Field research

MEDICI CON L'AFRICA CUAMM
Doctors with Africa

Scientific papers, abstracts and posters from cooperation activities in Africa – 2024

photo © Nicola Berti

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MEDICI CON L'AFRICA
CUAMM
Doctors with Africa

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"Despite the increasing frequency of extreme weather events, in fact, many communities continue to underestimate health risks, limiting the effectiveness of adaptation strategies. Moreover, particularly in rural areas, a lack of disaster preparedness hampers the disaster response ability of the most vulnerable populations."

"Infatti, nonostante la crescente frequenza degli eventi climatici estremi, molte comunità percepiscono questi rischi come improbabili, limitando l'efficacia delle strategie di adattamento. Inoltre, l'assenza di una preparazione strutturata ai disastri, specialmente nelle aree rurali, ostacola la capacità di risposta delle popolazioni più vulnerabili."

Giovanni Putoto,
Medici con l'Africa Cuamm

COMMUNITY RESILIENCE AND ADAPTATION TO CLIMATE CHANGE

Among the many challenges that Africa faces, climate change is one of the most daunting in terms of its impact on human health, particularly as regards the spread of waterborne diseases like cholera and vector-borne diseases like malaria. While predictive models can provide possible scenarios vis-à-vis climate change and epidemics, there has been little research on the ability of local communities to adapt to and mitigate these impacts.
A case in point is Mozambique, which copes with the consequences of recurrent cyclones and flooding, including the devastation of homes, disease outbreaks and malnutrition-related issues. Cyclones Idai (2019) and Freddy (2023) are just two examples of this broader trend of increasingly destructive weather patterns.
Climate-related emergencies continue to exacerbate the humanitarian crisis in the country's Cabo Delgado province, where prolonged conflict has led to the displacement of nearly one million people as well as a lack of access to basic resources and services such as safe water and sanitation. More than 43,000 cholera cases were reported by Mozambique's Ministry of Health between September 2022 and December 2023, underscoring the pressing need for targeted interventions.
It is against this challenging backdrop that Doctors with Africa CUAMM, in partnership with the Mozambican Health Ministry and UNICEF, is working to address new types of multifactorial emergencies with complex social dimensions. Operational research is being conducted to determine the most effective ways to enhance public health through social and behavior change (SBC) programs. Past disease outbreaks and pandemics such as COVID-19 and Ebola have highlighted the crucial role of such programs in containing the spread of infectious diseases by promoting practices such as handwashing and the use of safe water. Despite the increasing frequency of extreme weather events, in fact, many communities continue to underestimate health risks, limiting the effectiveness of adaptation strategies. Moreover, particularly in rural areas, a lack of disaster preparedness hampers the disaster response ability of the most vulnerable populations.
Our research in six districts of Cabo Delgado province started out by investigating cholera- and hygiene-related knowledge, attitudes and practices among displaced populations, i.e., in settings of great social disruption. We then looked into risk factors for cholera and acute watery diarrhea outbreaks, and assessed community preparedness for infectious disease outbreaks during climate change-related emergencies. We are currently focused on evaluating the impact of SBC in decreasing the risk of climate-sensitive diseases.
Our primary intervention, which is based on the Mozambican Ministry of Health's *Família Modelo* strategy, works to foster thirteen preventive behaviors. Involving 1,602 households, it takes an anthropological approach to community health education and has demonstrated how even simple changes can significantly bolster community resilience, with notable improvements in key preparedness indicators, especially vis-à-vis health facility availability, safe water management and the use of preventive tools including mosquito nets. But our research has also underscored the severe challenges faced by the internally displaced (IDPs), and the need for targeted support strategies for these populations.
CUAMM's commitment to the most vulnerable remains as strong as ever. Based on its proven effectiveness, we will now expand the *Família Modelo* strategy to other provinces in the country.

Giovanni Putoto

COMUNITÀ RESILIENTI E LA SFIDA DELL'ADATTAMENTO CLIMATICO

Tra le sfide con le quali l'Africa dovrà misurarsi a breve, il cambiamento climatico è quella con gli impatti sulla salute umana più preoccupanti, in particolare per quanto riguarda la diffusione di malattie epidemiche legate all'acqua, come il colera, e ai vettori, come la malaria. Modelli predittivi su clima e epidemie ci possono dire molto sugli scenari possibili, tuttavia rimane poco studiato l'aspetto legato alle comunità locali e al modo in cui riescono ad adattarsi e a mitigare gli effetti di questi cambiamenti.
Il Mozambico è un caso emblematico: colpito ripetutamente da cicloni e inondazioni, il Paese affronta conseguenze devastanti, tra cui la distruzione delle abitazioni, epidemie e problemi di malnutrizione.
I cicloni Idai del 2019 e Freddy del 2023 sono solo due esempi di una realtà sempre più pressante. Le emergenze climatiche aggravano una crisi umanitaria legata al conflitto nella provincia di Cabo Delgado, che ha causato lo sfollamento di quasi un milione di persone e ha compromesso l'accesso a risorse essenziali, come acqua sicura e servizi sanitari. Nel periodo tra settembre 2022 e dicembre 2023, il Ministero della Salute del Mozambico ha registrato oltre 43.000 casi di colera, sottolineando l'urgenza di interventi mirati.
In questo contesto, anche Medici con l'Africa Cuamm, in collaborazione con il Ministero della Salute e UNICEF, si è trovato ad affrontare situazioni nuove e multifattoriali, complesse e legate alla dimensione sociale. Per questo è stata avviata una ricerca operativa per migliorare la salute pubblica attraverso programmi di cambiamento comportamentale sociale (SBC): esperienze precedenti con epidemie e pandemie (Ebola, Covid19 e altre) hanno dimostrato come questi programmi siano fondamentali per promuovere pratiche igieniche, come l'uso di acqua sicura e il lavaggio delle mani, riducendo la diffusione di malattie infettive.
Infatti, nonostante la crescente frequenza degli eventi climatici estremi, molte comunità percepiscono questi rischi come improbabili, limitando l'efficacia delle strategie di adattamento. Inoltre, l'assenza di una preparazione strutturata ai disastri, specialmente nelle aree rurali, ostacola la capacità di risposta delle popolazioni più vulnerabili.
La ricerca di Cuamm in sei distretti della provincia di Cabo Delgado ha dapprima esaminato quali fossero conoscenze, atteggiamenti e pratiche relative a colera e igiene tra le persone sfollate, ovvero in contesti socialmente decostruiti. Poi ha studiato i fattori di rischio per epidemie di colera e diarrea acquosa acuta e indagato e valutato la preparazione delle comunità verso le malattie infettive in contesti di disastri climatici. Oggi, stiamo lavorando per valutare l'impatto dei cambiamenti comportamentali sociali sulla riduzione del rischio di malattie sensibili al clima.
L'intervento chiave, basato sulla strategia Família Modelo *del Ministero della Salute mozambicano, promuove tredici comportamenti preventivi. Questa iniziativa, che ha coinvolto 1.602 famiglie, combina un approccio antropologico con l'educazione alla salute comunitaria, dimostrando come semplici cambiamenti possano migliorare significativamente la resilienza delle comunità.*
I risultati evidenziano un significativo miglioramento nei principali indicatori di preparazione, in particolare nella disponibilità di strutture sanitarie, nella gestione sicura dell'acqua e nell'uso di strumenti preventivi come le zanzariere. Tuttavia, lo studio sottolinea le persistenti sfide affrontate dalle persone sfollate interne (IDP), mettendo in evidenza la necessità di strategie mirate per supportare questi gruppi. Per la sua affidabilità, la strategia della Família Modelo *sarà estesa in altre province del Mozambico.*
L'impegno di Medici con l'Africa Cuamm continua.

Giovanni Putoto

BRIDGING THE GAP BETWEEN KNOWLEDGE AND ACTION: OPERATIONAL RESEARCH IN AFRICA

2024 saw the publication of 31 studies in prominent international journals, the concrete outcome of Doctors with Africa CUAMM's multidisciplinary research in the countries where we are active.

Featuring the participation of some 118 international research centers and institutions, including 63 African partners, the goal of this synergic effort was to incorporate quality scientific research into health programs on the ground in low- and middle-resource countries.

In 2024, maternal and child health was our primary focus: we conducted research on best practices to ensure safe and accessible childbirth as well as on neonatology, to develop and bolster capacities to address critical childbirth-related issues in low-resource settings.

But we also explored other areas, analyzing innovative models for managing chronic noncommunicable diseases and generating fresh insights into infectious diseases such as malaria and tuberculosis. CUAMM's operational research also investigated climate-related and sociocultural health determinants linked to the attitudes, beliefs and practices of communities.

The journals that hosted our studies in 2024, including *BMJ* and *Frontiers* in *Public Health*, serve as a testament to our growing authority as global public health researchers and practitioners. Moreover, we were able to share our research findings with international practitioners and experts through oral presentations and poster sessions at conferences both in Italy and abroad, including the 2024 Eastern Africa Regional Conference on Early Childhood Development (ECD) and Congress of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).

CUAMM remains deeply committed to this dual approach – both in and from the field. It guides both our activities on the ground and our lines of research, as demonstrated by the many public occasions that we have organized for discussion with our partners and other experts. 2024 saw yet another such stimulating event in Padua, Italy – *"Research for quality health cooperation: an African perspective on lessons and results"* – which brought together both senior and junior researchers and practitioners from Italy and Africa to discuss innovative public health topics as well as our own field activities and research. To improve the quality of both our own health cooperation work and that of our peers, CUAMM will continue to implement and use research as a tool and strategic lever, integrating it progressively into our interventions on the ground.

COLMARE IL DIVARIO TRA CONOSCENZA E AZIONE: LA RICERCA OPERATIVA IN AFRICA

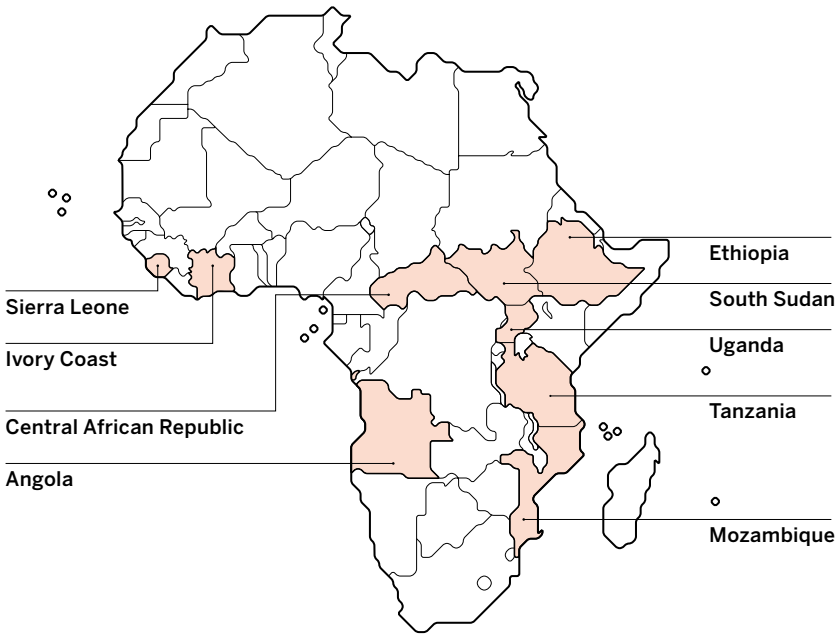
Sono 31 le ricerche pubblicate nel 2024 su riviste internazionali di alto spessore scientifico, risultato tangibile di un'attività di ricerca multidisciplinare e che rappresenta i Paesi in cui Cuamm opera. Un lavoro corale e sinergico che ha visto collaborazioni con 118 centri di ricerca e istituzioni internazionali, di cui 63 sono partner africani, e che ha l'obiettivo di integrare la ricerca scientifica di qualità nella programmazione sanitaria dei Paesi a basse e medie risorse.

Nel 2024 il focus maggiore è stato dedicato alla salute materno-infantile, con studi sul parto e sulle buone pratiche per renderlo sicuro e accessibile, e studi sulla neonatologia, per implementare le capacità di affrontare le criticità legate alla nascita in contesti a risorse limitate.
Lo sguardo delle ricerche pubblicate nel 2024 si è allargato anche all'analisi del tema delle malattie croniche non trasmissibili e di nuovi modelli per la loro gestione. Approfondimenti sulle malattie infettive, come la malaria e la tubercolosi, e sui sistemi sanitari,hanno arricchito questo anno di ricerche Cuamm, andando a considerare anche nuove forzanti sanitarie, come quelle derivate dai cambiamenti climatici o quelle di natura socio-culturale, legate intrinsecamente alle comunità e ai comportamenti socialmente influenzati.

Le riviste che hanno ospitato i lavori del Cuamm – tra cui BMJ *e* Frontiers in Public Health *– ne confermano l'autorevolezza e posizionano l'organizzazione come autore di ricerca accreditato. Inoltre, i progetti di ricerca di cui Cuamm è stato promotore e autore sono stati presentati a esperti e addetti ai lavori anche durante presentazioni orali e poster session di convegni in Italia e all'estero, come* East Africa Early Child Development Conference *e il* European Congress of Clinical Microbiology and Infectious Diseases.

Un approccio "sul campo" e "dal campo" in cui Cuamm crede fortemente e che orienta tutte le progettualità e le linee di ricerca, come è spesso emerso anche in diverse occasioni pubbliche di confronto tra esperti e partner, culminate nel 2024 con l'evento pubblico dedicato alla ricerca operativa "La ricerca per una cooperazione sanitaria di qualità: esperienze, evidenze e prospettive dall'Africa" *che ha riunito a Padova esperti e giovani ricercatori e ricercatrici italiani e africani, e posto l'attenzione su nuovi temi. Una modalità di coinvolgimento nuova, che testimonia l'importanza della ricerca come strumento di implementazione e leva strategica da integrare sempre di più alle azioni sul campo, non solo per Cuamm, ma anche a livello internazionale per una cooperazione sanitaria di qualità.*

Doctors with Africa CUAMM
Medici con l'Africa Cuamm



Doctors with Africa CUAMM is the largest Italian NGO working to **improve the health of vulnerable communities in Sub-Saharan Africa**. CUAMM carries out **long-term projects in 9 countries** in the region and partners with **universities and research centers** in Italy and abroad to raise awareness about people's right to health care. CUAMM also organizes **courses on global health** for medical students and health professionals and conducts **research** with international partners, convinced that such endeavors are vital to developing **quality international healthcare programs**.

*Medici con l'Africa Cuamm è la più grande organizzazione italiana per la **promozione e la tutela della salute delle popolazioni africane**. Medici con l'Africa Cuamm realizza **progetti a lungo termine in 9 Paesi** dell'Africa Sub-sahariana e collabora con **università e centri di ricerca in Italia e in Europa**. Organizza inoltre **corsi di Salute Globale** per studenti di Medicina e professionisti sanitari e lavora con partner internazionali a **progetti di ricerca**, nella convinzione che questi sforzi siano necessari per lo sviluppo di **programmi sanitari internazionali di qualità**.*

Doctors with Africa CUAMM currently operates in Angola, Central African Republic, Ethiopia, Ivory Coast, Mozambique, Sierra Leone, South Sudan, Tanzania and Uganda.
Medici con l'Africa Cuamm attualmente lavora in Angola, Costa d'Avorio, Etiopia, Mozambico, Republica Centrafricana, Sierra Leone, Sud Sudan, Tanzania e Uganda attraverso:

21
hospitals /
ospedali

116
districts (for public health activities, mother-child care, the fight against HIV/AIDS, tuberculosis and malaria, training) /
distretti (iniziative per la salute pubblica, assistenza e cure per la salute materna e infantile, lotta contro l'HIV/AID, la tubercolosi e la malaria)

4
nursing schools /
scuole per infermieri e ostetriche

1
university (Mozambique) /
università (Mozambico)

3,465
health workers, including /
collaboratori sanitari, che includono:

282
from Europe and abroad /
europei e internazionali

843
health facilities /
strutture sanitarie supportate

Reference: Annual Report 2023
Fonte: Bilancio Sociale 2023

Operational research in 2024
Ricerca operativa nel 2024

In 2024, thirty-one Doctors with Africa CUAMM studies made their way into distinguished international journals. As always, the guiding thread remained the key importance of interweaving research and programs on the ground, to enhance the quality of the latter and develop new insights and know-how thanks to the former.
While we focused in particular on maternal and child health, investigating issues related to childbirth and neonatology, we also conducted research on a more recent challenge for the African continent – chronic diseases – and explored issues related to infectious diseases, health systems and community health as we looked for practical solutions to health problems on the ground. Working side by side with **274** researchers in **118** Italian, African and international research centers, we generated valuable new know-how and partnered on projects in limited-resource countries.

*Nel 2024 sono stati **31** i lavori di ricerca Cuamm che hanno trovato spazio su riviste scientifiche di stampo internazionale. Il* fil rouge *continua a essere quello dell'integrazione tra ricerca e progettualità, tra studio e azione per sviluppare nuove conoscenze e competenze e per migliorare la qualità degli interventi. Quest'anno particolare attenzione è stata data ai temi della salute materna e infantile, approfondendo aspetti legati al parto e alla neonatologia, ma grande dedizione è stata rivolta alle malattie croniche, una nuova sfida per il continente africano. Malattie infettive, sistemi sanitari e nuove prospettive di salute di comunità sono stati ulteriori campi esplorati, provando a dare risposte alle domande di ricerca concrete provenienti dal campo.*
*Durante quest'anno abbiamo lavorato a fianco di **118** centri di ricerca italiani, africani e internazionali, coinvolgendo **274** ricercatori e ricercatrici che hanno collaborato per costruire nuova conoscenza e sviluppare progettualità condivise in Paesi con risorse limitate.*

- Maternal and child health
  Salute materna e infantile
- Infectious and tropical diseases
  Malattie infettive e tropicali
- Public health and universal coverage
  Copertura sanitaria universale ed equità
- Nutrition
  Nutrizione
- Chronic diseases
  Malattie croniche

OUR RESEARCH PARTNERS

The 118 research centers, universities and other organizations – in Africa, Europe (including Italy), and other countries around the world – with which Doctors with Africa CUAMM partnered on research 2024.
I 118 centri di ricerca, università e organizzazioni con cui Medici con l'Africa CUAMM ha collaborato per produrre la ricerca nel 2024.

AFRICA

1. Bombali District Ebola Response - Surveillance Team, Sierra Leone Ministry of Health and Sanitation, Bombali District, Makeni, Sierra Leone
2. Bugisi Health Centre, Shinyanga, Tanzania
3. Centre for Infectious Diseases Research in Zambia, Lusaka, Zambia
4. Centre Hospitalier Universitaire de Tengandogo (CHUT), Ouagadougou, Burkina Faso.
5. Clinton Health Access Initiative, Harare, Zimbabwe
6. College of Medicine and Allied Health Sciences, University of Sierra Leone, Freetown, Sierra Leone
7. Department of Agricultural Economics and Development, Universidade Eduardo Mondlane, Maputo, Mozambique
8. Department of Community Health, Universidade Eduardo Mondlane, Maputo, Mozambique
9. Department of Developmemt Studies, Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, Tanzania
10. Department of Diagnostic and Public Health, University of Verona, Verona, Italy
11. Department of Obstetrics and Gynecology, Central Hospital of Beira, Mozambique
12. Department of Obstetrics and Gynecology Princess Christian Maternity Hospital (PCMH), University of Sierra Leone, Freetown, Sierra Leone
13. Department of Research, Training and Health Surveys, National Institute of Health, Maputo, Mozambique
14. Department of Rural Development and Agricultural Extension, College of Agriculture and Natural Resource, Gambella University, Gambella, Ethiopia
15. Department of Statistics, College of Natural and Computational Sciences, Gambella University, Gambella, Ethiopia
16. Department of Statistics, College of Natural Sciences, Jimma University, Jimma, Ethiopia
17. Department of Internal Medicine, Maputo Central Hospital, Mozambique
18. Department of Neurology, Maputo Central Hospital, Maputo, Mozambique
19. Doctors with Africa CUAMM, Beira, Mozambique
20. Doctors with Africa CUAMM, Iringa, Tanzania
21. Doctors with Africa CUAMM, Kampala, Uganda
22. Doctors with Africa CUAMM, Maputo, Mozambique
23. Doctors with Africa CUAMM, Wolisso, Ethiopia
24. Ezintsha, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
25. Faculty of Medicine, Eduardo Mondlane University, Maputo, Mozambique
26. Government of Sierra Leone Ministry of Health and Sanitation, Freetown, Western Area, Sierra Leone
27. Health Department, Ileje District Council, Songwe Region, Tanzania.
28. Health Office, Oyam District Local Government, Loro, Uganda
29. Health Service Management, Doctors with Africa CAUMM, Kampala, Uganda
30. Hopital Saint Camille de Ouagadougou (HOSCO), Ouagadougou, Burkina Faso
31. Hospital Central de Mapoto, Ministerio da Saude de Mozambique, Maputo, Mozambique
32. Iringa District Council, Iringa, Tanzania
33. Mathiwos Wondu-Ye Ethiopia Cancer Society, Addis Ababa, Ethiopia
34. Mozambique Institute for Health Education and Research, Maputo, Mozambique
35. Muhimbili National Hospital, Dar-es-Salaam, Tanzania
36. Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
37. Jakaya Kikwete Cardiac Institute, Dar es Salaam, Tanzania
38. National Institute for Medical Research, Dar es Salaam, Tanzania
39. NCD Division, Ministry of Health, Lilongwe, Malawi
40. NCDI Poverty Network, Addis Ababa, Ethiopia
41. Ngokolo Health Centre, Shinyanga, Tanzania
42. Non-Communicable Diseases Alliance Kenya, Nairobi, Kenya
43. Noncommunicable Diseases and Mental Health Clinical Services, Malawi Ministry of Health, Lilongwe, Malawi
44. Noncommunicable Diseases and Mental Health, Sierra Leone Ministry of Health and Sanitation, Freetown, Sierra Leone
45. Operational Research Unit, African Network for Change, Kampala, Uganda
46. St. John's XXIII Hospital Aber, Jaber, Uganda
47. Oromia Regional Health Bureau, Addis Ababa, Ethiopia
48. Partners In Health Sierra Leone, Kono, Sierra Leone
49. Partners In Health, Maryland County, Liberia
50. Partners In Health, Neno, Malawi
51. Partners In Health/Inshuti Mu Buzima, Rwinkwavu, Rwanda
52. Reproductive Health and Family Planning Programme, Government of Sierra Leone Ministry of Health and Sanitation, Freetown, Western Area, Sierra Leone
53. Department of Epidemiology, Alliance for Africa Health Research, Dar es Salaam, Tanzania
54. Sofala Provincial Health Service, Ministry of Health, Beira, Mozambique
55. SolidarMed, Harare, Zimbabwe
56. St. Luke Catholic College of Nursing, Woliso, Ethiopia
57. Strategic Information Unit, National AIDS, STIs and Hepatitis Control Program, Ministry of Health, Dodoma, Tanzania
58. Tosamaganga Hospital, Tosamaganga, United Republic of Tanzania

59. Uganda Initiative for Integrated Management of Non-Communicable Diseases, Kampala, Uganda
60. UNICEF Mozambique, Maputo, Mozambique
61. Universidade Eduardo Mondlane, Maputo, Mozambique
62. Instituto Nacional de Saúde, Maputo, Mozambique and Instituto Nacional de Saúde, Maputo, Mozambique
63. Nucleo de Investigaçao Operacional del Pemba (NIOP), Pemba, Mozambique

ITALY

1. ANLAIDS Sezione Lombarda, Milano, Italy
2. Chair of Pediatrics, NESMOS department, Faculty of Medicine & Psychology, Sapienza University, Rome, Italy
3. Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy
4. CRIMEDIM - Research Center in Emergency and Disaster Medicine, Università degli Studi del Piemonte Orientale Amedeo Avogadro Scuola di Medicina, Novara, Piemonte, Italy
5. Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy
6. Department of Medical Sciences, Pediatric Section, S. Anna University Hospital, University of Ferrara, Ferrara, Italy
7. Department of Translational Medicine and Center for Research and Training in Disaster Medicine, Humanitarian Aid and Global Health, Università degli Studi del Piemonte Orientale Amedeo Avogadro Scuola di Medicina, Novara, Piemonte, Italy
8. Department of Woman's and Child's Health, University of Padua, Padua, Italy
9. Diagnostic Laboratory: Laboratorio analisi Dott.ssa Dell'Olio Nunzia, Trani, Italy and Department of Drug Chemistry and Technologies, Sapienza University of Rome
10. Division of Pediatric Infectious Diseases, Department of Women's and Children's Health, University of Padua, Padua, Italy
11. Section of Hygiene, Department of Diagnostics and Public Health, University of Verona
12. Division of Pediatric Infectious Diseases, Department of Women's and Children's Health, University of Padua, Padua, Italy
13. Doctors with Africa CUAMM, Bari, Italy
14. Epidemiolgy Unit, National Institute for Health Migration and Poverty (INMP), Rome, Italy
15. Fondazione IRCCS San Gerardo dei Tintori, Monza Brianza, Italy
16. Geriatric Unit, Department of Medicine, University of Palermo, Palermo, Italy
17. Health Mother and Child Department NICU, Poliambulanza Foundation Hospital Brescia, Brescia, Italy
18. Hygiene Unit, Policlinico Riuniti Foggia Hospital, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy
19. Infectious Diseases Unit, AUSL Romagna, Morgagni Pierantoni Hospital, Doctors with Africa CUAMM IT, Forlí, Italy
20. Institute for Maternal and Child Health-IRCCS Burlo Garofolo, Trieste, Italy; University of Trieste, Trieste, Italy
21. Interdisciplinary Department of Medicine, University of Bari, Bari, Italy
22. Internal Medicine and Gastroenterology-Hepatology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
23. Mangiagalli Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
24. MeS (Management and Health) Laboratory, Institute of Management, Sant'Anna School of Advanced Studies, Pisa, Italy
25. Division of Obstetrics and Gynecology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
26. Microbiology and Virology Unit, University of Bari, University Hospital Policlinico, Bari, Italy
27. Pediatric and Neonatology Unit, Iglesias Hospital, Iglesias, Italy.
28. School of Pediatrics, Department of Medical Sciences, University of Ferrara, Ferrara, Italy
29. Technologies for Respiration Laboratory, Electronics, Information and Bioengineering Department (DEIB), Politecnico di Milano
30. The BioRobotics Institute, Sant'Anna School of Advanced Studies, Pisa, Italy
31. Department of Excellence in Robotics and AI, Sant'Anna School of Advanced Studies, Pisa, Italy
32. Transfusion Medicine Department of Azienda Sanitaria Universitaria Giuliano Isontina (ASU GI), Trieste Italy and Doctors with Africa Cuamm, Padova, Italy
33. Unità Operativa Complessa di Epidemiologia Clinica con Registro Tumori, Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone", Palermo, Italy
34. Università degli Studi del Piemonte Orientale Amedeo Avogadro Scuola di Medicina, Novara, Italy

EUROPE

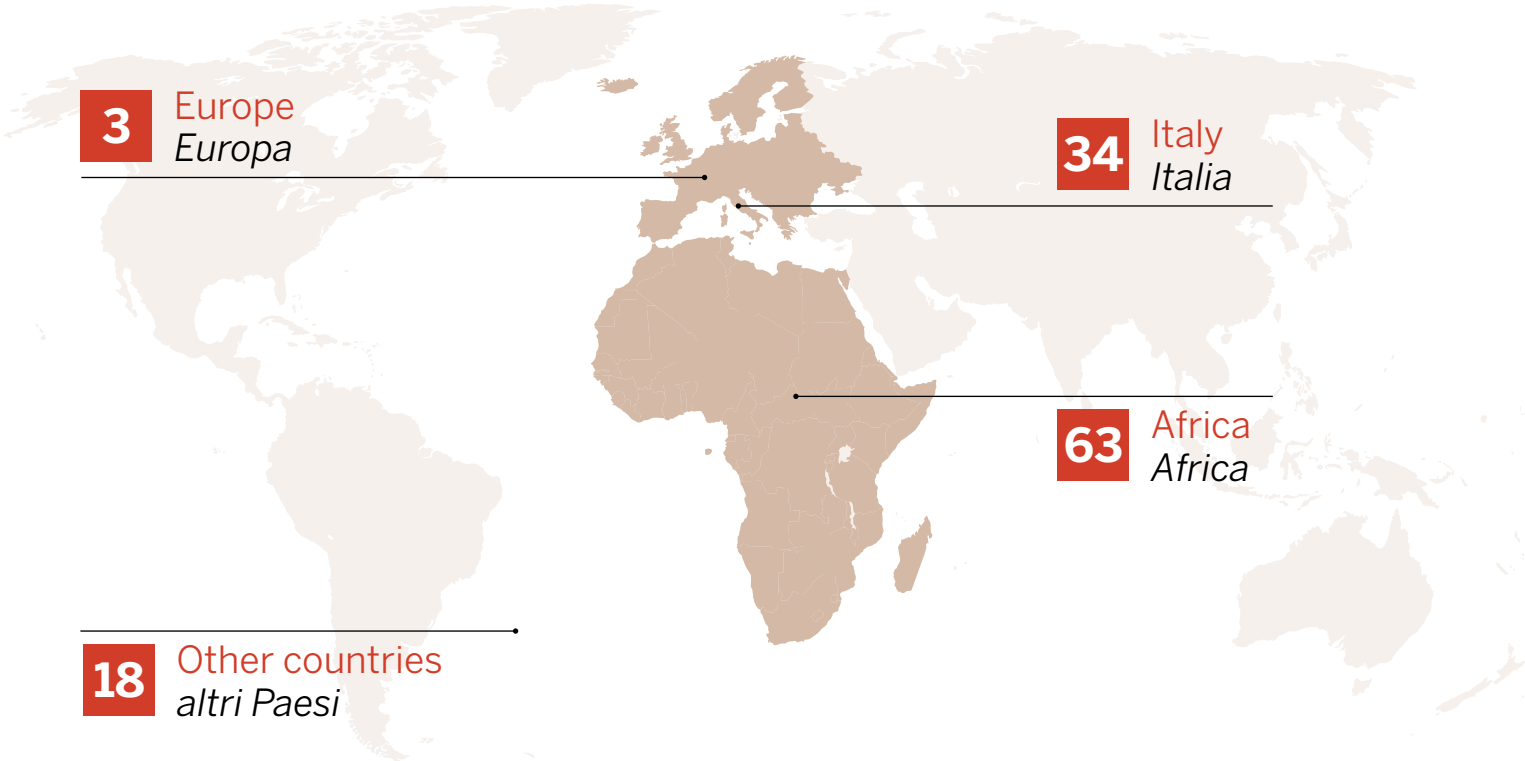
1. Department of Global Health, Amsterdam UMC, University of Amsterdam, the Netherlands
2. Amsterdam Institute for Global Health and Development, Amsterdam UMC, Amsterdam, the Netherlands
3. Centre for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Amsterdam UMC, Amsterdam, the Netherlands

OTHER COUNTRIES

1. Cardiovascular Health Research Unit, University of Washington, Seattle, Washington, USA
2. School of Medical Sciences, Kathmandu University, Kathmandu, Nepal
3. Center for Integration Science, Brigham and Women's Hospital, Boston, Massachusetts, USA
4. Center of Excellence for Trauma and Emergencies, The Aga Khan University, Karachi, Pakistan
5. Centre for Health, Performance and Wellbeing, Anglia Ruskin University, Cambridge, UK
6. Chhattisgarh NCD Plus Initiative, Ambikapur, Chhattisgarh, India
7. Department of Sexual and Reproductive Health and Research,

World Health Organization, Geneva, Switzerland
8. D'Or Institute for Research and Education, Rio de Janeiro, Brazil
9. HIV Department, Chelsea and Westminster Hospital NHS Foundation Trust, London, UK
10. Instituto de Medicina Integral Prof Fernando Figueira, Recife, Brazil
11. Kathmandu Institute of Child Health, Kathmandu, Nepal
12. NCDI Poverty Network, Surguja, Chhattisgarh, India
13. Nursing, Universidade de Pernambuco (UPE), Recife, Brazil.
14. Partners In Health, Boston, Massachusetts, USA
15. School of Nursing, Kinesiology, and Health Sciences, College of Health, Education and Human Services (CHEH), Wright State University, Dayton, OH, USA
16. Zamni Lasante, Croix-des-Bouquets, Haiti
17. Department of HIV and Department of Clinical Research, London School of Hygiene and Tropical Medicine, London, UK
18. Mahidol Oxford Tropical Medicine Research Unit, Bangkok, Thailand

118 Research partners
partner di ricerca



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Maternal and child health

Causes of maternal deaths in Sierra Leone from 2016 to 2019: analysis of districts' maternal death surveillance and response data

PAPER

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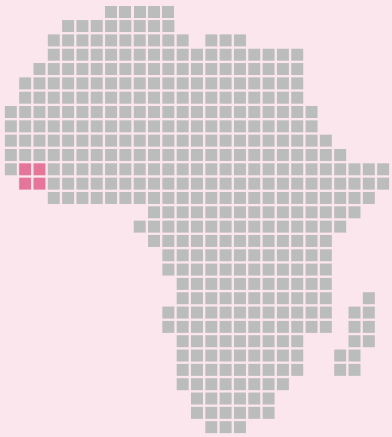

Open access Original research

BMJ Open

Causes of maternal deaths in Sierra Leone from 2016 to 2019: analysis of districts' maternal death surveillance and response data

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ABSTRACT

Introduction Sierra Leone is among the top countries with the highest maternal mortality rates. Although progress has been made in reducing maternal mortality, challenges remain, including limited access to skilled care and regional disparities in accessing quality care. This paper presents the first comprehensive analysis of the burden of different causes of maternal deaths reported in the Maternal Death Surveillance and Response (MDSR) system at the district level from 2016 to 2019.

Methods The MDSR data are accessed from the Ministry of Health and Sanitation, and the secondary data analysis was done to determine the causes of maternal death in Sierra Leone. The proportions of each leading cause of maternal deaths were estimated by districts. A subgroup analysis of the selected causes of death was also performed.

Results Overall, obstetric haemorrhage was the leading cause of maternal death (39.4%), followed by hypertensive disorders (15.8%) and pregnancy-related infections (10.1%). Within obstetric haemorrhage, postpartum haemorrhage was the leading cause in each district. The burden of death due to obstetric haemorrhage slightly increased over the study period, while hypertensive disorders showed a slightly decreasing trend. Disparities were found among districts for all causes of maternal death, but no clear geographical pattern emerged. Non-obstetric complications were reported in 11.5% of cases.

Conclusion The MDSR database provides an opportunity for shared learning and can be used to improve the quality of maternal health services. To improve the accuracy and availability of data, under-reporting must be addressed, and frontline community staff must be trained to accurately capture and report death events.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Employed comprehensive national Maternal Death Surveillance and Response (MDSR) data, ensuring a wide-ranging analysis of maternal deaths in Sierra Leone.
⇒ Used district-wise segregation of data for targeted regional insights into maternal mortality trends.
⇒ Faced significant under-reporting in the MDSR system, with about 76% of deaths potentially unrecorded in 2016–2017.
⇒ The retrospective nature of the data may limit the ability to capture all relevant factors influencing maternal mortality.
⇒ Reliance on existing reports and records could introduce bias if reporting practices varied across districts.

INTRODUCTION

The United Nations estimates suggest that life expectancy at birth in Sierra Leone is 60 years.[1] It remains among the top countries having the highest maternal mortality rate, and the lifetime risk of maternal death is 1 in 52.[2] The 2019 national survey data of Sierra Leone reported the maternal mortality ratio (MMR) of 717 per 100 000 live births, and the pregnancy-related mortality ratio was 796 per 100 000 live births.[3] However, the global data on trends of MMR showed decreasing MMR trends (443 per 100 000 live births in 2020 compared with 2480 per 100 000 live births in 2000) in Sierra Leone from 2000 to 2020.[2]

Sierra Leone has made strides in improving maternal health as part of its commitment to the Sustainable Development Goals, notably through enhancing healthcare access and community education.[4] However, challenges such as limited resources and cultural barriers continue to impede further progress in this critical area.[4 5] In previous years, the government of Sierra Leone, with the support of international partners, had implemented various initiatives to improve maternal health, including strengthening the health system and increasing the access to maternal care.[4–6] The Free Healthcare Initiative and the National Reproductive, Maternal, Neonatal, Child[7] and Adolescent Health strategy are the key programmes which aimed to improve

access to quality care.[6] In terms of major health indicators, the trends of facility births in the country have made significant progress, from 25% of deliveries that took place in health facilities in 2008 to 83% in 2019.[3 5 6] This trend varies by district, for instance, in Port Loko, 61% of births occur in health facilities, while in Kenema and Pujehun, the rate is as high as 97% in 2019.[3] However, access to skilled care on the continuum of maternal care during pregnancy, intrapartum and postnatal period remains limited, and many women in rural geographies have inequalities in accessing essential obstetric services.[7] Further confirmation of this gap is indicated by the differences in caesarean section rates among Sierra Leonean districts, which remain below the safety threshold of 10% at the population level indicated by WHO.[8] These regional disparities in accessing essential quality care are grossly linked to maternal death.[9]

In 2015–2016, the Maternal Death Surveillance and Response (MDSR) system in Sierra Leone was launched,[10] which aims to identify the causes of maternal deaths and inform targeted interventions.[10 11] MDSR assigns primary death causes to maternal deaths based on clinical/medical records from hospital/facility, in most of the cases, or through verbal autopsy (VA) data in a case where clinical or medical records are not available. The data on the cause of death are then coded according to the WHO classification.[12] Indeed, in many low-income and middle-income countries, VA is often the only available method to produce mortality statistics, as deaths often occur at home.[13] Moreover, many of these countries do not have a structured and reliable system of reporting death data.[14]

The first annual report on MDSR was published by the Ministry of Health and Sanitation (MOHS) of Sierra Leone, Reproductive and Child Health Directorate and partners in 2016.[10] Although these data are part of routine reporting and dissemination at MOHS to assess the trend and cumulative causes of maternal death,[10 15] so far the analysis has not investigated the differences and patterns between districts for the different causes of death. Therefore, this paper presents the first comprehensive analysis of the burden of different causes of maternal deaths reported in the MDSR system at the district level from 2016 to 2019. In a country with the highest maternal mortality and lowest life expectancy, a detailed presentation of the data by each participating district in MDSR is crucial for global health leadership. This paper is a joint effort of work on data analysis and synthesis in partnership with the Centre for Research and Training in Disaster Medicine, Humanitarian Aid, and Global Health at Università del Piemonte Orientale and Doctors with Africa CUAMM. These three are partners in one of the projects to evaluate the countrywide impact of National Emergency Medical Services (NEMS) on maternal health services.[16] The MDSR dataset is a key component of the impact evaluation of the NEMS project, and the scope of this paper falls under the umbrella of this work.

METHODS

This is the secondary data analysis of MDSR data. Access to the dataset was given by MOHS.

MDSR system

In Sierra Leone, MDSR is implemented through a multistakeholder approach involving MOHS, healthcare providers and both national and international non-governmental organisations. The key steps involved are (1) the identification of maternal deaths through various sources; (2) notification to key programme officials and clinicians; (3) verification and investigation of each maternal death, including periodical health facility-based death audits; and (4) review and clinical determination of the cause of death.

In the context of maternal mortality surveillance, the MOHS role in the identification and reporting of maternal deaths is pivotal.[10] Recognising maternal death as a notifiable event, the MOHS implemented a surveillance and reporting system, integrating the Civil Registration and Vital Statistics, the call system as well as community engagement, to capture maternal deaths irrespective of location.[10] This system is integral to the MDSR model, a comprehensive mechanism tracking maternal deaths and identifying underlying factors for targeted intervention.[10] MOHS has endeavoured to strengthen this system, addressing challenges such as under-reporting and coordination limitations.[10] They have developed national technical guidelines to fortify MDSR, incorporating a multifaceted approach that includes training clinicians for accurate death classification, supporting midwife investigators and ensuring continuous data validation.[10] This systematic approach aims to improve the quality of care and response strategies at both facility and community levels, reflecting a committed effort to reduce maternal mortality through enhanced surveillance and response initiatives.[10]

The process of assigning the cause of death for maternal fatalities adheres to a structured and methodical approach.[12] The International Statistical Classification of Diseases and Related Health Problems, 10 (ICD-10), is used to assign causes.[10 12] The investigation into suspected maternal deaths is triggered by reports to the Reproductive and Child Health unit, leading to a systematic inquiry by a multidisciplinary team comprising district surveillance officers, district health supervisors and midwife investigators.[10] This team is tasked with confirming the nature of death and elucidating the contributory factors.[10] The WHO ICD-10 definition of maternal death is employed, which encompasses deaths occurring during pregnancy or within 42 days of termination of pregnancy, attributable to pregnancy-related causes or its management, excluding incidental causes.[10 12] Maternal deaths are categorised into direct, indirect, incidental and unclassifiable types, facilitating a better understanding of each case.[10 12]

Nearly 90% of deaths recorded in the MDSR system occurred at health facilities; therefore, the cause of death is determined during review meetings by clinicians based

on clinical symptoms, examination findings and diagnosis in the case notes.[10] VA only applies to only 10% of deaths occurring and reported at the community level. At the facility level, periodic MDSR meetings allow incident reviews by the same multidisciplinary team. A district representative is usually invited to strengthen the collaboration between peripheral, basic and comprehensive healthcare facilities. Clinical/medical records or VA is used to determine the causes, and each cause was coded for the purpose of analysis.

Analysis

The data are cleaned, coded and assessed for missingness and outliers. In case of discrepancies, MOHS is contacted to resolve these. After consulting MOHS, the dataset for analysis was locked, and the main analysis was conducted using Stata SE 17. The proportion of each leading cause of maternal death with their 95% CI was estimated by districts for the period 2016–2019. CIs were calculated using the exact binomial method, chosen for its precision in estimating intervals for proportion data. This ensures robust and reliable statistical inference and provides an understanding of the variability and potential range of the observed proportions across different districts.

The direct and indirect causes are analysed and reported according to ICD guidelines, cumulative as well as by districts. Furthermore, a subgroup analysis of selected causes of death, such as obstetric haemorrhage and other direct and indirect obstetric complications, was performed as well. The denominator represented the total number of deaths reported in each district.

Patient and public involvement

Specific for MDSR system, MOHS and stakeholders engaged with the community to report the death events in the community. However, for this paper and analysis, there was no direct involvement of the patient and the public.

RESULTS

Direct causes of maternal death

Overall, 2428 maternal deaths were recorded and coded in the MDSR system from 2016 to 2019 in all 13 districts of Sierra Leone (online supplemental table S1). Obstetric haemorrhage was the leading cause of maternal death in Sierra Leone over the study period (n=956, 39.4%, 95% CI: 37.4, 41.3), followed by hypertensive disorders in pregnancy, childbirth and puerperium (n=384, 15.8%, 95% CI:14.4, 17.3), pregnancy-related infections (n=244, 10.1%, 95% CI: 8.9, 11.3), other obstetric complications (n=200, 8.2%, 95% CI: 7.1, 9.4) and pregnancy with abortive outcomes (n=71, 2.9%, 95% CI: 2.2, 3.3) (table 1).

Within the different subgroups of obstetric haemorrhages, postpartum haemorrhage was the leading cause (n=740, 30.5%, 95% CI: 28.6, 32.3) in each district, followed by antepartum haemorrhage (n=205, 8.4%, 95% CI: 7.3, 9.6) (table 2). Furthermore, the burden of death due to obstetric haemorrhage slightly increased over the study period, from 36.6% to 41.1% (figure 1). On the other hand, there was substantial variation in the proportion of obstetric haemorrhage over the total number of deaths among the different districts, ranging between 28.2% (Kono) and 60.0% (Kailahun), even if no clear geographical pattern emerged(figure 2).

Hypertensive disorders showed a slightly decreasing trend from 17.6% to 14.6% (figure 1). Even in this case, there was a large heterogeneity among districts, with figures ranging between 2.5% (Kailahun) and 22.1% (Moyamba), without a discernible spatial arrangement (online supplemental figure S1).

The yearly trend for pregnancy-related infections decreased slightly from 13.4% to 9.3% (figure 1). These infections also showed disparities among the districts, with proportions of 6.4% (Western Area) to 17.8% (Kono), with no distinct geographical arrangement observed (online supplemental figure S2).

Finally, among the group labelled as other obstetric complications, ruptured uterus (n=89, 3.7%, 95% CI: 2.9, 3.4) and obstructed labour (n=87, 3.6%, 95% CI: 2.8, 4.4) were the leading causes (online supplemental table S2). The trends almost doubled from 5.6% to 11.3% for all other obstetric complications (figure 1); the range of variability was also visible among districts, from 5.9% (Port Loko) to 12.3% (Kambia). No spatial pattern was observed (online supplemental figure S3).

Indirect causes of maternal death

The results indicated that non-obstetric complications were reported in 11.5% of the cases (n=278, 95% CI:10.2, 12.7) as shown in table 2. The most significant contributors to these complications included severe anaemia (n=111, 4.6%, 95% CI: 3.7, 5.4), malaria (n=55, 2.3%, 95% CI: 1.7, 2.9), HIV/AIDS (n=33, 1.4%, 95% CI: 0.9, 1.9) and heart failure, cardiomyopathy or stroke (n=34, 1.4%, 95% CI: 0.9, 1.9). For further analysis, a subgroup of non-obstetric complications by district is presented in online supplemental table S3.

DISCUSSION

Findings based on the MDSR platform between 2016 and 2019 suggest that more than half of the maternal deaths in Sierra Leone are attributable to haemorrhage, hypertensive disorders and sepsis. These results are consistent with those from a recent nationally representative mortality study which used Sierra Leone Sample Registration System of births and deaths.[17] This study also reported haemorrhage as the leading cause of maternal deaths (25.0% compared with 39.4% from MDSR), followed by infections and sepsis (15.0% vs 10.1% in MDSR) and hypertensive causes (9.0% vs 15.8% in MDSR).[17] Moreover, comparing our findings with reports from the Sierra Leone National Reproductive, Maternal, Newborn, Child, and Adolescent Health Strategy 2017–2021, the leading causes of maternal death reported were obstetric haemorrhage (46.0%),

Table 1 Proportion of maternal deaths in Sierra Leone due to different causes†

Causes*																	
	Pregnancy with abortive outcome		Hypertensive disorders in pregnancy, childbirth and the puerperium		Obstetric haemorrhage		Pregnancy-related infections		Other obstetric complications		Unanticipated complications of management		Non-obstetric complications		Total
Districts	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N
Western Area	16	2.9 (1.7, 4.7)	110	20.0 (16.7, 23.5)	220	40.0 (35.9, 44.2)	35	6.4 (4.5, 8.7)	34	6.2 (4.3, 8.5)	0	–	74	13.5 (10.7, 15.6)	550
Bo	7	2.9 (1.2, 5.9)	37	15.3 (11.1, 20.5)	102	42.2 (35.9, 48.6)	24	9.9 (6.5, 14.4)	19	7.9 (4.8, 12.9)	2	0.8 (0.1, 2.9)	30	12.4 (8.5, 17.2)	242
Bombali	7	4.1 (1.7, 8.2)	26	15.3 (10.2, 21.6)	55	32.4 (25.4, 39.9)	22	12.9 (8.2, 18.9)	15	8.8 (5.0, 14.1)	1	0.6 (0.01, 3.2)	27	15.9 (10.7, 22.2)	170
Bonthe	0	–	11	14.9 (7.7, 25.0)	36	48.7 (36.8, 60.5)	7	9.5 (3.9, 18.5)	6	8.1 (3.0, 16.8)	1	1.4 (0.03, 7.3)	2	2.7 (0.3,9. 4)	74
Kailahun	4	5.0 (1.3, 12.3)	2	2.5 (0.3, 8.7)	48	60.0 (48.4, 70.7)	7	8.8 (3.6, 17.2)	5	6.3 (2.0, 13.9)	0	–	10	12.5 (6.2, 21.8)	80
Kambia	1	0.7 (0.01, 3.5)	22	14.2 (9.1, 20.7)	51	32.9 (25.6, 40.9)	10	6.5 (3.1, 11.5)	19	12.3 (7.5, 18.4)	1	0.7 (0.01, 3.5)	26	16.8 (11.2, 23.6)	155
Kenema	15	6.7 (3.8, 10.7)	34	15.1 (10.7, 20.4)	73	32.4 (26.3, 38.9)	21	9.3 (5.9, 13.9)	22	9.8 (6.2, 14.4)	2	0.9 (0.1, 3.1)	36	16.0 (11.4, 21.4)	225
Koinadugu	2	1.5 (0.1, 5.1)	19	13.8 (8.4, 20.6)	57	41.3 (32.9, 49.9)	20	14.5 (9.0, 21.5)	12	8.7 (4.5, 14.6)	2	1.5 1.5 (0.1, 5.1)	16	11.6 (6.7, 18.1)	138
Kono	6	3.5 (1.2, 7.3)	25	14.4 (9.5, 20.4)	49	28.2 (21.6, 35.4)	31	17.8 (12.4, 24.3)	20	11.5 (7.1, 17.1)	0	–	26	14.9 (9.9, 21.1)	174
Moyamba	0	–	28	22.1 (15.1, 30.2)	54	42.5 (33.7, 51.6)	10	7.9 (3.8, 14.0)	10	7.9 (3.8, 14.0)	0	–	7	5.5 (2.2, 11.0)	127
Port Loko	2	1.1 (0.1, 3.8)	34	18.2 (12.9, 24.4)	88	47.1 (39.7, 54.4)	19	10.2 (6.2, 15.4)	11	5.9 (2.9, 10.2)	0	–	7	3.7 (1.5, 7.5)	187
Pujehun	7	6.0 (2.4, 12.0)	19	16.4 (10.1, 24.3)	39	33.6 (25.1, 42.9)	13	11.2 (6.1, 18.4)	12	10.3 (5.4, 17.3)	1	0.9 (0.2, 4.7)	8	6.9 (3.0, 13.1)	116
Tonkolili	4	2.1 (0.5, 5.3)	17	9.0 (5.2, 13.9)	84	44.2 (37.0, 51.5)	25	13.2 (8.6, 18.8)	15	7.9 (4.4, 12.6)	1	0.5 (0.01, 2.8)	9	4.7 (2.1, 8.8)	190
Countrywide	71	2.9 (2.2, 3.6)	384	15.8 (14.3, 17.3)	956	39.4 (37.4, 41.3)	244	10.1 (8.8, 11.3)	200	8.2 (7.1, 9.4)	11	0.5 (0.2, 0.8)	278	11.5 (10.2, 12.7)	2428

*Data on 'coincidental causes (n=1, 0.04%)' and 'unknown/undetermined causes (n=283, 11.7%)' are not included in the table and reported in online supplemental table 4.
†Data shown are the proportion of cause of death (%) with 95% CI for each district in the MDSR data.

Table 2 Subgroup analysis of obstetric haemorrhage†

Causes									
	Postpartum haemorrhage		Antepartum haemorrhage		Intrapartum haemorrhage		Obstetric haemorrhage	
Districts	N	% (95% CI)	N	N	N	% (95% CI)	N	% (95% CI)
Western Area	166	30.2 (26.6, 34.2)	53	9.6 (7.3, 12.4)	1	0.2 (0.004, 1.0)	220	40.0 (35.9, 44.2)
Bo	84	34.7 (28.7, 41.0)	17	7.0 (4.1, 11.0)	1	0.4 (0.01, 2.2)	102	42.2 (35.9, 48.6)
Bombali	45	26.5 (20.0, 33.7)	9	5.3 (2.4, 9.8)	1	0.6 (0.01, 3.3)	55	32.4 (25.4, 39.9)
Bonthe	27	36.5 (25.5, 48.4)	9	12.2 (5.7, 21.8)	0	–	36	48.7 (36.8, 60.5)
Kailahun	40	50.0 (38.6, 61.3)	8	10.0 (4.4, 18.7)	0	–	48	60.0 (48.4, 70.7)
Kambia	38	24.5 (17.9, 32.0)	13	8.4 (4.5, 13.9)	0	–	51	32.9 (25.6, 40.9)
Kenema	62	27.6 (21.8, 33.8)	11	4.9 (2.4, 8.5)	0	–	73	32.4 (26.3, 38.9)
Koinadugu	37	26.8 (19.6, 35.0)	19	13.8 (8.4, 20.6)	1	0.7 (0.01, 3.9)	57	41.3 (32.9, 49.9)
Kono	38	21.8 (15.9, 28.7)	10	5.7 (2.7, 10.3)	1	0.6 (0.1, 3.1)	49	28.2 (21.6, 35.4)
Moyamba	40	31.5 (23.5, 40.3)	13	10.2 (5.5, 16.8)	1	0.8 (0.1, 4.3)	54	42.5 (33.7, 51.6)
Port Loko	73	39.0 (32.0, 46.4)	14	7.5 (4.1, 12.2)	1	0.5 (0.1, 2.9)	88	47.1 (39.7, 54.4)
Pujehun	32	27.6 (19.6, 36.6)	6	5.2 (1.9, 10.9)	1	0.9 (0.02, 4.7)	39	33.6 (25.1, 42.9)
Tonkolili	58	30.5 (24.0, 37.6)	23	12.1 (7.8, 17.6)	3	1.6 (0.3, 4.5)	84	44.2 (37.0, 51.5)
Countrywide	740	30.5 (28.6, 32.3)	205	8.4 (7.3, 9.6)	11	0.5 (0.2, 0.8)	956	39.4 (35.9, 44.2)

†Data shown are the proportion of cause of death (%) with 95% CI for each district.

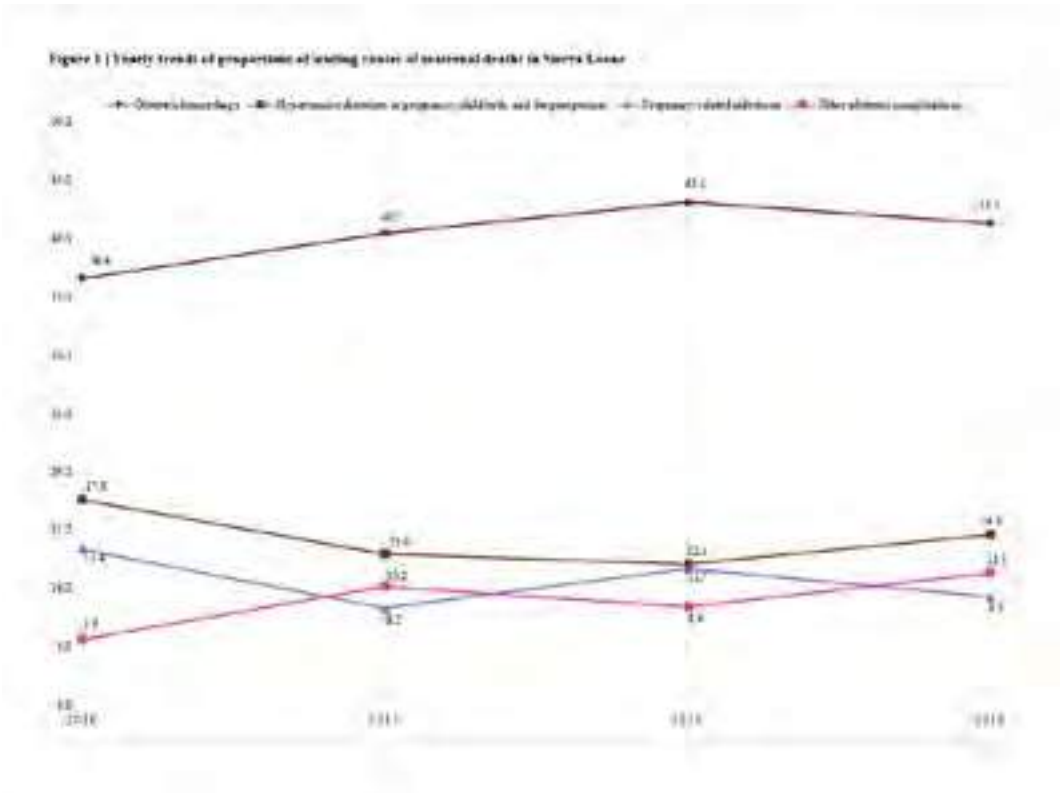

Figure 1 Yearly trends of proportions of leading causes of maternal deaths in Sierra Leone.

hypertension (22.0%), obstructed labour (21.0%) and sepsis (11.0%).[18] The regional comparison of our findings suggests that in the West African countries, obstetric haemorrhage is also the leading cause of deaths (31.4%), followed by hypertension (22.7%), non-obstetric causes (14.1%) and infections (10.3%).[19] Likewise, data from sub-Saharan Africa on maternal deaths suggest a similar pattern. A WHO systematic analysis revealed obstetric haemorrhage (24.5%), hypertension (16.0%), obstructed labour (2.1%) and sepsis (10.3%).[20]

Figure 2 Map of proportions of maternal deaths due to obstetric haemorrhage in each district.

A time-trend analysis of the major causes of maternal death failed to reveal any major patterns. A potential explanation could be that the observation period was relatively short to detect a temporal trend in maternal mortality at the population level.[21] The extent of the changes to be measured depends on numerous factors, such as the frequency with which the data are collected, the accuracy of the data and the magnitude of the changes to be measured.[21] Data spanning at least 5 years are recommended to detect trends in maternal mortality.[22] Even in high-mortality settings, maternal mortality is a relatively rare event; therefore, data accuracy is particularly relevant.[22] Thus, in addition to the quantity of data, it is crucial to ensure data quality and consider any changes in data collection methods or definitions that occur during the observation period. Additionally, despite the heterogeneity in the burden of the specific causes of death, no clear geographical pattern emerged. The reason for this may be associated with the fact that the total number of deaths reported in MDSR may vary from district to district, and the validity of how the MDSR team assigns the cause of death in each district could differ due to the field-related challenges.

This study presented comprehensive findings on causes of maternal deaths using the national dataset of MDSR Sierra Leone segregated by districts. This is crucial for policymakers, decision-makers and programme implementers to understand the targeted interventions. However, it should be noted that the MDSR platform has the major constraint of under-reporting deaths in the system. Approximately 76% of deaths were not recorded by this system in 2016 and 2017 due to several challenges in reporting.[10] This is a well-known limitation of systems like MDRS, which have been documented to have under-reporting rates ranging between 58 and 76 in other settings.[23–25] Nonetheless, such systems remain integral in developing countries to evaluate the performance of health systems and population-level issues. A similar evaluation of the cause as well as an in-depth analysis of these maternal deaths by districts could help policymaker and programme implementers to track the maternal health indicators.[26]

The introduction of monitoring and evaluation (M&E) mechanisms, together with the efforts to tackle reporting challenges within the community, limited organisational capacity and motivation, and difficulties in implementing the programme in the field, can substantially improve the performance of MDSR.[26 27] Moreover, a differential under-reporting rate among the specific causes of death seems unlikely. Thus, an analysis based on relative numbers (proportions over the total number of deaths) rather than absolute numbers should be less sensitive to this limitation.

Finally, the quality of assigning the cause of death using clinical/medical records as well as VA data may have affected the results in specific districts. However, the percentage of VA is low because of the lack of data on maternal death from the community. Therefore, the MDSR system in Sierra Leone has a great opportunity to strengthen the community reporting system within MDSR.

CONCLUSION

To reduce maternal mortality in Sierra Leone, there is a pressing need for more robust strategies in districts with a high burden of top preventable causes. There is an enormous opportunity for shared learning from the MDSR database, which can be used by different stakeholders to provide better-quality services to high-risk women. Although this platform and data have limitations, they can still be used to advance health policies, programmes and innovations aimed at reducing maternal deaths. This can be accomplished by applying the knowledge obtained from these findings. The issue of under-reporting must be addressed to improve the availability and quality of data on maternal deaths and their causes. Capacity building and motivating frontline staff to capture the death event across different scenarios are crucial for improving mortality estimation at the district level. Effective M&E within the MDSR system will be ensured by strengthening the synergy between the national, district, facility and community levels to improve the reporting system and assess the impact of the improvement strategies. Furthermore, longitudinal data on maternal deaths and causes will ensure time-trend analysis of the causes of maternal mortality and design targeted interventions in different districts.

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Toward the design of a tailored training course for birth assistance: an Ethiopian experience

PAPER

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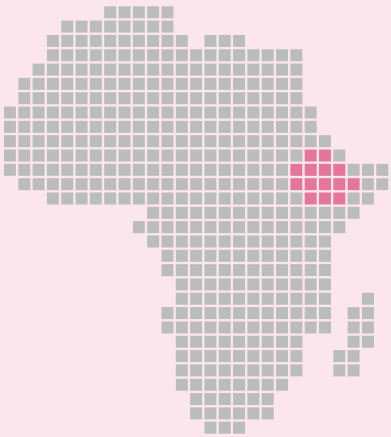

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Short communication

Toward the design of a tailored training course for birth assistance: an Ethiopian experience

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Toward the design of a tailored training course for birth assistance: an Ethiopian experience

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Abstract

Simulation in healthcare has already demonstrated extraordinary potential in high-income countries. However, to date, few authors have explored the possibility of applying simulation-based training in African settings, highlighting the necessity of need-based training protocols capable of addressing economic, social, and cultural aspects. In this framework, this research investigates the main features a simulation training course on umbilical cord care and placenta management should be considered effective and sustainable in an African healthcare environment. Local facilitators were identified as the best resources for defining course contents and providing technical lectures to mitigate cultural, linguistic, and social issues. For

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the training program, the design of a new low-cost medium-fidelity simulator was explored and a preliminary evaluation was performed. Finally, the propensity of 25 students to attend a simulation training course was investigated using a questionnaire. The attitude of the enrolled students was positive, endorsing the future introduction of simulation training into the educational offers of Ethiopian colleges.

Introduction

Simulation in healthcare links classroom learning and real-life clinical experiences [1,2]. Patient safety, error prevention, replicable cases, confidence-building, and team training are the most recognized benefits of simulation [3]. In the past decade, some authors have questioned whether there is room for medical simulation in the African healthcare system [1-6], whereas others have implemented simulation experiences with medical students or trainees [7-9] The establishment of a simulation center in Rwanda has also been documented [10]. These data demonstrate a concrete opportunity for medical simulation in Africa. The participants were engaged and satisfied with the training, although some limitations were identified. Financial and personnel shortages, as well as technical issues such as limited power and internet access, have hindered the development and spread of health simulation. To address these limitations, methodologies that actively involve local resources and technologies to ensure training sustainability are required [6]. Moreover, effective training must be patient-centered and realistic [5]; thus, socio-cultural factors and their influence on learning and teaching must be considered [4].

Following these clear literature indications, this study was designed to create a need-based training course on umbilical cord care and placenta management during childbirth. This specific topic allows the merging of the experiences gained by engineers in high-income countries´ hospitals and the local needs of African clinicians. The study was conducted at St. Luke Catholic Hospital and College of Nursing and Midwifery (Wolisso, Ethiopia) involving both permanent staff and students. The presence of students also allows us to investigate the propensity to include these specific training activities in future education plans. Developing an effective need-based training program in Africa entails identifying the most critical elements to guarantee an affordable and sustainable course. As previously reported, the literature has shown successful results with low-fidelity manikins in some African centers [3-5,10] identifying low-cost, high-fidelity models as the most promising technical solution [5]. Thus, the main aims of this study were as follows: i) define course contents according to local guidelines and resources; ii) find or realize a low-cost, high-fidelity, and sustainable manikin; iii) define teaching and administration modalities tailored to local experiences; iv) examine St. Luke College students' inclination to use physical manikin simulation training.

Methods

The course contents and teaching modalities were defined through regular online meetings between the clinicians and engineering team at Scuola Superiore Sant´Anna (Pisa, Italy). Literature and market analysis showed some training manikins potentially adequate for umbilical cord management. However, some are expensive and clinically incomplete, whereas others are cheaper but still incomplete from an operative point of view. Therefore, by exploiting our experience in the field of high-fidelity simulators for healthcare, a dedicated simulator of the human umbilical cord and placenta was created using rapid prototyping techniques and silicone materials. The medical team and 25 third-year St. Luke College students were asked to perform umbilical cord ligation, cutting, and cleaning, and to examine simulator fidelity and usability for placental lobes, vessels, and membranes assessment tasks. Their feedback was noted and reorganized in a report revised and approved by the clinical team. Finally, the attitude of the St. Luke College students to attend a

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complete simulation-based training course with the simulator was assessed with an anonymous online questionnaire created by Google Forms (Google Inc., USA). No sensitive information was provided on this form.

Results

Daily umbilical cord and placental care procedures used at St. Luke Hospital - in agreement with the Ethiopian guidelines - were chosen as reference for the training course contents. St. Luke teachers were identified as facilitators to ensure course alignment with local teaching methods and to overcome cultural and linguistic barriers. The course was held on February 6, 2023, at St. Luke spaces to ensure student comfort and long-term sustainability.

The new simulator (Figure 1) consisted of a reusable part and a disposable part connected through a 20 mm deep cylindrical hole exploiting the friction between the two silicone surfaces. The disposable part, a 150 mm long and 13 mm diameter cylinder, mimics the proximal part of the umbilical cord with three cylindrical holes resembling the two arteries (3 mm diameter) and one vein (3.5 mm diameter). This part is cut during the training and, due to design constraints, it can be used no more than 3-5 times, then it must be replaced. The reusable part was a 320 mm long, 15 mm diameter cylinder with a conical end 55 mm tall and 130 mm maximum diameter. It replicates the distal part of the umbilical cord and placenta and can be used repeatedly. The components were made of uncolored Ecoflex 0010 silicone (Smooth-On, USA) using molding techniques. This inexpensive silicone exhibits a balance between softness and integrity, thereby mimicking the tactile feedback of human tissues. The molds, designed using Fusion 360 CAD software (Autodesk, USA), were 3D printed using a Prusa MK3S+ printer (Prusa Research, Czech Republic) with PLA (RS Components, UK).

During simulator use, the limitations due to the absence of crucial anatomical structures, i.e. the placenta lobes and membranes, have appeared as evident, and the physiological tissue colors necessary for teaching. The material softness and possibility of being cut were appreciated. However, the high stretchability of silicone has been identified as a problem. The questionnaire was completed by 25 students, 12 nurses, and 13 midwives, and the results are presented in Table 1. Overall, the students had a positive attitude. The 24% were unaware of simulation-based education. All participants enjoyed the simulator despite its limitations and wanted to include the simulation in their study plan. They felt confident using the simulator for future re-training. 96% of the students recognized the simulation´s potential to improve their skills and confidence.

Discussion

The key findings of this study are summarized in Figure 2. The research results suggest that local facilitators should define course content and teaching methods to ensure socio-cultural-linguistic compliance. Internet discussions between the two teams, clinical and engineering, experienced connectivity issues, with challenges in mutual comprehension. These issues were promptly resolved during an in-person meeting before the course. Similar connection difficulties arose during the online survey, which were eventually solved by local teachers. It is clear that Internet connectivity in Africa is still unreliable; therefore, printed surveys and in-person meetings should be preferred whenever possible.

Regarding language barriers, students were able to read English sentences, but they had difficulties speaking. Local facilitators helped address this issue. It is crucial that each participant fully understands the concepts taught because incomplete or misinterpreted information may have serious consequences for patient safety in future clinical practice. In conclusion, working with local teachers is mandatory to provide an effective tailored training course because a foreign facilitator would not be able to properly address local language, cultural, and social factors. If local

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teachers have no prior experience with simulation, it is recommended to 'train the trainers' before delivering the course, as demonstrated in [9].

The simulator material and manufacturing choices were selected to keep the final cost low, resulting in a medium-fidelity solution for umbilical cord cutting and basic umbilical cord care training. Owing to the limited fidelity of the simulator, healthcare students cannot learn all the steps of placenta management and umbilical cord care, such as evaluating the right color of umbilical cord structures and identifying placental components. The silicone tactile feedback in compression resembles human tissues, but its high stretchability does not replicate reality. The real umbilical cord is inextensible and usually pulled to help deliver the placenta, which cannot be achieved using this simulator. Thus, improvements in anatomical and appearance fidelity are required. Finally, silicone, which is affordable in wealthy countries, is difficult to obtain in Ethiopia. At the same time, disposable part delivery is costly and unsustainable. Therefore, to create a locally manufactured and sustainable product, the identification of another material for the simulator is required. Further design choices should target a compromise between fidelity, affordability, and local manufacturability to lean toward the low-cost high-fidelity sustainable models demanded, e.g. by Campain *et al.* [5].

Conclusion

Literature shows that there is potential for the use of medical simulations in Africa, provided that local socio-cultural-economic factors are considered. The design of a sustainable and need-based simulation training course was investigated. Procedural guidelines and best teaching and administration practices were identified. A new medium-fidelity low-cost simulator was developed and assessed by the local clinical team and students. It showed a few strong limitations that require further improvement before being used in a training course. Students showed a generally positive behavior toward simulation, demonstrating that there is space for simulation training in the educational offer of Ethiopian colleges.

What is known about this topic

- *The utilization of simulation as a teaching tool in medical education is considered to be effective in African nations;*
- *It is necessary to employ methodologies that actively engage local resources and technologies to ensure the sustainability of training.*

What this study adds

- *Guidelines for structuring a tailored training course for African medical students are provided;*
- *It is recommended that low-cost, high-fidelity simulators be utilized for effective training courses in low-income countries.*

Competing interests

The authors declare no competing interests.

Authors' contributions

All authors have read and approved the final version of the manuscript and contributed equally to its content.

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Table and figures

Table 1: list of questions provided to 25 students using the questionnaire; the results are shown as percentages
Figure 1: new simulator of the umbilical cord and placenta, made of silicone, with labels pointing to the main components

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Figure 2: summary of key research findings; main features a simulation training course tailored to the Ethiopian needs should present

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Table 1: list of questions provided to 25 students using the questionnaire; the results are shown as percentages	
Question	**Results**
Did you know what the training with simulation was before today?	24%; no
	76%; yes
What are your feelings regarding simulation?	100%; positive
	0%; negative
	0%; neutral
Did you like the experience with the new simulator?	100%; yes
	0%; no
Do you think simulation can help you improve your skills?	96% yes
	4%; maybe, not sure
	0%; no
Do you think simulation can help you improve your confidence?	96%; yes
	4%; maybe, not sure
	0%; no
Would you like to introduce the simulation into your curriculum?	100%; yes
	0%; no
Would you like to have periodical training sessions on umbilical cord management?	96%; yes
	4%; no
Would you be comfortable using the simulator on your own for future individual retraining?	100%; yes
	0%; no
Would you like to participate in additional training sessions with other simulators to enhance your proficiency in other areas?	100%; yes
	0%; no

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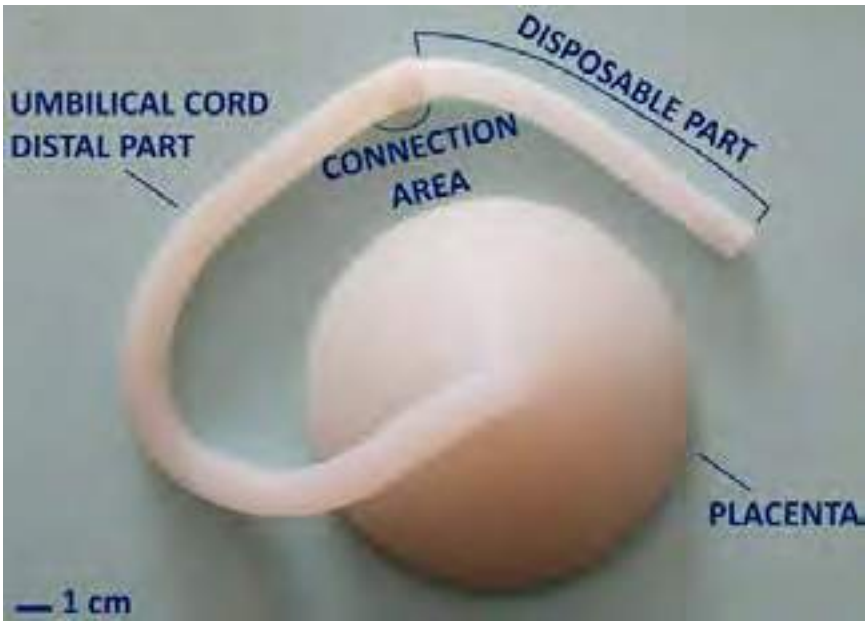

Figure 1: new simulator of the umbilical cord and placenta, made of silicone, with labels pointing to the main components

Figure 2: summary of key research findings; main features a simulation training course tailored to the Ethiopian needs should present

Traditional Herbal Medicine in the Central African Republic: Ethnobotanical Survey and Prognosis of Children Hospitalized at the Centre Hospitalier Universitaire

PAPER

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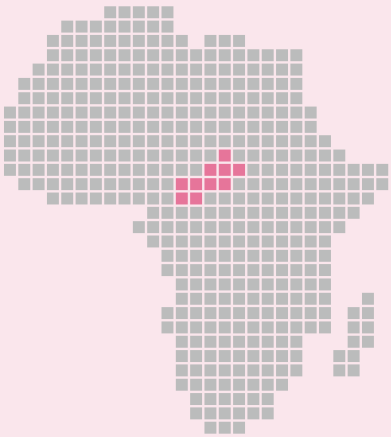

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Traditional Herbal Medicine in the Central African Republic : Ethnobotanical Survey And Prognosis of Children Hospitalized at the Centre Hospitalier Universitaire

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Abstract

Context : *Medicinal plants are a precious heritage for mankind, and more particularly for the majority of poor communities in developing countries who depend on them for their primary health care and subsistence.*

Objective : *To carry out a hospital-based ethnobotanical survey among parents of children having benefited from traditional phytotherapy prior to admission to the Centre Hospitalier Universitaire (CHUPB) in order to identify the prevalence, the nature of the product used, the proportion of prescriptions of plants presumed to be toxic, while assessing the effects on the children.*

Materials And Methods : *Cross-sectional study conducted at CHUPB over a 2-month period (March 1 to April 30, 2021). All children aged between 1 month and 15 years, admitted to intensive care regardless of diagnosis, with notion of exclusive traditional phytotherapy at home prior to therapeutic admission, were included. Data were analyzed using Epi-info software.*

Results : *Hospital frequency was 1.85% (n=50/2702) and mean age 2.2 years. The sex ratio was 1.38 and 62% of children lived in urban areas. Most parents were out of school (64%) and 80% lived in poor socio-economic conditions. The symptoms that prompted phytotherapy were anal pruritus (58%) and skin pallor (18%). The average duration of phytotherapy was 68.4 hours. It was administered by the parents in 86% of cases. The main route of administration was intra-rectal (36%). The plants used were harvested in the forest in 42% of cases. The main plants used were: Chromolaena odorata "BARABOKASSA" (22%) - Vernonia amygdalina "HONCKA" (14%) - Solanum lycopersicum "TOMATE" (12%) - Ocimum gratissimum "MATETE" (6%) - Jatropha curcas "KADA MONO" (4%) - Cassia siamea o Senna siamea "CASSIA" (2%) and Dioscorea bulbifera "KERERE" (2%). Organ failure was neurological in (62%), hepatic (48%), hematological (38%) and renal (16%) cases. Mortality rate was 26.0%.*

Conclusion: *Phytotherapy is frequently used in Bangui. The medicinal plants used must, like "conventional medicines", obey strict rules of cultivation, control and dispensing.*

Keywords: Phytotherapy, Children, CHUPB.

Abbreviations

CHUPB	:	Complexe Hospitalier Pédiatrique de Bangui	**%**	:	Percentage
CAR	:	Central African Republic	**g/l**	:	grams per liter
INR	:	International Normalised Ratio	**h**	:	hour
WHO	:	World Health Organization	**j**	:	Day
mg/dl	:	Milligrams per deciliter	**g**	:	Grams
mm^3	:	Cubic millimeter	>	:	Superior
g/dl	:	Grams per decilitre	≥	:	Greater than or equal to
dl	:	Deciliter	<	:	Lower
°C	:	Degrees Celsius	≤	:	Less than or equal to

1. Introduction

Medicinal plants are a precious heritage for mankind, and particularly for the majority of poor communities in developing countries, who depend on them for their primary health care and livelihood [1]. Traditional phythotherapy, which is not based on evidence-based medicine, is considered by the scientific community to be an unconventional medicine which, depending on the plants used, carries risks of toxicity, interaction with other medicines, or pollution by chemicals or heavy metals [2]. Its origins can be very ancient, based on the use of plants with virtues discovered empirically [3]. Whether they were healers, shamans, sorcerers or druids, the wise men of each people studied all the herbs they had at hand and passed on their knowledge, usually orally, to subsequent generations [3]. La phytothérapie moderne qui se base sur des preuves scientifiques sans récuser la tradition, fait appel aux recherches pour valider l'efficacité des principes actifs extraits des plantes mais les études et surtout les essais cliniques sont encore trop peu nombreux [4]. According to the WHO, in certain developing countries in Asia, Africa and Latin America, 80% of the population depends on traditional medicine, especially in rural areas, due to the proximity and accessibility of this type of care at affordable cost, and above all because of the lack of access to modern medicine for these populations [5-10]. In Africa, little is known about the toxic principles of plants, mainly due to their natural complexity. Like "conventional medicines", these medicinal plants must therefore obey strict rules governing cultivation, control and dispensing [10]. The World Health Organization has drawn up a list of monographs on medicinal plants, which is divided into three categories : plants whose use is supported by clinical data, those whose use is supported by pharmacopoeias and traditional systems of medicine, and those whose use is described in popular circles but not supported by clinical and experimental data [11]. In paediatric hospitals, it is often very difficult to get parents to confess to using traditional herbal medicine before admitting their child to hospital. According to a German study, patients rarely spontaneously inform nurses of their use of herbal medicine. Yet the risks of interactions between herbal medicines and drugs are real [9]. Several studies have shown that phytotherapy is not without risk. Toxic effects affect most organs. Examples include renal failure linked to Chinese plants, cardiac damage caused by aconite intoxication, and pulmonary damage linked to certain mints [10,12,13]. In many parts of the world, authorities, health professionals and the general public are grappling with issues relating to the safety, efficacy, quality, availability, preservation and regulation of traditional medicine [14]. In the Central African Republic, there are no data on the use of traditional herbal medicine in paediatrics, hence the aim of this study, which was to carry out a hospital survey of parents of children who had used this practice on their children prior to admission to the CHUPB in order to identify the prevalence, the nature of the product used, the proportion of use of plants thought to be toxic, and to gather information on the effects on children.

2. Patient And Method

The survey was carried out at the Centre Hospitalier Universitaire Pédiatrique de Bangui, the only referral hospital and facility specializing in the care of children in vital distress in the CAR. It receives children aged between zero and 15, from home or referred from a public or private health center in the capital and the provinces. The study was carried out in the intensive care unit. It was a monocentric, cross-sectional, descriptive and analytical study covering the two-month period (March 1 to April 30, 2021). We included in the study, after informed consent from parents or guardians, children aged from 1 month to 15 years, admitted to the intensive care unit of the CHUPB regardless of diagnosis with notion of exclusive traditional herbal medicine for therapeutic purposes at home prior to admission. We did not include in the study children who had received traditional phytotherapy combined with animal products or pharmaceutical molecules, or those who had received phytotherapy for preventive purposes.

• **Data Collection Began By Obtaining Research Authorization from the Deanship of The Faculty of Health Sciences in Bangui (CAR) ;** we then introduced ourselves to the head of the CHUPB intensive care unit. After explaining the purpose of the study, we were given access to the children's medical records, to their parents or legal guardians, and to the intensive care hospital wards. Confidentiality was also assured. Thus, for each child, data were collected from a pre-established survey form and entered using SPSS 20.0 statistical software. For word processing, we used Microsoft Word 2003. Results, presented in tabular and graphical form, were produced using Excel version 2003. The statistical test used was Pearson's chi^2. A value of $p < 0.05$ was considered statistically significant, and the Odds ratio was calculated with a 95% confidence interval. There were no conflicts of interest.

3. Results

3.1. Epidemiological Data

3.1.1. Hospital Frequency

Of the 2.702 children hospitalized during the study period, 50

had received traditional phytotherapy prior to admission, giving a hospital frequency of 1.85%.

3.1.2. Gender, Age and Place of Residence

The average age of the children was 2.2 years, ranging from 1 month to 13 years. Eighty-four percent of children 84%(n=42) were under 3 years of age, versus 16% (n=8) aged 3 years or over. There was a male predominance of 58.0% (n=29) versus 42.0% (n=21) for female children, with a sex ratio of 1.38. The children lived in Bangui's urban area in 62% (n=31) of cases, and in rural areas in 38% (n=19).

3.1.1. Socio-Demographic Characteristics of the Parents

The average age of the mothers was 28.5 years, ranging from 16 to 45 years. The average age of the fathers was 35.1 years, ranging from 17 to 56 years. Most of the mothers were unschooled or had primary education in 68% (n=34) of cases. Sixty percent of fathers (n=30) had no schooling or some education. Parents worked in the informal sector : 78% (n=39) of mothers versus 62% (n=31) of fathers. Eighty percent (n=40) of children lived in unfavorable socio-economic conditions. The distribution of children according to their parents' socio-demographic characteristics is shown in **Table I**.

Determinants (N=50)	Parents			
	Father Mother		Father Mother	
	(n)	%	(n)	%
Age in years				
<25	12	24	13	26
26-35	17	34	23	46
36-45	15	30	11	22
≥46	6	12	3	6
Education level				
Primary	16	32	17	34
Out of school	14	28	17	34
Secondary	18	36	16	32
Higher	2	4	0	0
Professions				
Informal sector	31	62	39	78
Manual/worker	13	26	1	2
No profession	5	10	10	20
Senior executive	1	2	0	0
Socioeconomic level				
Low	40	80	40	80
Medium	9	18	9	18
High	1	2	1	2

Table I: Distribution of children according to parents' socio-demographic characteristics.

3.2. Clinical data

3.2.1. Anamnestic data

The symptoms that prompted traditional phytotherapy were anal pruritus in 58% (n=29) of cases, skin pallor in 18% (n=9), suspected splenomegaly in 14% (n=7), fever in 6% (n=3) and diarrhea in 4% (n=4).

The average duration of traditional phytotherapy was 68.4 hours, with extremes ranging from 21.9 to 120 hours. The duration of phytotherapy was greater than or equal to 72 hours in 46% (n=23) of children, and less than 24 hours in only 4% (n=2). Traditional phytotherapy was administered by parents in 86% (n=43) of cases, and by the traditional phytotherapist in 24% (n=7). The two main modes of preparation of plants used for phytotherapy were decoctions in 74% (n=37) versus infusion in 26% (n=13). The main routes of administration of phytotherapy were intra-rectal in 36% (n=18) of cases, mixed in 28% (n=14) of cases, oral in 24%(n=12), nasal in 6%(n=3) and transcutaneous by scarification in 6%(n=3) of cases. The plants used were harvested in the forest in 42% (n=21) and in the family plot garden in 24% (n=12). In 20% (n=10), they were bought freely at the market by the parents, and in 8% (n=4) they were supplied by the phytotherapist, versus 6% (n=3) by a neighbor. The distribution of children according to anamnestic data is shown in Table II.

Parameters (N=50)	Number (n)	Percentage
Traditional herbal medicine motif		
Anal pruritus	29	58
Skin pallor	9	18
Suspicion of splenomegaly	7	14
Fever	3	6
Diarrhea	2	4
Duration of traditional phytotherapy in hours		
<24	2	4
[24-48[	15	30
[48-72[	10	20
≥72	23	46
Actors of the Phytotherapist		
Parents	43	86
Herbal therapists	7	24
Plant preparation methods		
Décoction	37	74
Infusion	13	26
Herbal medicine's path of admiration		
Intra-rectal	18	36
Mixed	14	28
Oral	12	24
Nasal	3	6
Transcutaneous (scarification)	3	6
Access to plants		
Forest	21	42
Family garden	12	24
Free purchase at the market	10	20
Provided by herbalist	4	8
Supplied by a neighbor	3	6

Table II : Distribution of children according to anamnestic data.

3.2.2. Taxonomy of Plants Used for Phytotherapy

The scientific names and families of plants used for phytotherapy were identified by the botanical department of the University of Bangui in 62% (n=31) versus 38% (n=19) whose scientific names did not exist in the botanical repertory of the University of Bangui. For cases whose names (families) could be clearly identified (N=31), these were ***Chromolaena odorata (Asteraceae)*** with the Central African vernicular name "BARABOKASSA" in 35, 48% (n=11) of cases - ***Vernonia amygdalina (Asteraceae)*** of the Central African vernicular name "HONCKA" in 22.58% (n=7) of cases - ***Solanum lycopersicum (Solanaceae)*** of the Central African vernicular name "TOMATE" in 19, 35% (n=6) of cases - ***Ocimum gratissimum (Lamiaceae)*** of the Central African vernicular name "MATETE" in 9.68% (n=3) of cases - ***Jatropha curcas (Euphorbiaceae)*** of the Central African vernicular name "KADA MONO" in 6, 45% (n=2) of cases - ***Cassia siamea o Senna siamea (Fabaceae)*** of the Central African vernicular name "CASSIA" in 3.23% (n=1) of cases and ***Dioscorea bulbifera (Dioscoraceae)*** of the Central African vernicular name "KERERE" in 3.23% (n=1) of cases.

The remaining plants used for traditional phytotherapy (N=19) were known only by their Central African vernicular name: "BERA o BERERA" in 36.84% (n=7) of cases - "BOBO" in 21, 05% (n=4) of cases - "DIN" in 10.52% (n=2) of cases - "KIERE" in 10.52% (n=2) of cases - "NDIRI" in 10.52% (n=2) of cases and "NGBANDA" in 10.52% (n=2) of cases. The distribution of children according to the plants used for traditional phytotherapy is shown in figure 1.

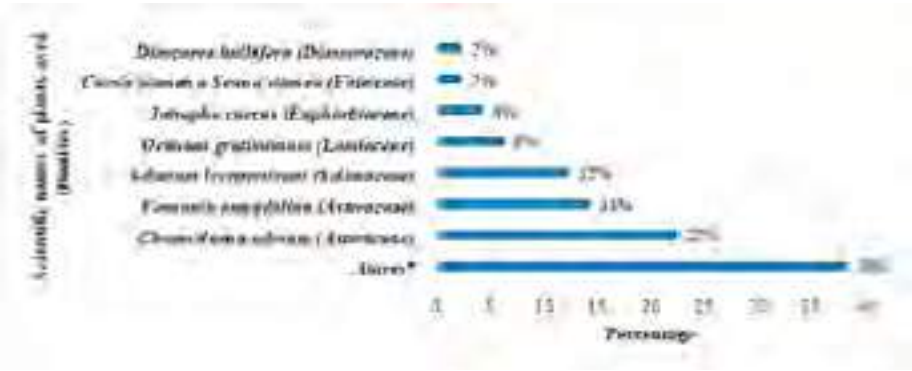

Figure 1 : Distribution of children according to plants used for traditional herbal medicine.

2.2.3. Reason for Consultation

Reasons for consultation included fever 92% (n=46), convulsions 40% (n=20), skin pallor 24% (n=12), agitation 24% (n=12), breathing difficulties 22% (n=11), level gaze 18% (n=9), dark urine 18% (n=9), diarrhea associated with vomiting in 10% (n=5), jaundice 10% (n=5), hemorrhage 4% (n=2), behavioral disorder 2% (n=1). The same child could have several reasons for consultation.

2.2.4. Vital Parameters

The children had fever in 92% (n=46) of cases, normal fever in 6% (n=3) of cases and below-normal fever in 2% (n=1) of cases. Tachycardia was noted in 90% (n=45), normo-thermia in 12% (n=6) and bradycardia in 2% (n=1). Children were eupneic in 78% (n=39), had tachycardia in 18% (n=9) and bradypnea in 4% (n=2). Desaturation was noted in 16% (n=8). Coma was noted in 62% (n=31) of cases, stage I in 26% (n=13), stage II in 18% (n=9), stage III in 7% (n=14) and stage IV in 4% (n=2). Vital parameters are shown in Table III.

Parameters (N=50)	Number (n)	Percentage
Temperature :		
High temperature	46	92
Normal temperature	3	6
Hypothermia	1	2
Heart rate :		
Tachycardia	45	90
Normal	6	12
Bradycardia	1	2
Respiratory frequency:		
Eupnea	39	78
Tachypnea	9	18
Bradypnéa	2	4
Oxygen saturation :		
≥ 95%	42	84
< 95%	8	16
Glasgow :		
15 14	19	38
13 - 10	13	26
9 - 6	9	18
5 - 4	7	14
3	2	4

Table III : Distribution of children according to vital parameters.

2.2.5. Physical Examination

The main signs on physical examination were splenomegaly in 54% (n=27) of cases, hepatomegaly in 46% (n=23), mucocutaneous pallor in 24% (n=12) of children, skin recoloration time greater than 3 seconds in 12% (n=6), severe respiratory distress syndrome in 12% (n=6) and cold extremities in 12% (n=6). Physical examination findings are shown in figure 2.

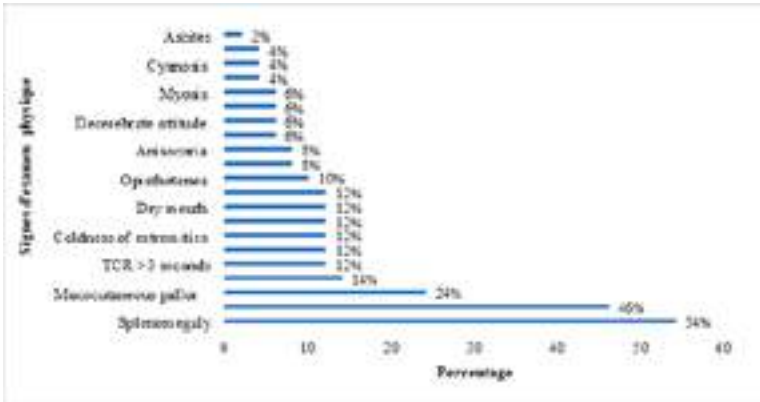

Figure 2 : Distribution of children according to physical examination signs

3.2. 6. Paraclinical Data

The malaria rapid diagnostic test was performed in all cases on admission and was positive in 50% (n=25) of patients. Thick drop tests for haematozoa were carried out in all cases and were positive in 40% (n=20) of cases. Mean parasite density was 118.5/mm3 with extremes [80- 1300/mm3]. A blood glucose test was performed on admission in all cases. The mean blood glucose level was 67.8±6.6 mg/dl with extremes (Lo - 270 mg/dl). A glycemic abnormality was noted in 22% (n=11) of cases. Refractory hypoglycemia was noted in 16% (n=8) of cases, and hyperglycemia in 6% (n=3). Lumbar puncture was performed in 12% (n=6) of cases. The appearance was clear in 6%(n=3), cloudy in 4%(n=2) and. All children had a complete blood count (CBC). The mean white blood cell count was 5955.5/mm3 with extremes (221 - 77000/mm3). They were normal in 46% (n=23) of cases, hyperleukocytosis in 38% (n=19) and leukopenia in 16 (n=8). The mean hemoglobin level was 8.8 g/dl with extremes (2.3 - 13.4 g/dl). This level was normal for age in 40% (n=20) of cases and less than or equal to 5g/dl in 22% (n=11). Hemoglobin levels were below normal for age, but above 5g/dl in 38(n=19). Mean Figurelet count was 146,000.68/mm3; extremes (1240 - 410000/mm3). Thrombocytopenia was noted in 38% (n=19) of cases. Blood ionograms were performed in 22% (n=11) of patients, with abnormalities noted in 12% (n=6). Creatinine levels were measured in 46(92%) children, with a mean value of 74.6±3 micromole/l. Mean glomerular filtration rate was 122 ± 29 ml/min/1.75m2. Decreased glomerular filtration rate was noted in 17.39% (8/46) of cases. Renal failure was mild in 37.5% (3/8) of cases, moderate in 25% (2/8), preterminal in 25% (2/8) and end-stage in 12.5% (1/8). Among the 47(94%) cases of International Normalized Ratio (INR) performed, hepatocellular insufficiency was noted in 51.06% (24/47) of cases. GeneXpert was performed in 3(6%) children. The result was positive in one case (2%). Bilirubinemia was performed in 37(74%) children, with a mean level of 5.79±3.3 extremes (0.7- 18.4 mg/dl).

3.2.7 Principal Organ Failures Noted

Organ failure was neurological in 62% (n=31) of cases, hepatic in 48% (n=24), hematological in 38% (n=19) and renal in 16% (n=8). It should be noted that the same child could have one or several organ failures.

3.2.8. Etiological Data

The main etiologies associated with phytotherapy were neuromalaria in 28% (n=14) of cases, sepsis in 18% (n=9), severe malaria anemia in 12% (n=6) of cases, septic shock in 10% (n=5) of cases, acute gastroenteritis with dehydration in 10% (n=5) of cases, severe acute pneumonia in 10% (n=5), bacterial meningitis in 4% (n=2), meningoencephalitis in 4% (n=2), febrile convulsion in 4% (n=2), hypoglycemia with severe emaciation in 4% (n=2) and pulmonary tuberculosis in 4% (n=2).

3.3. Progression

Progression was favorable in 68.0% (n=33) of cases. Complications occurred in 34.0% (n=17) of cases, with 8.0% (n=4) suffering neurological sequelae and 26.0% (n=13) dying. The mean time to death was 18.33±1.3 hours (range 2.6 - 123.3 hours), with 69.24% (n=9) of cases within the first 48 hours and 30.76% (n=4) after the 48th hour. The average hospital stay was 168.22 hours, ranging from 72.7 to 360.9 hours. It was less than 72 hours in 16%(n=8) of cases, between [72 - 120 hours] in 64%(n=32) of cases, between [120-168 hours] in 6%(n=3) and greater than or equal to 168 in 14%(n=7).

3.4. Study of the Sample's Sub-Populations According to The Specific Use of Traditional Plants Whose Scientific Name Was Known

The 11 children who received phytotherapy with ***Chromolaena Odorata (Apolo o Barabokassa)***, the average age was 1.06 years, seven lived in rural areas, the plant was administered

exclusively by the parents (11), the route of administration was exclusively rectal for 5 children and mixed (per os and rectal) for 6 children. Plants were collected from the forest in the case of 7 children, and from the family garden in the case of 4. The average duration of treatment was 1.09 days and the average number of administrations was 1.09 per day. Malfunctions were multiplied in 4 children (hepatic/neurological in 3 cases and hepatic/renal in 1). They were exclusively hepatic in 3 children and neurological in one. The main diagnoses were: neuromalaria (9), sepsis (1) and severe acute pneumonia (1). Five of the 11 children died (45%). Of the 7 children who benefited from ***Vernonia Amygdalina (Honcka)*** phytotherapy, the average age was 3.07 years, five lived in urban areas, the plant was administered exclusively by the parents (7), the route of administration was exclusively rectal for 5 children and mixed (per os and rectal) for two children. Plants were collected from the forest in the case of 5 children, and from the family garden in the case of 2. The average duration of treatment was 1.02 days, and the average number of administrations was 1.14 per day. 3 children had multiple failures (hepatic/neurological/ hematological). Failure was exclusively hematological in 2 cases, hepatic in 2 and renal in one child. The main diagnoses were : Severe malaria anemia (3), Bacterial meningitis (2), Acute gastroenteritis (2). One child out of 7 died (14.28%). Of the 6 children who benefited from phytotherapy with ***Solanum Lycopersicum (Tomato),*** the average age was 1.2 years, four of them lived in urban areas, the plant was administered exclusively by the parents (6), the route of administration was exclusively oral for 3 children, rectal for one child and mixed (per os and rectal) for two children. Plants were collected from the family garden in 4 children and from the forest in 2. The average duration of treatment was 1.16 days, and the average number of administrations was 1.11 per day. Multiple failures occurred in 3 children (hepatic/ neurological/ hematological). Failure was exclusively hematological in 2 cases, hepatic in 2 and renal in one child. No child died. Of the 3 children treated with ***Ocimum Gratissimum (Matete)*** phytotherapy, the average age was 0.63 years, all lived in urban areas, the plant was taken by the parents (3), and the route of administration was mixed (per os and rectal) in all children. All children had their plants collected in the forest. The average duration of treatment was one day, and the average number of administrations was one per day. Multiple organ failure was observed in all children (hepatic and neurological) in one and (hepatic and renal) in two. One child out of three died (33.33%). The average age of the two children treated with Jatropha Curcas (Kada-Mono) was 3.35. The route of administration was mixed oral and rectal. Both cases had hepatic failure and the discharge diagnosis was neuromalaria. No deaths were observed. The child who received phytotherapy with ***Senna Siamea o Cassia Siamea (Cassia)*** was 4 years old, had no organ failure and was discharged alive with a diagnosis of pulmonary tuberculosis. Finally, the child who had received ***Dioscorea Bulbifera (Kerere)*** phytotherapy had liver failure and was discharged with a diagnosis of simple febrile convulsion.

3.5. Analytical Data

Death in children receiving traditional phototherapy was influenced by the young age of children under 3 (p=0.01 - OR=0.1[0.02-0.81]), parental administration of phytotherapy (p=0.004 - OR=0.09[0.01-0.055]), mixed route of administration (p=0.001 - OR=0.06[0.01-0.43]) and coma depth p=001. Septic shock increased the probability of death by a factor of 14 (p= 0.03 - OR=14[0.9-201.6]), severe malaria in the anemic form increased the risk of death by a factor of 20 (p=0.034 - OR=20[0.93-429.9]) and the neurological form by a factor of 24 (p=0.008 - OR= 24[1.6-341]), acute gastroenteritis with dehydration increased the risk of death by 16 (p=0.05 - OR= 16[0.72-354.8]), and long hospital stays of 72 hours or more multiplied the risk of death by 42 (p=0.00- OR=42[4.35-405.14]). Analytical data are shown in **Table IV.**

Features	Deaths (n=13)	Living (n=37)	P	OR	X^2
Male	6	23	0,16	0,5[0,14-1,87	1,01
Female	7	14			
Origin					
Urban	6	25	0,09	0,4[0,11-1,49]	1,87
Rural	7	12			
Age in years					
< 3	9	35	**0,01**	**0,1[0,02-0,81]**	**5,86**
≥3	4	2			
Duration of traditional phytotherapy					
<24	1	1			
[24-48[	2	13	0,17	6,5[0,27-151,1]	1,63
[48-72[	4	6	0,41	1.5[0,07-31,57]	0,06
≥72	6	17	0,28	2,8[0,15-52,7]	0,52
Actors of the Phytotherapists					
Parents	8	35	**0,004**	**0,09[0,01-055]**	**8,73**
Herbal therapists	5	2			

How to use					
Intra-rectal	2	16			
Mixed	9	5	0,001	0,06[0,01-0,43]	9,8
Oral	1	11	0,42	1,3[0,11-17,09]	0,06
Nasal	1	2	0,21	0,25[0,01-4,17]	1,03
Transcutaneous (scarification)	0	3	0,36	----------	0,36
Coma staging					
Stage I	1	18			
Stage II	5	8	0,01	0,08[0,008-0,8]	5.580
Stage III	6	3	0,0007	0,02[0,002-0,32]	12,28
Stage IV	1	1	0,09	0,05[0,001-1,7]	4,20
Diagnosis associated with intoxication					
Septic shock	4	1			
Sepsis	2	7	0,03	14[0,9-201,6]	4,38
Severe neurological malaria	2	12	0,008	24[1,6-341]	7,36
Severe malaria, anemic form	1	5	0,034	20[0,93-429,9]	4,41
Acute gastroenteritis with dehydration	1	4	0,05	16[0,72-354,8]	3,6
Bacterial meningitis	1	1	0,28	4[0,11-136,9]	0,63
Other	2	7	0,03	14[0,94-207,6]	4,38
Main organ failures					
Neurological	3	28			
Hematological	3	16	0,27	0,57[0,1-3,17]	0,41
Hepatic	5	19	0,13	0,4[0,86-1,9	1,35
Renal	2	6	0,15	0,32[0,04-2,36]	1,33
Hospital stay in hours					
≥72	7	1	0,00	42[4,35-405,14]	18,72
< 72	6	36			

Table IV: Distribution of children according to analytical data.

4. Discussion

4.1. Epidemiological Aspects

Herbal medicine is one of the foundations of popular medicine and, like other alternative medicines, is considered particularly attractive in Africa. It is an important and often underestimated component of health services [9,10,13,14]. The WHO estimates that a considerable number of people in sub-Saharan Africa use traditional herbal medicine as a complementary and alternative means of meeting their primary healthcare needs [15]. The vast majority of the population, estimated at between 65% and 80%, rely on indigenous systems of medicine and use medicinal plants as first-line medicines [16,17]. In our series, the hospital frequency of use of traditional herbal medicine was 1.85%. This frequency does not reflect the use of herbal medicine among Central African children, as it is underestimated due to the fact that our work was carried out in a hospital setting with a short timeframe. On the other hand, Ethiopian highlanders reported the use of traditional herbal medicine among children in 71% of cases during a community study [18]. Several studies carried out in the same unit noted that the late admission of children to the CHUPB was explained by the importance attached to traditional phytotherapy inherited from ancestral cultures, the efficacy of which was not always proven [19,20]. Traditional medicine is still widely used in most countries, and its adoption is accelerating in others. At the same time, interest in this medicine is moving beyond products to practices and practitioners [21]. Various factors have contributed to the popularity of medicinal plants, in particular : the ecological movement that has been developing for several years in industrialized countries ; the idea that what is natural can only be beneficial ; the notion that medicinal plants, if not very effective, are at least completely harmless, unlike conventional medicines [10,12,13]. At the International Conference on Traditional Medicine for South-East Asian Countries, in February 2013, the Director General of the WHO, had asserted that "For many millions of people, herbal medicines, traditional treatments and traditional practitioners are the main if not the only source of health care. They are close to people, easily accessible and affordable. They are also culturally acceptable and trusted by a large number of people. Traditional medicine also appears to be a way of coping with the inexorable rise in chronic non-communicable diseases" [14]. The use of traditional herbal treatments in young children is a major concern ; therapeutic regimens, indeterminate dosage, immaturity of metabolic and excretory organs, content, preparation, quality of mixtures and duration of treatment may be important risk factors for adverse effects in this age group [22]. Early childhood was

the most affected by the traditional herbal medicine phenomenon in our series, with 84% under 3 years of age and 20% under 6 months. This observation corroborates the Nigerian study, which reports the use of phytotherapy in infants and children from the age of 6 months. The predominance of under-3s is probably due to this age group's greater susceptibility to fever-producing infections, which motivates parents to use plants as a therapeutic means. This is borne out in our study by fever (58%), which is the main reason for using phytotherapy. In addition, the martial deficiency that is rife in certain regions of the world, including the Central African Republic [23]. Is generally responsible for pallor, which was the second most common cause of phytotherapy in our series (18%). The low density of health facilities in certain regions of the country led the 38% of parents in our study who lived in rural areas to resort to phytotherapy, which was facilitated by their proximity to traditional healers. On the other hand, the 62% of parents living in urban Bangui resort to traditional herbal medicine to compensate for the long queues in Bangui's public health establishments for the 20% whose study had noted average socio-economic conditions. On the other hand, for the other 80% of parents with low socio-economic conditions, the use of herbal medicine is justified by the lack of means to access care in health facilities, although it must be stressed that the journey to these health facilities often depends on the availability of public or private motorized transport, which implies additional costs to be added to health costs. The low level of education observed in our series (68%) would also explain the use of herbal medicine by parents. Like our series, several African authors have noted in their work that the use of traditional herbal medicine was significantly associated with parental profiles : low level of education, unemployment or low-skilled jobs, low monthly income, ease of access, residence in rural areas, literacy with ancestral cultural belief in the merits of herbal medicine [15,18, 24].

4.2. Main Traditional Plants Identified and Their Phyto-Therapeutic Properties

Phytotherapy is an integral part of the development of modern civilization, and continues to be important worldwide [25]. Chromolaena Odorata (vernacular name in Sango common in the Bangui region: APOLLO or BARABOKASSA) was the most widely used plant in our series (22%). It is a tropical and subtropical plant belonging to the Asteraceae family, native to the Americas and widely introduced into western and central sub-Saharan Africa, tropical Asia and parts of Australia. [25,26]. Chromolaena odorata is a fast-growing, climbing perennial herb that can reach several meters in height. Leaves are opposite, triangular to elliptical with serrated margins. Flowers are tubular, white to pale pink in color Figure 1.

Figure 1 : Chromolaena odorata plant, leaves, fruits and seeds

With regard to the phyto-therapeutic properties of Chromolaena odorata, its leaves contain flavonoids (quercetin, kaempferol), terpenes, terpenoids, saponins and tannins responsible for antimicrobial, anti-inflammatory, antioxidant, healing, anti-parasitic, antioxidant, anti-convulsant and haemostatic properties [27,28]. They are used in the treatment of skin infections, burns, wounds, malaria, liver pathology, dysentery, headaches and toothache [25, 27]. While the use of Chromolaena odorata seems relatively safe at low doses, biochemical and histological evidence of its toxicity is beginning to emerge at high dose levels [29]. Among the 11 children who benefited from Chromolaena odorata phytotherapy in our series, multivisceral failure was noted in four cases, notably hepatorenal failure in one child and neuro-hepatic failure in 3. They were exclusively hepatic in 3 children and neurological in one. This finding corroborates the results of in vitro studies on albino rats, which showed hepatic, renal and intestinal toxicity, especially at high doses of Chromolaena odorata extract and for prolonged periods [25,29]. In our series, the average duration of Chromolaena odorata treatment was 1.09 days. The neurological failure noted in our series in children having received Chromolaena odorata could have a bias linked to neuromalaria (9/11 cases) or sepsis (1/11). The second most frequently used plant in our series was ***Vernonia Amygdalina,*** with the Central African vermicular name "**HONCKA**" in 14% (n=7) of cases. This medicinal herb is commonly known as bitter leaf in tropical Africa **[30,31].** Belonging to the Asteraceae family of the ***Vernonia genus***, named after the English botanist Sir William Vernon, who first characterized it. It grows throughout sub-Saharan Africa and much of South America, preferring forest, woodland or meadow edges in moist, sunny environments [31,32].

Figure 2 : Plant, leaves and flowers of ***Vernonia amygdalina***

The bioactive compounds identified in phytochemical and pharmacological studies of Vernonia amygdalina belong mainly to the flavonoids, terpenoids, saponins and tannins [31,32]. Extracts and compounds isolated from Vernonia amygdalina have been reported to possess several pharmacological properties, including cytotoxic and thus anticancer, antioxidant, anti-inflammatory, antimicrobial and antidiabetic activities [31,32]. The plant has a broad spectrum of uses in phytotherapy in Africa in the treatment of conditions such as malaria, fever, diabetes, constipation, hypertension and intestinal parasitosis [30]. With regard to toxicity, our series noted multiple toxicity with Vernonia amygdalina in 3 children, associating hepatic, neurological and hematological failure. This toxicity was mono-organic in five children, notably haematological in 2 cases, hepatic in 2 and renal in one. In our series, the fatality rate was 14.28%. Toxicity studies have shown that Vernonia amygdalina, commonly found in Malaysia, can only be harmful if consumed in very large quantities, and the presence of flavonoids as powerful antioxidants and terpenoids may contribute to the absence of direct organ toxicity at common ingestion doses [30]. Solanum lycopersicum was the third plant used in our series (6 cases). Widely known as the tomato, it is a plant belonging to the Solanaceae family, genus Solanum, to which other plants such as potatoes and eggplants belong [33]. This herbaceous perennial plant produces a large number of berries with 2-12 locules containing numerous small seeds. Most tomato varieties are red when ripe. **Figure 3.**

Figure 3 : Solanum lycopersicum plant, leaves, flowers and berries

The plant is commonly used in parts of Africa for the treatment of anemia, notably as an oral and rectal infusion of the leaves ; the red, blood-like color of the berries has led to the plant being thought to regenerate blood tissue [33]. Most sporadic cases of solanine toxicity involve children who have ingested toxic wild plant parts [33]. Clinical features of solanine intoxication include gastrointestinal symptoms and neurological symptoms, including vomiting, headache and flushing [33]. In our series, no deaths were reported in the seven children treated with Solanum lycopersicum physiotherapy. Liver damage was noted in 4 patients, renal failure in 1 patient, and nerve damage with reduced GCS in 2 patients and serous miosis in 2 patients, the seizures recorded being traceable to cerebral malaria. The fourth plant commonly used by parents in phytotherapy was ***Ocimum gratissimum (Lamiaceae),*** with the Central African vermicular name "MATETE" in 6% (n=3) of cases. It is also known as African basil (from the ancient Greek Okimon, basil). It is an annual herbaceous plant belonging to the Lamiaceae family. It is native to sub-Saharan Africa and widespread throughout much of Southeast Asia and South America [34]. It is a highly branched plant with a woody stem at the base, 1 to 3 meters high, with long-stalked opposite leaves and an elliptical to oval blade with a serrated margin and acute apex. The inflorescence is a whorl arranged in a single or branched terminal branch. The fruit is divided into 4 chambers, with one seed per chamber, **Figure 4 :**

Figure 4 : Detail of ***Ocimum gratissimum*** plant, leaves, inflorescence and flower.

In addition to its use as a food flavoring, Ocimum gratissimum is used in traditional medicine to treat a variety of ailments [34]. Leaves prepared by soaking, decoction or infusion in water or alcohol are used to treat inflammatory disorders such as rheumatism, arthritis and stomatitis [34]. In our series, the routes of administration were mixed (per os and rectal) in all children. Photochemical studies showed the presence of several classes of metabolites, including flavonoids, terpenes, fatty acids, saponins, tannins, alkaloids and oligosaccharides [35,36]. Recent work has identified and demonstrated that pomolic acid and tormic acid are the main anti-inflammatory constituents of Ocimum gratissimum extract [34]. Rare animal toxicity studies warn of the possibility of secondary effects on the liver and kidneys [35]. In our study, multiple organ failure was observed in all children. One child suffered from hepatic and neurological failure, while the other two suffered from hepatic and renal failure. One in three children treated with Ocimum gratissimum phytotherapy died. The fifth most commonly used plant in our study was ***Jatropha curcas (Euphorbiaceae),*** whose Central African vermicular name is "KADA MONO" in 4% (n=2) of cases. Jatropha curcas is a large, perennial, drought-tolerant shrub up to 5 meters tall. It belongs to the Euphorbiaceae family and is native to Central America, from where it has spread to several other tropical and subtropical regions. Jatropha curcas is a multi-purpose plant, important both medicinally and biotechnologically [37]. The plant is also known in some countries as the Barbados hazelnut, due to the shape of the fruit, which can be confused with the normal edible hazelnut. **Figure 5.**

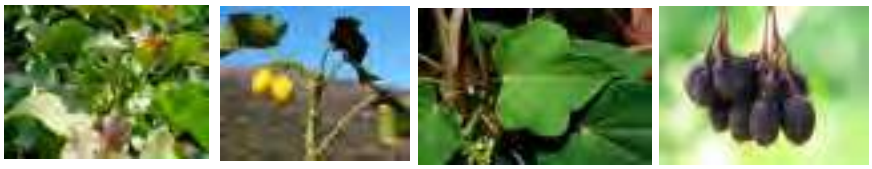

Figure 5 : Jatropha curcas plant, leaves, fruits and seeds.

In phytotherapy, this plant has been applied since ancient times for the treatment of various ailments ranging from simple fevers to infectious diseases, including sexually transmitted diseases, in many African and Asian countries [37,38]. Photochemical studies on Jatropha curcas have isolated numerous compounds, including diterpenes, sterols, flavonoids, alkaloids and peptides [37,38]. Many of these compounds have shown diverse biological activities ranging from antimicrobial to anti-tumor cytotoxic actions. Among these compounds, an important role is played by curcosone isolated from stems, which has shown anti-tumoral activities and also suppression of metastatic processes [37,38]. The route of administration of the plant was mixed oral and rectal. Case reports of children presenting intestinal symptoms (abdominal pain, nausea and vomiting) following ingestion of Jatropha curcas seeds are reported in the literature [39]. In our series, both cases had hepatic failure and no deaths were observed. ***Cassia siamea o Senna siamea (Fabaceae),*** with the Central African vermicular name "CASSIA", was the sixth plant frequently used 2% (n=1) of the time. It belongs to the Fabaceae family and is native to South and Southeast Asia. The name Senna is derived from the Arabic word "sana", which designates certain medicinal properties, while "siamea" is an epitope alluding to the ancient name of Thailand, the plant's country of origin [40]. It is an evergreen tree of medium height, reaching 18 meters, with alternate, pinnate, reddish-green leaves, yellow flowers and pods containing edible seeds. Figure 6.

Figure 6 : Senna Siamea Plant, Leaves, Flowers And Pods

Its bark is traditionally used against fever and malaria, the roots are used as an antipyretic and the leaves for constipation, hypertension, insomnia and asthma [40,41]. Its analgesic and anti-inflammatory properties are attributed to four major families of compounds present in the plant : triterpenes (lupeol, oleanolic acid, ursolic acid (friedeline, betulin), flavonoids (apigenin, kaempferol, luteolin), anthraquinones (emodin), phytosterols (stigmasterol, beta-sitosterol) [40]. Strong antimalarial activity has also been demonstrated in vitro [42]. The various side effects associated with a possible toxicity profile appear to be reduced [41]. In our series, no side effects were noted. Finally, Dioscorea bulbifera (Dioscoraceae), with the Central African vermicular name "KERERE", was also used in a child. Commonly known as "air potato", it belongs to the Dioscoreaceaes family, a name

dedicated to Padanio Dioscorides Anazardeo, a Greek physician, botanist and pharmacist who lived in the 1st century AD [43]. Dioscorea bulbifera is a perennial vine that can reach over 60 feet in length when climbing trees; it has broad leaves and forms bulbils when the leaves emerge from the stem and tubers underground, some of which are edible. Figure 7.

Figure 7 : Dioscorea bulbifera plant, leaves and bulblets

Dioscorea bulbifera bulblets are traditionally used in Thai folk medicine as a diuretic and anthelmintic, in longevity preparations and for the treatment of wounds and inflammation [43]. In traditional Indian and Chinese medicine, the plant is also commonly used to treat sore throats, gastric cancer, rectal carcinoma and goiter [43]. In Cameroon and Madagascar, crushed bulbs are applied to abscesses, boils and wound infections [43]. Due to its many clinical uses, Dioscorea bulbifera has attracted increasing attention in recent decades ; numerous phytochemical and pharmacological studies have been carried out, leading to the isolation of numerous compounds from the plant, including steroids (diosgenin, beta-sitosterol, stigmasterol, etc.), terpenoids (disobulbin B, epidisiobulbin E acetate) and flavonoids (kempferol and quercetin) [43,44]. The flavonoids contained in the plant are the components with the greatest antioxidant, anti-inflammatory, antibacterial and even antioxidant activity [44]. Toxicity is also common. Clinically, hepatotoxicity is the most typical form of this plant's toxicity, manifesting itself mainly as nausea, vomiting, liver dysfunction or jaundice [44]. The terpenoids contained in Dioscorea bulbifera, in particular Diosbulin B, are thought to be the main cause of liver damage [44]. The mechanism of hepatotoxicity is linked to its inhibition of antioxidant enzymes in liver mitochondria, and to the activity of metabolic enzymes such as glutathione transferase, glutathione peroxidase, superoxide dismutase and glucose-6-phosphate dehydrogenase, which play a key role in the metabolism of components of many herbs [45]. According to clinical pathology studies, kidney damage caused by ***Dioscorea bulbifera*** takes longer to manifest itself, and tubular lesions are more frequent. The plant's toxic effects on the liver and kidneys, mainly due to diosbulbin B and epidioxibulbin E acetate, limit its therapeutic potential. Numerous cases of liver damage, often associated with mortality, have also been described, the latter being linked to excessive or prolonged exposure to diosbulbin [44,45]. In our series, the child who had received phytotherapy with DIOSCOREA BULBIFERA (Kerere) had liver failure and was cured.

5. Conclusion

The present study, which represents the first on the practice of herbal medicine in paediatric settings in the Central African Republic, has enabled us to note that it is a common practice among people with low levels of education and low monthly incomes. It is also used by people living in rural areas. Phytotherapy is not without risk, as this study shows, and like conventional medicine, it must obey strict rules of cultivation, control and dispensing.

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Factors associated with hospitalization in a pediatric population of rural Tanzania: findings from a retrospective cohort study

PAPER

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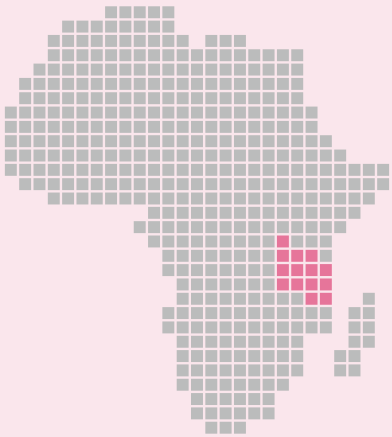

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Factors associated with hospitalization in a pediatric population of rural Tanzania: findings from a retrospective cohort study

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Abstract

Background Despite pediatric acute illnesses being leading causes of death and disability among children, acute and critical care services are not universally available in low-middle income countries, such as Tanzania, even if in this country significant progress has been made in child survival, over the last 20 years. In these countries, the hospital emergency departments may represent the only or the main point of access to health-care services. Thus, the hospitalization rates may reflect both the health system organization and the patients' health status. The purpose of the study is to describe the characteristics of clinical presentations to a pediatric Outpatient Department (OPD) in Tanzania and to identify the predictive factors for hospitalization.

Methods Retrospective cohort study based on 4,324 accesses in the OPD at Tosamaganga Voluntary Agency Hospital (Tanzania). Data were collected for all 2,810 children (aged 0–13) who accessed the OPD services, within the period 1 January – 30 September 2022. The association between the hospitalization (main outcome) and potential confounding covariates (demographic, socio-contextual and clinical factors) was evaluated using univariate and multivariate logistic regression models.

Results Five hundred three (11.6%) of OPD accesses were hospitalized and 17 (0.4%) died during hospitalization. A higher ($p < 0.001$) risk of hospitalization was observed for children without health insurance (OR = 3.26), coming from more distant districts (OR = 2.83), not visited by a pediatric trained staff (OR = 3.58), and who accessed for the following conditions: burn/wound (OR = 70.63), cardiovascular (OR = 27.36), constitutional/malnutrition (OR = 62.71), fever (OR = 9.79), gastrointestinal (OR = 8.01), respiratory (OR = 12.86), ingestion/inhalation (OR = 17.00), injury (OR = 6.84).

Conclusions The higher risk of hospitalization for children without health insurance, and living far from the district capital underline the necessity to promote the implementation of primary care, particularly in small villages, and the establishment of an efficient emergency call and transport system. The observation of lower hospitalization risk for children attended by a pediatric trained staff confirm the necessity of preventing admissions for conditions that could be managed in other health settings, if timely evaluated.

Keywords Pediatrics, Emergency services, Hospitalization, Predictive factors, Low-income country, Tanzania

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Background

Annually, more than 80 per cent of the 6.4 million deaths in children under 14 years of age occur in low- and middle-income countries (LMICs) [1]. These deaths are predominantly due to acute illnesses (such as sepsis, pneumonia, infections, trauma, etc.) that could be successfully managed with basic intensive care interventions, including fluid resuscitation, ventilatory support and blood product transfusion [2, 3]. Although pediatric acute illnesses are globally the leading causes of death and disability for children outside the neonatal period, acute and critical care services remain inconsistently available in resource-limited settings [2–6]. Therefore, it is essential to gather specific data on the etiology of acute critical illness to facilitate the development of evidence-based intervention plans and proper allocation of the available yet limited resources in LMICs.

Tanzania is a LMIC in sub-Saharan Africa [7]. Over the last 20 years, significant progress has been made in child survival, bringing Tanzania close to the target set by the Millennium Development Goals (MDGs) of reducing child mortality by two-thirds. Specifically, from 1999 to 2022, neonatal and under-five mortality rates decreased from 47 deaths to 20 deaths per 1,000 live births and from 147 to 49 deaths per 1,000 live births, respectively [8, 9].

To improve the access to basic health services, Tanzania implemented a primary health service development program (2007–2017) by renovating and building at least one dispensary per village and one health center per municipal unit throughout the country [10].

Despite the presence of exemption and waiver policies witch protect poor and vulnerable groups (e.g. pregnant women, children and the elderly), the implementation of these policies remains ineffective in many areas of Tanzania [11, 12].

Tanzania is divided in 21 regions, housing 369 hospitals [13]. The Iringa District Council (Iringa DC) is a district in the Iringa Region in southern Tanzania, where The Tosamaganga Voluntary Agency Hospital (Tosamaganga Hospital) operates since '80s.

In Iringa region, like other Tanzanian regions, the hospital emergency departments often remain the only or the main points of access to health-care services. The hospitalization rates after an access to Emergency department may reflect the lack of preventive and primary care for conditions that could be managed and treated in a setting other than a hospital, in particular for pediatric patients [14].

Therefore, it may be important to assess for which conditions a pediatric population in a developing country uses hospital's emergency services and may need hospitalization, to support health policy choices to promote interventions for the purpose of improving outcomes for children with acute and critical illnesses.

This study aims to describe the clinical profile and outcomes of pediatric presentations to Tosamaganga Hospital OPD departments over a 9-month period, and to identify predictors of hospitalization in a pediatric OPD care services in a LMIC.

Methods

Study design and population

We retrospectively collected data on children population (aged 0–13 years old) accessing to the OPD (pediatric and general) at Tosamaganga Hospital, over a 9-month period, within the period 1 January – 30 September 2022. The upper age limit for the inclusion of patients was 13 years old, because hospital policy dictates that from the age of 14 years old, patients have been seen at general Outpatient Department (OPD) and admitted to the adult wards. Data were collected for all patients who accessed the OPD services, both general (with non-pediatric trained staff) and pediatric (with pediatric trained staff).

We have obtained from the institution of Tosamaganga Hospital the necessary permissions to carry out the study. The Health Management Team of Tosamaganga Voluntary Agency Hospital formally approved the ethical aspects of the study.

Setting

The Tosamaganga Voluntary Agency Hospital (Tosamaganga Hospital) owned by the Diocese of Iringa is located about 16 km from the capital city, Iringa. The Region spans an area of 35,503 km2 and it is divided into 5 districts, namely Iringa Urban, Iringa DC, Kilolo, Mufindi District Council and Mafinga. The population of the region exceeds 1,000,000.

The hospital has a capacity of 192 beds and in 2022 it registered about 33,000 outpatient visits, 9,500 admissions and 3,500 deliveries. In addition to inpatient activities, the hospital provides outpatient services (known as Outpatient Department, OPD), which operates 24/7 and caters to patients from outside the hospital. An OPD dedicated exclusively to pediatric patients (pediatric OPD) is present since 2019, where patients are examined by a clinical officer trained in the management of pediatric acute conditions. The pediatric OPD operates from 8 a.m. to 4 p.m. approximately, Monday to Friday. Outside these hours (nights and holidays), patients are examined in the general OPD.

Data collected

The data examined in this study were extrapolated from the Health Information Management System (HMIS) currently in use at Tosamaganga Hospital. The following data were collected from the HMIS: gender, age, area of

residence, whether insured or uninsured, visiting clinic, access symptoms, outcome (discharge, admission, transfer, or death).

The variable of the area of residence was classified based on the distance (in kilometers) to travel from the village of residence to the hospital. For statistical analysis, the accesses were divided according to the districts of greatest influx: Iringa DC, Iringa Urban, and the other areas.

Information on access symptomatology was classified based on the diagnosis reported by the health professional who visited the child, dividing them into two main medical categories:

1) Non-traumatic disorders: infectious diseases such as gastrointestinal infections (viral, bacterial or parasitic), lower respiratory tract diseases (pneumonia, bronchitis, bronchiolitis), skin infections, sensory organ-related infections (tonsillitis, sinusitis, otitis and conjunctivitis), urinary tract infections, malaria, sepsis, meningitis and encephalitis. Non-infectious diseases include malnutrition, sickle cell anaemia, epilepsy, febrile seizures, heart failure due to congenital heart disease or rheumatic disease, umbilical hernia, appendicitis, and neonatal jaundice.
2) Injury-related presentations, classified as an accident, trauma, injury, violence, ingestion and inhalation of foreign bodies, or burns.

Additionally, information about transfer to another facility and death was also collected.

The primary outcome studied was hospital admission to Tosamaganga Children Ward.

Statistical analysis

All the analyses are referred to the accesses to the OPD service as statistical analysis unit.

In particular, the descriptive analysis presents absolute and relative frequencies for categorical variables, while the mean, standard deviation, median, interquartile range of the distribution are shown for continuous variables.

Differences in the proportions of the distribution of the qualitative variables, in the mean and median values of the distribution of the quantitative variables, between OPD services accesses that did or did not result in a hospital admission, death, or transfer, were assessed.

The chi-square test was used for qualitative variables, while for quantitative variables the non-parametric Wilcoxon-Mann-Whitney test was performed, as the assumption of normality distribution was not formally verified.

The *p*-values presented in the analyses are derived from two-tailed tests (95% confidence interval).

The association between the outcome (hospitalization) and potential confounding covariates (demographic, socio-contextual and clinical factors) was evaluated using univariate and multivariate logistic regression models.

As each subject can potentially experience multiple access to OPD service, logistic regression models with robust standard errors were performed. In this way, we took into account that the individual observations were not independent from each other, allowing for intragroup correlation and accounting for heteroscedasticity.

Multivariate model was carried out including age in months and sex as a priori risk factors, and all the variables that at univariate analysis were associated with the outcome with a p-value < 0.10.

Statistical data analyses were performed using Stata 16 software [15].

Results

Among the 9-month study period, a total of 2,810 children were visited, accounting for 4,324 accesses in the OPD. Of these, 2,331 (53.9%) were males and 1,993 were females (46.1%), with a male-to-female ratio of 1.17 to 1. The mean age at access was 43.2 months (SD 41.6), with a median age of 27.2 months (IQR 9.6–68.6).

Among children at visit, 185 (4.3%) were in neonatal age (0–28 days), 1,094 (25.3%) in post-neonatal age (29–365 days), 1,831 (42.4%) in pre-scholar age (1–4 years) and 1,214 (28.1%) in scholar age (6–13 years).

Most of accesses were referred to children who came from the districts of Iringa DC (68.1%) and Iringa Urban (25.4%), 6.5% from other districts.

The mean distance to the hospital was 33.1 km (SD 39.7), with a median of 20 km (IQR 12–36). The average travel time to the hospital was 43.4 min (SD 42.7), with a median of 31 min (IQR 19–53).

Out of the total number of accesses, 70.8% of patients did not have health insurance, whereas 29.2% had health insurance policies covering the expenses of services provided.

Overall, 87.9% of accesses to OPD were performed from Monday to Friday and 12.1% on weekend. Pediatric-trained personnel attended to 61.8% of the accesses, while the remaining 38.2% were attended to by personnel without pediatric training.

Data on the presenting symptoms of the access were available in 93.0% of the cases, while for 7.0% of accesses, there was no information about the admission symptomatology.

Medical symptomatology accounted for the reason for presentation in 90.5% of cases, while 9.5% were due to injury. The most common reasons for presentation were sensory organ-related disorders (symptomatology involving nose, ear, eye, and throat for 19.2%), followed by genitourinary symptoms (14.1%), post-therapy follow-up,

post-hospitalization or anthropometric and neurodevelopmental assessment (12.3%), and gastrointestinal disorders (10.9%).

For inpatients, on the other hand, the most common admission diagnoses were related to malnutrition (20.1%), respiratory disorders (12.2%), osteo-articular injuries (11.2%) and skin disorders and infections (9.0%).

Among all the OPD accesses,, 503 (11.6%) were admitted at Tosamaganga Hospital, 17 (0.4%) were transferred to other facilities to allow further investigation and treatment, and 17 (0.4%) died during hospitalization. Among the 503 hospitalized patients, 14 (2,8%) were referred to higher centers or developed a need for intensive care. The causes of admission to OPD for the 17 deaths, were the following: 8 (47.1%) respiratory disease, 4 (23.5%) malnutrition, 2 (11.8%) genitourinary infection, 1 (5.9%) heart failure, 1 (5.9%) skin infection, 1 (5.9%) injury.

The children admitted to the hospital were in average younger ($p<0.001$) than those not admitted: 44.5 (SD 42.1) vs. 34.7 (SD 36.8) months old (median 30 [IQR 10–70] vs. 19 [IQR 9–51]) (Fig. 1).

Table 1 summarizes the demographic, social, and clinical characteristics of subjects admitted to OPD by hospitalization.

A higher percentage of hospitalization was observed among males than among females (12.4% vs. 10.7%, $p=0.07$).

A higher percentage of hospitalizations was observed among those who did not have insurance than among those who did (14.9% vs. 3.8%, $p<0.001$).

A higher percentage of inpatients was observed among those who came from the districts furthest from the hospital, compared to those who came from the rural Iringa district and the urban Iringa district, 23.5%, 12.0%, 7.6% ($p<0.001$), respectively.

An association between the distance of residence from the hospital and hospitalization was confirmed (Fig. 2) by the finding that the distance in kilometers was higher ($p<0.001$) among hospitalized than not hospitalized (mean 46.9 [SD 55.2] vs. 31.3 [36.9] km (median 36 [IQR 12-61.5] vs. 19 [IQR 12–36)).

A lower percentage of inpatients was observed among those who were visited in the outpatient clinic in the presence of pediatric-trained health personnel, compared to those who were visited by non-pediatric-trained personnel (6.3% vs. 20.2%, $p<0.001$).

In relation to symptoms at the time of admission to OPD, a higher percentage ($p<0.001$) of inpatients was observed among those who had or did not have one of the following symptoms: burn/wound (72.4% vs. 11.2%), cardiovascular (37.5% vs. 11.5), constitutional/malnutrition (65.0% vs. 9.3%), fever (22.4% vs. 11.0%), gastrointestinal (18.5% vs. 10.8%), respiratory (30.4% vs. 10.5%), ingestion/inhalation (41.7% vs. 11.6), injury (19.4% vs. 11.1%). On the contrary, we observed a lower percentage ($p<0.001$) of inpatients if the following symptoms at

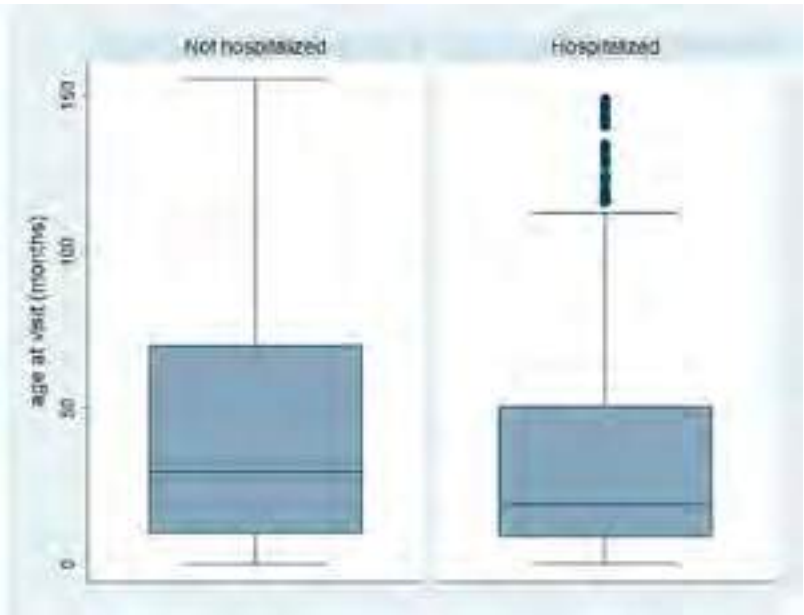

Fig. 1 Age at visit of subjects admitted to OPD, by hospitalization

Table 1 Demographic, social, and clinical characteristics of subjects admitted to OPD, by hospitalization

		Hospitalization						
		Not		Yes		Total		
		N.	%	N.	%	N.	%	*P*-value
Sex	Males	2,041	87.6	290	12.4	2,331	100	0.07
	Females	1,780	89.3	213	10.7	1,993	100	
Insurance	Not	2,605	85.1	455	14.9	3,060	100	< 0.001
	Yes	1,216	96.2	48	3.8	1,264	100	
District of residence	Iringa urban	1,015	92.4	84	7.6	1,099	100	< 0.001
	Iringa DC	2,591	88.0	353	12.0	2,944	100	
	Other	215	76.5	66	23.5	281	100	
Presence of paediatric trained staff	Not	1,319	79.8	334	20.2	1,653	100	< 0.001
	Yes	2,502	93.7	169	6.3	2,671	100	
Burn / Wound	Not	3,813	88.8	482	11.2	4,295	100	< 0.001
	Yes	8	27.6	21	72.4	29	100	
Cardiovascular	Not	3,806	88.5	494	11.5	4,300	100	< 0.001
	Yes	15	62.5	9	37.5	24	100	
Constitutional / malnutrition	Not	3,757	90.7	384	9.3	4,141	100	< 0.001
	Yes	64	35.0	119	65.0	183	100	
Fever	Not	3,644	89.0	452	11.0	4,096	100	< 0.001
	Yes	177	77.6	51	22.4	228	100	
Gastrointestinal	Not	3,437	89.2	416	10.8	3,853	100	< 0.001
	Yes	384	81.5	87	18.5	471	100	
Respiratory	Not	3,647	89.5	427	10.5	4,074	100	< 0.001
	Yes	174	69.6	76	30.4	250	100	
Dermatological	Not	3,471	87.7	488	12.3	3,959	100	< 0.001
	Yes	350	95.9	15	4.1	365	100	
Genitourinary	Not	3,228	86.9	485	13.1	3,713	100	< 0.001
	Yes	593	97.0	18	3.0	611	100	
Neurological	Not	3725	88.4	488	11.6	4,213	100	0.53
	Yes	96	86.5	15	13.5	111	100	
Eye, ear, nose, throat medical complaints	Not	3,008	86.1	485	13.9	3,493	100	< 0.001
	Yes	813	97.8	18	2.2	831	100	
Ingestion / Inhalation	Not	3,814	88.4	498	11.6	4,312	100	0.001
	Yes	7	58.3	5	41.7	12	100	
Injury	Not	3,593	88.9	448	11.1	4,041	100	< 0.001
	Yes	228	80.6	55	19.4	283	100	
Wound / Violence	Not	3,813	88.3	503	11.7	4,316	100	0.30
	Yes	8	100.0	0	0.00	8	100	
Month of the admission to OPD	January	251	86.9	38	13.1	289	100	< 0.001
	February	337	91.3	32	8.7	369	100	
	March	507	85.9	83	14.1	590	100	
	April	499	83.9	96	16.1	595	100	
	May	461	88.7	59	11.3	520	100	
	June	417	89.5	49	10.5	466	100	
	July	395	92.3	33	7.7	428	100	
	August	488	90.9	49	9.1	537	100	
	September	463	87.9	64	12.1	527	100	

access to OPD were present and not absent: dermatological (4.1% vs. 12.3%), genitourinary (3.0% vs. 13.1%), eye, ear, nose, throat medical complaints (2.2% vs. 13.9%).

Table 2 summarizes the results of univariate logistic regression models performed to evaluate the association between demographic, social, and clinical characteristics of subjects admitted to OPD with the risk of hospitalization. A higher risk of hospitalization for the admissions to OPD was observed for the subjects without insurance (OR 4.42), coming from more distant districts (OR

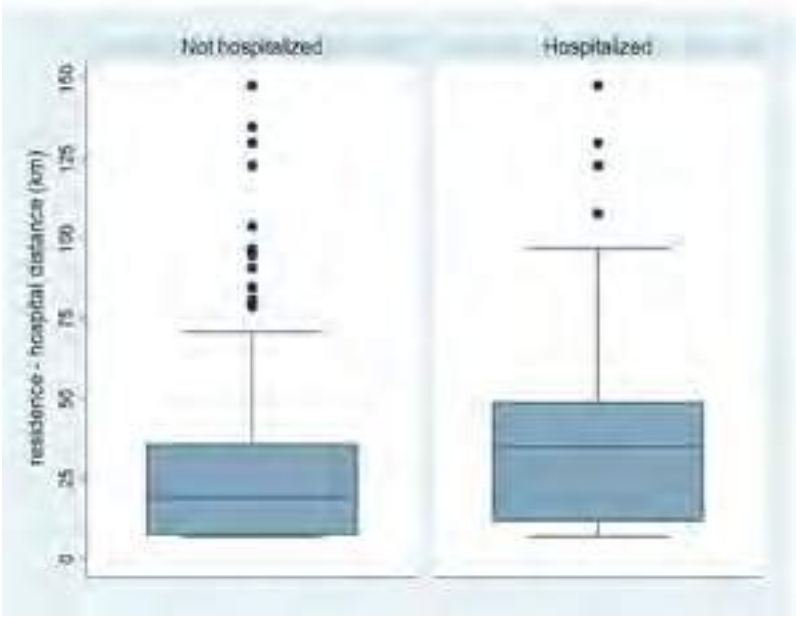

Fig. 2 Distance from residence to hospital of subjects admitted to OPD, by hospitalization

3.71) and from Iringa rural (OR 1.65) compared to Iringa urban, coming from a village with more distance from residence to hospital (for each additional km traveled OR 1.01), for those visited by a not pediatric trained staff (OR 3.75) and who accessed to OPD for the following symptoms: burn/wound (OR 20.77), cardiovascular (OR 4.62), constitutional/malnutrition (OR 18.19), fever (OR 2.32), gastrointestinal (OR 1.87), respiratory (OR 3.73), ingestion/inhalation (OR 5.47), injury (OR 1.93). Furthermore, males had higher risk ($p=0.07$) compared to women, while a lower risk of hospitalization was found for age (in months) increase (OR 0.994), for those with genitourinary symptoms (OR 0.20) and for children who had access to OPD in July (OR 0.55, $p=0.02$), February (OR 0.63, $p=0.06$), and August (OR 0.66, $p=0.08$) compared to January, which was considered the reference month.

Multivariate logistic regression analysis (Fig. 3) confirm the results of univariate logistic regression analysis, showing a higher ($p<0.001$) risk of hospitalization for the admissions to OPD without insurance (OR 3.26, 95%CI 2.18–4.89), coming from more distant districts (OR 2.83, 95%CI 1.76–4.53), for distance (in kilometers) from residence to hospital increase (OR 1.003, 95%CI 1.001–1.006), for those visited by a not pediatric trained staff (OR 3.58, 95%CI 2.82–4.55), and who accessed to OPD for the following symptoms: burn/wound (OR 70.63, 95%CI 30.41-164.06), cardiovascular (OR 27.36 95%CI 7.68–97.44), constitutional/malnutrition (OR 62.71, 95%CI 41.04–95.82), fever (OR 9.79, 95%CI 5.86–13.18), gastrointestinal (OR 8.01, 95%CI 5.69–11.28), respiratory (OR 12.86, 95%CI 8.80-18.79), ingestion/inhalation (OR 17.00, 95% CI 4.53–63.77), injury (OR 6.84, 95%CI 4.54–10.32). A lower risk of hospitalization was found for age (in months) increase (OR 0.993, 95%CI 0.989–0.996).

Discussion

In this study, we present the first dataset on pediatric emergency visits to an OPD of a district-level hospital in rural Tanzania.

Overall, we observed a hospitalization rate of approximately 12% among the OPD, which was lower than the rates previously reported in other studies [16–19]. Instead, the mortality rate (0.4%) was higher than reported in high-income countries (1.5/100,000 visits) [20], but it was comparable to the rate found by Enyuma et al. [16], where in their study (0.5%), and even lower compared to other sub-Saharan countries like Nigeria where the rates was ranged 2-17.5% [21–25] or Cameroon where Chiabi et al. found a mortality rate of 1,6−1,9% [19] and Chelo et al. found a rate of 5,76% [26]. Our findings revealed a higher risk of hospitalization for the admissions to OPD among patients without insurance, those from more distant districts, those attended by a non-paediatric trained staff and those accessing the OPD for burn/wound, cardiovascular, constitutional/malnutrition, fever, gastrointestinal, respiratory,

Table 2 Factors associated to hospitalization. Results of univariate logistic regression models

VARIABLES		Odds Ratio	95CI%	*P*
age at visit	each 1 month more	0.994	0.991–0.996	< 0.001
sex	females	1.00	-	-
	males	1.19	0.97–1.45	0.094
insurance	yes	1.00	-	-
	not	4.42	3.20–6.12	< 0.001
district of residence	Iringa urban	1.00	-	-
	Iringa DC	1.65	1.28–2.12	< 0.001
	other districts	3.71	2.57–5.36	< 0.001
distance from residence to hospital	each 1 km more	1.007	1.005–1.009	< 0.001
presence of paediatric trained staff	yes	1.00	-	-
	not	3.75	3.07–4.58	< 0.001
burn / wound	not	1.00	-	-
	yes	20.77	7.64–56.45	< 0.001
cardiovascular	not	1.00	-	-
	yes	4.62	1.96–10.93	< 0.001
constitutional / malnutrition	not	1.00	-	-
	yes	18.19	13.14–25.18	< 0.001
fever	not	1.00	-	-
	yes	2.32	1.67–3.23	< 0.001
gastrointestinal	not	1.00	-	-
	yes	1.87	1.44–2.43	< 0.001
respiratory	not	1.00	-	-
	yes	3.73	2.78–5.01	< 0.001
ingestion / inhalation	not	1.00	-	-
	yes	5.47	1.73–17.31	0.004
injury	not	1.00	-	-
	yes	1.93	1.41–2.66	< 0.001
month of the admission to OPD	January	1.00	-	-
	February	0.63	0.38–1.02	0.062
	March	1.08	0.71–1.64	0.713
	April	1.27	0.84–1.93	0.262
	May	0.85	0.54–1.32	0.457
	June	0.78	0.49–1.24	0.285
	July	0.55	0.34–0.91	0.019
	August	0.66	0.42–1.05	0.079
	September	0.91	0.59–1.42	0.687

ingestion/inhalation, injury. Conversely, we observed a lower risk of hospitalization when the age of children increased.

The findings suggest that living in suburban or otherwise remote areas, far from health centers, is a risk factor for hospitalization. Juran et al. found that 92.5% of the sub-Saharan African population lived within 2 h of a major hospital for surgical procedures [27]. The increased risk is likely due to the greater distance to the hospital, which may lead to a delayed access to OPD for the children. Manongi and colleagues in Tanzania found that hospitalised children who came from areas less than 3 h away from the hospital had a mortality rate of 3.4% compared to 8.0% for children who came from areas more than 3 h away [28]. These delays can be attributed to socioeconomic factors related to high costs of transportation, inadequate transportation infrastructures and vehicles, which in turn may result in the exacerbation of the disease not treated in a timely manner. This observation may also reflect the large number of challenges in traveling to the hospital that children face even when they are seriously ill [29]. A WHO report on quality of care recommends timely referral for every child with conditions that cannot be managed effectively at first-level facilities [30].

Previous studies highlighted that the reasons for late presentations at pediatric emergency units includes poor identification of early sign of disease severity by care givers of low level health facilities, high costs of hospital treatments as patient pay out of pocket, poor health seeking behaviors and beliefs in remedies with unproven efficacy [31, 32].

Although challenging and costly, the establishment of an efficient emergency call and ambulance transport service would be crucial to ensure that critically ill children from both suburban and urban areas have timely access to OPD. Safe transport is required by many sick children seen in primary care facilities to referral hospitals. However, implementing such a service may not always be feasible, and this need to be balanced against the potential risk of transport, distance to referral hospital, costs and the needs of other patients. In Tanzania, transportation from primary care health posts to hospitals is even more difficult, and other modes of emergency transport are employed; these included bicycles with trailers, tricycles with platforms, motorboats and ox carts [33].

Another relevant observation of the present study is that owning health insurance is a protective factor for hospitalization risk. The existing health insurance schemes in Tanzania only cover medical costs at healthcare facilities, but do not compensate patients for travel and time costs incurred in accessing care, resulting in financial burden on households and delayed access to care [34]. The health financing system in Tanzania is highly fragmented involving different resource providers including general taxation (34%), private donors, non-governmental organizations (NGOs), foreign states etc. (36%), direct payments (22%) and health insurance contributions (8%) [35]. According to a 2018 analysis of the health sector only 33% of Tanzanians are covered by health insurance, leaving the remaining two-thirds 2/3 of population exposed to financial arising from direct health care payments [35]. This finding could be partly correlated with the above, assuming that the family with health insurance is in better economic condition and

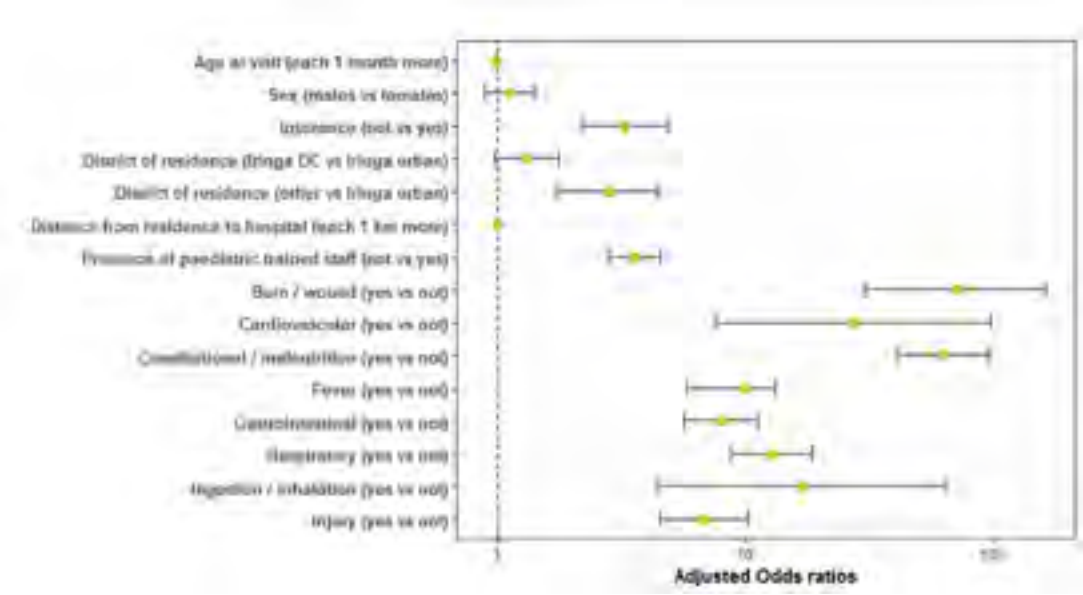

Fig. 3 Demographic, socio-contextual and clinical factors associated with hospitalization. Multivariate logistic regression model

thus can more easily afford transportation to the hospital. In addition, by not having to pay for the health service, the parent would tend to bring the child in early for a medical examination as shown by Huang at al. in Taiwan [36], with opportunities then for health personnel to intervene early on the ongoing condition. Moreover, we can hypothesize that the higher level of education of families with health insurance may also play a role, being more aware of the warning signs/symptoms of the child's pathology. As demonstrated by Agelebe at al [37]., children who were socially disadvantaged presented significantly later to the hospital than their non-socially disadvantaged counterparts following onset of illnesses. Low utilization of healthcare services due to delay in making decision and delay in assessing medical services is because of the ripple effects of unemployment and poverty [37].

Our study showed that children were more likely to be hospitalized if they had cardiovascular, constitutional, neurological, gastrointestinal, respiratory symptoms, or had burns. In the literature other studies in LMICs report found similar rates. Specifically, in LMICs the prevalence of preventable communicable diseases (such as malaria, pneumonia and diarrheal diseases) and acute and chronic malnutrition is high in sub-Saharan African Countries [19, 21, 26, 38–41].

In addition to the high burden of pediatric infectious disease, there is at present an increasing incidence of non-communicable and hereditary diseases and their complications, that require special care by specialized personnel. Such symptomatology in the pediatric patient takes on different peculiarities and complexity than in the adult one, thus emphasizing that specific expertise is needed [16, 23, 42–44].

Our study supports this hypothesis, as it indicates that visiting an outpatient clinic not specifically dedicated to pediatric care is predictive of an increased risk of hospitalization. Indeed, our findings may suggest that better management of the pediatric patient even at the OPD level could reduce avoidable hospitalizations, which can cause stress and economic burden to families, as well as increase the risk of hospital-acquired infections. Several studies have shown that children that arrived at emergency departments during off hours tend to experience longer stays [21, 45–46]. This is attributed to the unavailability of highly skilled personnel and certain investigations during such periods of the day [31, 32]. Also, healthcare personnel trained in pediatric emergency medicine principles are shown to reduce childhood mortality in LMICs likely through dissemination of education, practice patterns, and advocacy measures [47].

Training health personnel in early identification of critical illness is a crucial step in improving disease prognosis, as shown by several studies [48, 49]. Priority should be given to training in the early recognition and management of pediatric conditions that most commonly lead to death in the local area. This issue holds particular significance in LMICs [50], such as Tanzania, where, like

many sub-Saharan Africa countries, there is a shortage of trained healthcare professionals with an estimated 3 doctors and 39 nurses per 100 000 inhabitants in the country [51, 52].

Early triage assessment and prompt identification of signs of critical illness, and rapid initiation of appropriate treatment should be top priorities for all hospitals providing emergency care for children [53]. However, according to the study of Ardsby et al. [54], only 9.1% of the hospitals reported specific triage protocols for children < 5 years of age. Inadequate triage is a widespread problem in LMICs and represents an important challenge in addressing emergency conditions in hospitals [55, 56].

Finally, our study revealed that the children admitted to hospital were in average younger than not admitted (about 10 months older), a result in agreement with what other studies have observed [18]. However, in our study are included children who came for follow up for post-therapy, post hospitalization or anthropometric and neurodevelopmental assessment (12.3% of the total population examined).

Strengths

This study provides information about pediatric emergency visits to an OPD of a district-level hospital in Tanzania on a large sample of children, a still under-researched field of research that needs as much work as possible for reduce preventable deaths.

Moreover, the availability of data collected through dedicated software is another strength of our study. Optimization of data recording is an important area on which to focus resources to obtain increasingly accurate data. The data collection was done through the new HMIS introduced in early 2022 at Tosamaganga Hospital. The availability of this software allowed to collect good quality information in terms of accuracy, reliability, consistency. In fact, the current data recording system that is used in the hospital allows for good data recording with minimal gaps that are likely to be reduced over time. The HMIS proved to be effective and easily usable in the data collection process, confirming that having better data quality simplifies the monitoring of health care delivery and evaluation of the impact of health interventions [57].

Limitations

This is a single-center study of a district-level hospital; it may not represent the rest of Tanzania or other LMICs, but it is reasonable to assume that our data provide some useful information about pediatric emergency care at the local and national levels that can help optimize the distribution and use of resources, as well as plan more appropriate feasible and effective interventions to improve pediatric emergency care within an integrated system of care.

For some variables we could not collect information for all subjects because they had not been registered in the electronic database, which became operational just in January 2022, when the study started. Furthermore, we could not collect information on the last three months of 2022, a limitation that did not allow to assess whether there are seasonal differences on the outcome. However, we performed analyses by month of admission to OPD.

Moreover, data on comorbidities different from those collected are not reported in the OPD database, thus in the inpatient database they are mentioned inconsistently and, therefore, could not be analyzed.

This would be extremely valuable information to include in multivariate analysis, as underlying conditions such as malnutrition, HIV, and other infectious or chronic diseases have been shown to be associated with need for hospitalization and mortality [58, 59]. Systematic collection of major comorbidities should be pursued to be able to properly interpret the data to improve care and optimize organization and resource utilization.

Finally, it was not possible to define the aetiological diagnosis of the diseases due to instrumental and laboratory diagnostic limitations.

Conclusions

The findings of higher risk of hospitalization for children without health insurance, and living far from the hospital underline the necessity to promote health education and policies aimed at extending the universality of health care, through the implementation of primary care as close as possible to the population, in particular in little villages. The establishment of an efficient emergency call and transport system could support this healthcare priority.

The observation that children visited by staff including health care personnel specifically trained on pediatric patient management confirm the necessity to improve the quality of care provided to children with acute and critical illness, avoiding admissions for pathologies that could be treated in other health settings, such as primary care, if timely evaluated. The presence of a triage system, not currently present at Tosamaganga Hospital, could facilitate a more specific access to emergency care.

The experience of the Tosamaganga Hospital, with the presence of an electronic database suggests that optimizing data recording is central in the development of a health care system, because a monitoring system can produce information useful for health care providers and for policy makers. In fact, the possibility of identifying some relevant risk factors of hospitalization, as our study did, may support the health policy choices useful to promote interventions such as family health education, training of

health staff, implementation of a triage system and of an emergency care transport system useful to the development of pediatric care system in Tanzania and in other medium-low-resource country, improving outcomes for children with acute and critical illnesses.

Abbreviations

CI	Confidence Interval
DC	District Council
HIV	Human immunodeficiency virus
HMIS	Health Information Management System
IQR	Interquartile Range
KM	Kilometer
LMIC	Low and Middle-Income Country
MDG	Millennium Development Goal
N	Number
NGO	Non-Governmental Organization
OPD	Outpatient Department
OR	Odds Ratio
P	*P*-Value
SD	Standard Deviation
VS	Versus
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1

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Authors' contributions
VM contributed to conceptualization/design, methodology, investigation, supervision/oversight, and data curation; he participated in drafting the initial manuscript and in review and editing the final manuscript. MB contributed to investigation, supervision/oversight, and data curation; she participated in review the final manuscript. PB contributed to investigation, supervision/oversight, and data curation; he participated in review the final manuscript. MCC contributed to methodology, and supervision/oversight; she participated in review and editing the final manuscript. EYK contributed to investigation, supervision/oversight, and data curation; he participated in review the final manuscript. CM contributed to investigation, supervision/oversight, and data curation; she participated in review the final manuscript. DM contributed to investigation, supervision/oversight, and data curation; he participated in review the final manuscript. PP contributed to conceptualization/design, methodology, and supervision/oversight; he participated in review and editing the final manuscript. ADN contributed to conceptualization/design, methodology, and investigation, supervision/oversight, data curation and formal analysis; he participated in drafting the initial manuscript and in review and editing the final manuscript.

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Data availability
The database that support the findings of this study were used under license by Tosamanga Voluntary Agency Hospital for the current study, and are thus not publicly available. Specifical statistical analysis can be requested and agreed with Tosamanga Voluntary Agency Hospital. However, all data relevant to the study have been included in the paper.

Declarations

Ethics approval and consent to participate
All methods were performed in accordance with the ethical standards as laid down in the Declaration of Helsinki and its later amendments or comparable ethical standards. The study has been formally approved for ethical aspects by the Health Management Team of Tosamaganga Voluntary Agency Hospital that declared: "The above mentioned retrospective study proposal "Factors Associated with Hospitalization in a Pediatric Population of Rural Tanzania: Findings from a Retrospective Cohort" has been evaluated. Data were collected from the hospital's electronic medical records. Particularly, patients related information were retrieved for the purposes of the management of health care services provision through the consent given by legal representative of the patient when accessing the hospital. The protocol of the research, its tools, means of data collection, and materials have been examined and found adequate, respectful of national and international standards and regulations for health-related research activities, and consistent with the Mission of Tosamaganga Voluntary Agency Hospital. Therefore, the Health Management Team of Tosamaganga Voluntary Agency Hospital authorizes the researchers to use the data collected and the relative findings of the research for further elaboration and publication". We attached the declaration of the Health Management Team of Tosamaganga Voluntary Agency Hospital (REF: NO DOIRA/TVAH/VOL/56/01, December 6th 2023).

Consent for publication
Not applicable.

Competing interests
All the authors do not have any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within that could inappropriately influence and bias their work.

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Publisher's Note

Successful management of prolonged abdominal pregnancy in low-resource setting: a case report

PAPER

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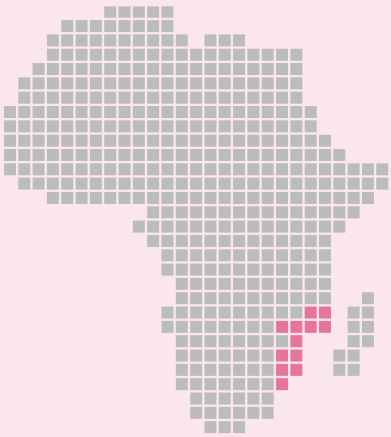

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Case Report

Case Report

Successful management of prolonged abdominal pregnancy in low-resource setting: a case report

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Abstract

Ectopic pregnancy is a life-threatening complication of pregnancy and represents the leading cause of maternal mortality in the first trimester. In developing countries early diagnosis, necessary for favorable outcomes, is often unavailable and women are often not aware of possible conditions and associated complications. Moreover, access to sexual and reproductive health services and antenatal care are limited in such settings. Finally, management options are restricted and often performed in emergency with higher risk of complications and mortality. We report here a 33-year-old woman presenting a 41 weeks abdominal pregnancy successfully managed in a low-resource setting.

Keywords: prolonged pregnancy; ectopic pregnancy; low-resource setting; case report

Introduction

Ectopic pregnancy (EP) is a complication of pregnancy where the embryo implants outside the uterine cavity, mainly in the Fallopian tube but also in the cervix, ovaries, and abdomen [1]. EP is life-threatening for the mother especially due to the possible consequent internal hemorrhage and it represents the leading cause of maternal mortality in the first trimester, with an estimated incidence of 5–10% of all pregnancy-related deaths [1]. Reliable epidemiological data are available only in developed countries with well-established healthcare and it is estimated that EP accounts for ∼2% of all pregnancies in Europe and North America [2]. On the contrary, in developing countries, due to poor medical and economic conditions, limited antenatal visits and prevention programs, not only it is difficult to find epidemiological data but there are important limitations in the understanding of the risk factors and management of EP [2]. The main risk factors for EP are the use of an intrauterine device at the time of conception, *Chlamydia trachomatis* and Neisseria gonorrhea infections, current or past history of pelvic inflammatory disease, previous EP, iron deficiency, and smoking cigarettes [3]. The gold standard for diagnosis is the serum concentrations of human β chorionic gonadotropin (hCG) and transvaginal ultrasound while clinical evaluation is not reliable as many women with EP report no pain nor adnexal tenderness and often it may be confused with miscarriage or induced abortion, a problem with the ovary or with a pelvic inflammatory disease [3]. In developing countries not only the gold standard is often unavailable, but women are often not aware of possible conditions and their complications and have no access to proper sexual and reproductive health services nor antenatal care [4]. Likewise, the EP management in developed countries is standardized both for stable patients, which can be treated medically with methotrexate injection, or surgically with the removal of the fallopian tube, both for unstable patients requiring emergency surgery to stop life-threatening hemorrhage [5]. In limited resources settings, instead, surgery, mostly performed by laparotomy, remains the main treatment and, due to late diagnosis, it is often performed in emergency with frequent tubal rupture and hemoperitoneum and, thus, higher risk of complications and mortality [3].

We reported a 33-year-old woman presenting a 41 weeks abdominal pregnancy successfully managed in a low-resource setting.

Case report

A 33-year-old woman presented with a prolonged (41 weeks) pregnancy without labor and history of fourth pregnancy with three births, one stillbirth and two live children.

At admission, the patient reported abdominal pain and discomfort due to fetal mobilization, with good baby movement, anorexia, and no other complaints. She presented a prenatal record of 10 consultations carried out in a rural context with no ultrasound availability and no complication. She was HIV positive on treatment with Tenofovir, Lamivudine, and Dolutegravir and

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Figure 1. Live newborn after prolonged abdominal pregnancy (A), placenta adhesions to the left annex of the uterus (B), and adnexectomy (C).

tested negative for syphilis. At clinical examination, blood pressure levels were normal (115/83 mmHg), heart rate 106 bpm, respiratory rate 18 cpm, temperature 36.5°C, and cardiopulmonary auscultation unchanged. The abdomen was painful on superficial and deep palpation, the fetus was palpated in a longitudinal position, breech presentation, fundus height of 37 cm, auscultation of the fetal cardiac focus in the right hypochondrium at 130 bpm, without uterine dynamics. Upon vaginal examination, the posterior cervix was long and impervious. The ultrasound revealed a single intrauterine fetus, fetal heartbeat positive, breech presentation, biparietal diameter of 9.3 cm, femur length of 7.2 cm, and occlusive placenta previa and severe oligoamnios. Emergency cesarean section was performed. The abdominal cavity was accessed where the gestational sac was found, the empty uterus next to the gestational sac slightly increased in size. The amniotic membrane was opened and the newborn, a live male weight 2600 g was delivered with Apgar score of 6 at first minute and 8 at fifth minute (Fig. 1A). A small amount of clear amniotic fluid was observed, the placenta was inserted into the left interstitial region, with adhesions to the left annex of the uterus (Fig. 1B). Thus, the left adnexectomy was performed (Fig. 1C). Surgery was uneventful, postoperative course had no complication, and the mother and child were discharged 4 days after surgery. Importantly, 1 week follow up was regular for both.

Discussion

EP represents a potential highly preventable and treatable condition and, especially when early detected, the chances of successful treatment are high, leading to a low risk of complications and mortality. However, these optimal conditions are characteristics of high-income countries while in undeveloped and developing countries EP remains an underestimated and underdiagnosed condition leading to urgency and fatal outcomes. The main reasons are the lack of diagnostic tools as hCG and transvaginal ultrasound and limited access to proper health care system and service. However, the higher rate of morbidity and mortality seems also related to country or region's combined educational, economic, and medical levels reflecting a strong role of social determinants of health [3].

The successful management of this case represents a rare and extraordinary case that reflects the poor social-economic context, limited resources but also the appropriateness of the care provided in this complex case.

Considering the limited scientific literature available especially in low-income countries, further research and investigation are necessary to better understand the underlying factors contributing to EP in low-resource settings. Moreover, considering the various factors such as ethnicity, economic status, and educational levels, it is mandatory to develop effective public health policies that address these disparities and provide enhanced protection for vulnerable women. Finally, it is crucial to promote early diagnosis and treatment of EP especially in low-resource settings to mitigate its impact on women and child health.

Conflict of interest statement

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Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Guarantor

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Unknown advanced abdominal pregnancy in low resource setting: A case report

PAPER

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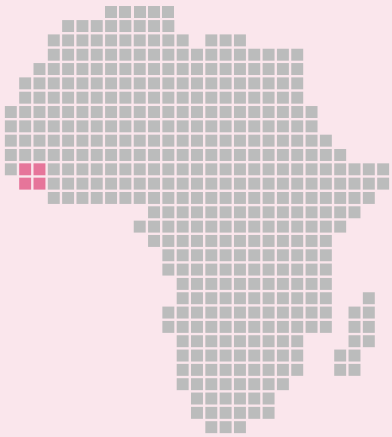

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Unknown advanced abdominal pregnancy in low resource setting: A case report

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Abstract
Background: Abdominal pregnancy is a rare, life-threatening condition.
Case: A 39-year-old pregnant, gravida 2, para 1 (spontaneous vaginal delivery), was presented to hospital at 36+6 weeks gestation on account of abdominal pain. She underwent an emergency caesarean section due to foetal distress. The diagnosis of abdominal pregnancy was not made until intrasurgical operation was carried out and a live baby of 2.8 kg was delivered via laparotomy with an intact uterus. However, to avoid major bleeding the placenta was left in situ along with gauze packs to achieve hemostasis. A second laparotomy was eventually carried out to remove the gauzes after one week, but the placenta, since being firmly attached to the postero-lateral pelvic wall, was not removed.
Conclusions: The present case recalls the attention to the possible misdiagnosed abdominal pregnancy in low resource settings where ultrasound scan is often not available and to the management of placenta after delivering the foetus.

Keywords: Abdominal pregnancy, expectant management, low-resource setting.

Introduction

Nowadays, ectopic pregnancy is a crucial cause of mortality and morbidity, with an incidence rate of 2% of all pregnancies and accounting for 10% of all pregnancy-related deaths [1, 2]. While in the ectopic pregnancy the fertilized ovum grows in an area outside the uterus (fallopian tubes, ovaries, cervix, vagina), in the abdominal ectopic pregnancy the implantation occurs in a site inside the peritoneal cavity: Omentum, peritoneal membrane, uterine surface and abdominal organs as intestinal loops, spleen, liver and blood vessels. Most of cases of ectopic pregnancy reported in literature are found in the fallopian tubes, with a high risk of maternal mortality in the first trimester, while the incidence rate of abdominal pregnancy accounts for <1% [1].

The difference between primary and secondary abdominal pregnancy is due to the site of ovum fertilisation in the abdomen. In the first case, it occurs directly in the abdominal cavity while in the second case it is consequent to a uterine perforation of an intrauterine pregnancy or an early rupture of a tubal pregnancy [2]. The diagnosis is usually arduous, since the non-specificity of symptoms like vaginal bleeding or generalized abdominal pain, which usually shift the diagnosis to a tubal pregnancy.

AEPs diagnosed after the twentieth week of gestation, caused by an abnormal implantation of the placenta, are a significant cause of maternal-fetal mortality due to the high risk of a major obstetric haemorrhage and coagulopathy following partial or total placental detachment [3].

As reported by Atrash *et al*. in 1987, out of 5221 total cases of abdominal pregnancy, preoperative diagnosis could be made in only 11% of patients, despite multiple obstetric evaluations, antenatal visits and ultrasound scans [4]. Nowadays radiologic techniques have improved, as clinician awareness has increased throughout the years. In a more recent study, 26 advanced abdominal pregnancies were reviewed and in 56% of the cases a prior diagnosis was done and in all the cases a conservative management was done with a 100% rate of live births [5].

The radiologic methods which could help in the diagnosis are the pelvic ultrasound scan and magnetic resonance imaging (MRI). In a case of abdominal pregnancy, ultrasonography could be the primary diagnostic modality. The most common signs are the loss of the visualization of the myometrial wall between the gestational sac and the bladder, the unusual position of the foetus with foetal parts uncommonly close to the abdominal wall and sometimes the abnormal placental vascularization [6].

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Otherwise, MRI can be useful to delineate the relationship and sometimes the invasion of placenta to the adjacent organs [7, 8].
AEP is extremely risky to the patient due to the high mortality rate; this is the reason why all the recent guidelines [9] recommend the termination of pregnancy at first diagnosis in all cases of ectopic pregnancy. The management of these patients could be either medical, surgical or a combination of these, according to the gestational age, the patient's clinical conditions, the professional skills of the in-charged doctors, the hospital setting and the patient's desires and personal obstetrical history. Surgical treatment options include a laparoscopic or a laparotomic surgery, while the medical treatment involves intramuscular or intralesional methotrexate and/or intracardiac potassium chloride. Abdominal pregnancies frequently terminate during early gestational age, when the placenta spontaneously detaches from the implantation site, causing abdominal bleeding and consequent peritoneal irritation by hemoperitoneum followed by abdominal pain.
Nonetheless, in rare cases, the pregnancy can progress to late stages and the foetus must be delivered via laparotomy. Once the foetus is delivered, the options for the placental management are mainly two: either the placenta is removed or it is left in place for its spontaneous regression, with or without the use of methotrexate. However, no guidelines provide specific recommendations, therefore the choice is taken according to the surgeon's skills, the location of the placenta and its vascular supply, and the availability of materials and blood.

Clinical Case
A 31-year-old gravida 2 para 1 at 36 weeks + 6 days gestational age (from 1st trimester ultrasound scan) was admitted to Princess Christian Maternity Hospital, Freetown, Sierra Leone, on November 29th, 2023, on account of abdominal pain, gradual, intermittent and increasing in frequency and severity, consistent with labour pain. She had been diagnosed with HIV from the first pregnancy, from when she was under antiretroviral medication, and had an otherwise unremarkable family and social history. No past surgical and gynaecological intervention were reported. Her obstetric history accounted for one spontaneous vaginal delivery in 2011 at term, after that she inserted a contraceptive subcutaneous implant for 5 years. During her pregnancy she had three antenatal clinic visits, one for every trimester, where vitals, symphysis fundal height (SFH), weight and fetal heart rate (FHR) were always exanimated while only at the first one visit Hb value, HIV and syphilis status were checked. Only the 1st trimester ultrasound scan was done during the pregnancy.
At the time she arrived in OPD (Outpatient Department) on examination, the patient was alert, afebrile, acyanosed, anicteric, not pale and not dehydrated. No pedal edema was reported. Her blood pressure was 133/79 mmHg, pulse rate was 104 bpm, respiratory rate was 26/min, temperature was 36 °C and SpO2 was 98%. Abdominal examination revealed an estimated foetal weight of 3.7 kg, SFH 37 cm, abdominal gut (AG) 104 cm. Foetal heart rate by Doppler was 98 bpm. Vaginal examination showed a cervix posterior, 20% effaced, soft consistency and closed, station-2 (Bishop score 3/13). The last bedside ultrasound scan recorded a breech presentation.
Due to the unfavourable cervix, together with the lack of opportunity of continuous monitoring by cardiotocography and to avoid further delaying the surgery, the decision for an emergency cesarean section on account of foetal distress was taken. While awaiting surgery, the patient received intrauterine resuscitation man oeuvres (placed on O_2 support, nursed in left lateral position, intravenous fluids were administered).
Surgery was performed after 5 hours from the diagnosis. Intraoperatively, the surgeon described an abdominal pregnancy and managed to deliver a healthy live male in breech presentation, Apgar score was 7 in 1 minute and 8 in 5 minutes. Birth weight resulted 2.8 kg. The newborn showed no major anatomical abnormalities. Uterus was normal for size and morphology as well as ovaries and tubes. The placenta was found firmly adherent to the posterolateral abdomino-pelvic wall. After the ligation of the umbilical cord, due to the high risk of intraoperative massive haemorrhage, the decision to leave the placenta in situ and to pack the abdominal cavity with gauzes was made, for a re-laparotomy to be performed in the following days. Total estimated blood loss was 1200 milliliters, and two emergency units of whole blood were transfused intraoperatively.
The post-operatory plan was to transfer the patient to HDU, PCMH's high intensity care unit, where broad spectrum antibiotics, analgesics, intramuscular methotrexate 50 mg and intravenous fluids were administered. During postoperative day 1, Hb was 6 g/dL, so the patient received two more units of cross matched blood. She was taken back to the operating theatre after one week: since the concern of major bleeding, we opted to wait for the placenta to regress spontaneously. During the surgery, the abdominal packs were removed, adequate hemostasis was checked, intraoperative abdominal washing was performed, and placenta was left in situ.
Both the mother and the baby recovered well and were discharged home after two weeks from the first laparotomy, in good general conditions. Unfortunately, the baby passed away after one month of life due to unexplained fever. At the follow up, she reported a wound dehiscence for which she was followed by nurses to do wound dressing and that ultimately closed by secondary intention.
She underwent a both transvaginal and transabdominal ultrasound scan after 4 months from the surgery from which the placenta could not be identified. She hadn't resumed her usual menstrual period yet at the moment of the ultrasound scan. No further investigations were possible due to financial constraints.

Discussion
The present case reflects a poor management of pregnancies and an overall lack of resources in this kind of setting. The main issue with this patient was that the abdominal pregnancy was only diagnosed intraoperatively; so, no adequate materials to face any complications during surgery were provided, nor blood units were stocked in case of need. Therefore, the decision not to attempt to cleave the placenta from its site on the abdominopelvic wall was due to its firm attachment and the impossibility to eventually deal with a major haemorrhage, which should have been ultimately caused by the deep invasion of tissue on abdominal organs not meant to host it, and the lack of hemostatic mechanisms exerted by myometrial contractions.
Our case raises questions such as: "Could we have tried to remove the placenta from its site, if materials and surgical skills consented to it?" or "What would our management have been if we knew antepartum that this was an abdominal pregnancy?". At a review of the literature on good-outcome abdominal pregnancies, sporadic cases of known abdominal pregnancies, held up to the viability of the foetus, were carried out through a watchful, close follow-up [10-12] nonetheless, in most of the cases it has been a rather surprising intraoperatively diagnosis while performing an emergency caesarean section for other obstetric reasons [13-18]. Certainly, if the surgeon knows about the

abdominal location of the pregnancy, much attention must be paid during surgery to the high risk of abdominal organs and abdominal vessels injury, since the possible displacement of the same in the abdominal cavity due to the presence of the foetus with its placenta, membranes and amniotic fluid.

One similar case reported [19] a large bowel injury inadvertently made to the sigmoid colon due to the adhesions between the large bowel and the ectopic mass.

No guideline provides recommendations on how to deal with the placental removal after the extraction of the baby. One case report from Burundi [20] showed a conservative approach with the placenta left in the abdomen, since the removal of the ectopic placenta may have been associated with life-threatening complications. Moreover, the placental vascularization is often difficult to discern and clearly identify. The use and timing of methotrexate is still controversial, as it has been correlated with lobular necrosis and, while decreasing bHCG level quickly, it does not modify the degree of placental reabsorption, which is poor [21]. Abdominal packing with gauzes during the caesarean section followed by a second laparotomy to remove the gauzes has been described to be successful in the event of major bleeding, whether the placenta was removed or not [15, 22]. If the facility permits so, a specific radiological embolization of the placental bed vessels has been demonstrated to be a useful tool to control the bleeding.

Conclusions

The present study showed that

- Unlike tubal ectopic pregnancies, abdominal uncomplicated pregnancies may not be detected until late gestational ages and even to term. In a low-resource setting where most patients accomplish with one, if none, ultrasound scan throughout all the duration of the pregnancy, it is hard to have a suspicion of ectopic in absence of symptoms.
- In a public academic hospital, the only diagnostic tools available are point-of-care hemoglobin value, without the possibility of performing for free any other hematological laboratory tests or imaging investigations. These must be carried out in other private facilities, but often they are unavailable to patients due to financial constraints. The free healthcare obstetrical program provided by the government barely guarantees antenatal clinic visits where blood pressure is recorded, but no ultrasound scans are available.
- A first trimester ultrasound scan showing an empty uterus is warranted to detect ectopic pregnancies, but attention should be paid in performing it, as with any other diagnostic procedure. As the pregnancy advances and the foetus gets to more advanced gestational ages, it could be more likely missed that the location of the pregnancy is not inside the uterus.
- According to guidelines, a patient with a first trimester vital ectopic pregnancy should promptly undergo its termination, either medical or surgical. In the case of misdiagnosed abdominal pregnancies which luckily manage to get more advanced, it is advised to carefully balance the benefits and risks of letting the pregnancy proceed, according to the mother's will and the healthcare providers' skills, whether to term or to the age of viability of the foetus. An ethical dilemma of terminating an ectopic pregnancy must be considered in infertile women with no possibility of access to assisted reproductive techniques in low resource settings [10].

It was deemed safer in our setting to leave the placenta in situ to avoid a major bleeding for which we were not prepared, but further investigation and long-term follow up is needed to confirm whether it is safer to perform a conservative management aiming for spontaneous regression, with or without the use of methotrexate, or to attempt its surgical removal in a tertiary care centre with the availability of adequate blood supply, a trained anaesthetist équipe and a skilled abdominal surgeon.

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Conflict of Interest:

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Suctioning with a bulb syringe or suction catheter after delivery?

PAPER

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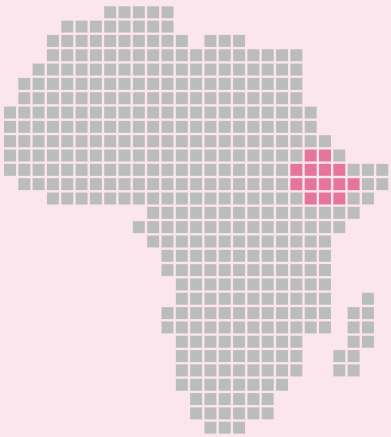

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A Novel CPAP Device With an Integrated Oxygen Concentrator for Low Resource Countries: In Vitro Validation and Usability Test in Field

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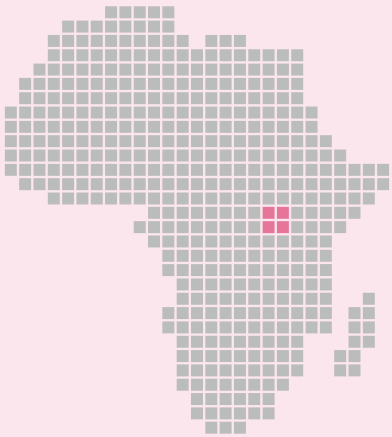

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A Novel CPAP Device With an Integrated Oxygen Concentrator for Low Resource Countries: In Vitro Validation and Usability Test in Field

Poletto Sofia, Zannin Emanuela, Ghilotti Emanuele, Putoto Giovanni, Ichto Jerry, Lochoro Peter, Obizu Moses, Okori Samuel, Corno Matteo, and Dellacà Raffaele

Abstract*—*Goal: **To develop and validate a novel neonatal non-invasive respiratory support device prototype designed to operate in low-resource settings.** ***Methods:*** **The device integrates a blower-based ventilator and a portable oxygen concentrator. A novel control algorithm was designed to achieve the desired fraction of inspired oxygen (FiO_2) while minimizing power consumption. The accuracy of the delivered FiO_2 and the device power consumption were evaluated in vitro, and a formative usability test was conducted in a rural hospital in Uganda.** ***Results:*** **The agreement between the set and delivered FiO2 was high (limit of agreement: −5.6 ÷ 3.8%). For FiO2 below 60%, the control algorithm reduced the power drain by 50%. The device was also appreciated by intended users.** ***Conclusion:*** **The prototype proved effective in delivering oxygen-enriched continuous positive airway pressure in the absence of compressed air and oxygen, holding promise for a sustainable and effective implementation of neonatal respiratory support in low-resource settings.**

***Index Terms*—Continuous positive airway pressure, low- and middle-income countries, respiratory distress syndrome, under-5 mortality, usability test.**

***Impact Statement*—The proposed device may provide a relevant impact on improving survival and respiratory outcomes of infants with respiratory distress in LMICs.**

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I. Introduction

EVERY year, approximately 5.2 million children under 5 die, and 98% of these deaths occur in low- and middle-income countries (LMICs) [1], [2]. Approximately 46% of these deaths are related to hypoxemia or acute respiratory distress and could be prevented by a more spread and effective implementation of respiratory support [1], [3], [4].

Non-invasive respiratory support is relatively low-cost and feasible across a wide range of low-resource settings [6], [7]. In particular, nasal Continuous Positive Airway Pressure (nCPAP) is widely used to reduce the work of breathing and improve blood oxygenation [8].

There are several methods to generate CPAP [9], bubble CPAP (bCPAP) being the simplest and most common CPAP method in LMICs [10]. However, several factors still limit the widespread implementation of CPAP in LMICs, especially in peripheral centers [5]. Effective CPAP requires compressed medical air and oxygen. Standard CPAP systems use large bias flows and waste large amounts of compressed medical air and oxygen, which are expensive and limited in low-resource settings.

The most common sources of medical oxygen in LMICs are cylinders and oxygen concentrators. Cylinders are expensive, poorly sustainable and require a reliable distribution network, which is uncommon in LMICs [11]. Oxygen concentrators are cost-effective compared to cylinders but are cumbersome, need stable power sources, and typically cannot be used with standard ventilators [12], [13]. Moreover, connecting an oxygen concentrator to a ventilator's gas supply is ineffective for two reasons: first, a significant amount of oxygen is wasted through the expiratory pathway; second, standard oxygen concentrators cannot adjust oxygen production for patients needing low fractions of inspired oxygen, leading to energy waste and quicker deterioration of molecular sieves like zeolite.

Compressed medical air is less common than oxygen in LMICs. Therefore, inexpensive bCPAP systems that connect modified oxygen prongs and water bottles to a pure oxygen source are often used [5]. Even though these solutions are effective [10], they carry important limitations. Indeed, pure oxygen carries risks of oxygen toxicity, including but not limited

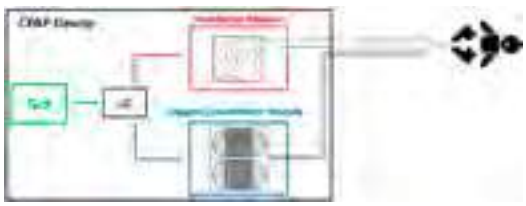

Fig. 1. Schematic of the device. Red: ventilation module, blu; oxygen concentrator module; green: Graphic User Interface (GUI). The core microcontroller (μC) controls all the units.

Fig. 2. Structure of the ventilation module. PNT: pneumotachograph. P_{blower}, $\dot{V}_{blower}$: pressure and flow at the blower outlet. P_{awo}, $\dot{V}_{awo}$: pressure and flow at the patient's airways opening.

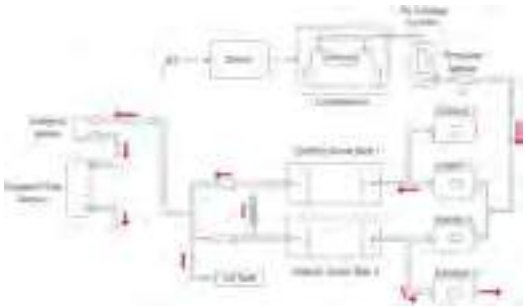

Fig. 3. Schematic of the oxygen concentrator. The microcontroller drives the compressor, which pressurizes ambient air into the two zeolite sieve beds through two pairs of supply/exhaust valves. Two solenoid valves arranged in parallel control the output oxygen-enriched gas flow. An oxygen and flow sensor measures the oxygen concentration and gas flow at the output of the module. Purple arrows show the gas flow direction in case bed 1 is under adsorption and bed 2 under desorption.

to retinopathy of prematurity, and necessitates high oxygen flows to work properly [14]. CPAP devices specifically developed for low-resource settings are also available, but they either require an external source of oxygen or continuous stable electricity [20].

To overcome the abovementioned technical limitations to the safe and effective implementation of CPAP in low-resource settings, we developed a novel non-invasive neonatal mechanical ventilator independent from compressed medical air and oxygen sources. The device integrates a blower-based ventilation module and a small oxygen concentrator. The latter delivers an oxygen-enriched gas mixture directly at the inlet of the patient interface, avoiding oxygen waste through the expiratory pathway. Moreover, the oxygen concentrator is modulated based on the required fraction of inspired oxygen to produce only the needed amount of oxygen and minimize power consumption.

This paper presents 1) the design of the device, 2) its in vitro validation in terms of range and accuracy of the delivered fraction of inspired oxygen and power drain and 3) a formative field usability test.

II. Materials and Methods

Study design and setting

The device design and development and the in vitro validation study were performed at the TechRes Lab, Politecnico di Milano.

A. Device Development

1) System Architecture: The device is made of four modules: the ventilation platform, the oxygen concentrator, the Graphic User Interface (Supplementary Material), and the control unit (Fig. 1).

The ventilation module is based on a radial blower, while the oxygen concentrator produces an oxygen-enriched gas mixture that is blended with the air from the ventilation module to achieve the desired fraction of inspired oxygen at the patient interface. The oxygen-enriched gas mixture is injected between the intentional leak and the patient interface to minimize oxygen waste. An intuitive GUI allows the user to set the respiratory support settings, visualize the pressure and flow tracings, and manage the alarms. All the device units are controlled via a custom-made board, which hosts the main microcontroller (μC, STM32F746ZG; ST Microelectronics, Geneva, CH), the power drivers for actuators and the circuits for data communication with the sensors. This unit is powered by a switching 24 V AC/DC power supply (RSP-500-24; Mean Well, New Taipei, TW). A rechargeable lithium battery (24V DC-6000 mAh, Aftertech, Reggio Emilia, IT) guarantees a 30- to 60-minute backup.

2) Ventilation Module: Fig. 3 shows the structure of the ventilation module. The core is a mono-stage radial blower powered by a brushless DC motor with three Hall-effect sensors that allow highly accurate control of the rotor position (U65MN; Micronel, Tagelswangen, CH). Pressure and flow are measured at the blower outlet (P_{blower}, $\dot{V}_{blower}$) using a ±75 mbar differential piezoresistive pressure transducer (HCLA0075B; First Sensor, Berlin, DE) and a custom-made 3D printed pneumotachograph (resistance ∼0.3 $cmH_2O{\cdot}s/L$) coupled with a ±2.5 mbar differential pressure transducer (HCLA02X5B; First Sensor, Berlin, DE). The breathing circuit has a single-limb configuration with an intentional leak that allows carbon dioxide washout and generates the desired pressure into the circuit. A customized 3D-printed connector incorporates an intentional leak and an inlet for the oxygen-enriched gas from the oxygen concentrator (Supplementary Fig. 5).

The intentional leak has a non-linear characteristic that allows the generation of 5 cmH_2O of pressure with a bias flow of 3 L/min.

Pressure and flow sensors measure the variables at the inlet of the breathing circuit. The airway opening pressure and flow

(P_{awo} and $\dot{V}_{awo}$) are estimated based on the resistance of the single-limb breathing tube (R_{tube}) and the flow through the intentional leak.

$$P_{awo} = P_{blower} - -R_{tube}\ \dot{V}_{blower} \quad (1)$$

$$\dot{V}_{awo} = \dot{V}_{blower} - \dot{V}_{leak} \quad (2)$$

We approximated R_{tube} as a constant and the pressure-flow characteristic of the intentional leak as follows:

$$\dot{V}_{leak} = 0.013 \cdot P_{blower}^{0.704} \quad (3)$$

Note that $\dot{V}_{awo}$ does not account for the flow coming from the oxygen concentrator.

We implemented a PID controller in the main microcontroller that uses the difference between the desired P_{awo} from the GUI and the measured P_{awo} as input to adjust the speed of the radial blower. The PID output is converted into an analog signal using a 12-bit Digital to Analog peripheral of the microcontroller and sent as target speed to a dedicated servo-controller (Escon module 50/5; Maxon Motor, Sachseln, CH) that implements a four-quadrant closed-loop control system of the blower speed.

3) Oxygen Concentrator Module: Fig. 3 shows the schematic of the oxygen concentrator.

The oxygen concentrator operates on the Pressure Swing Adsorption (PSA) principle using two molecular sieves made of zeolites, porous materials that selectively adsorb nitrogen from ambient air when pressure increases [15]. In each cycle, one molecular sieve is in the adsorption stage (pressurized to produce an oxygen-enriched gas flow), while the other is in the desorption stage (depressurized to ambient pressure to release the previously adsorbed nitrogen). Part of the oxygen-enriched gas produced by the sieve in the adsorption phase is used to wash out the nitrogen from the sieve in the desorption phase to increase output oxygen concentration. In the subsequent cycle, the role of the two sieves is reversed.

The oxygen concentrator core component is the compressor (BD-08AB-D; Shenzhen Boden Technology Development Co., Shenzhen, Guangdong, CH), an oil-free, brushless dual head medical air pump driven by its proprietary servo controller electronics with a speed set point set by a digital Pulse Width Modulation (PWM) signal. A copper tube and a small aluminium cylinder filled with alumina (100 ml) cool and dry the pressurized air. The air is driven alternatively in the two zeolite-filled (JLOX 101A; Luoyang Jalon Micro-nano New Materials Co., Yanshi, Henan, CN) 300 ml-molecular sieves. Each sieve is coupled with two diaphragm valves (DXT474; SMC, Tokyo, JP), called supply and exhaust valves. When a sieve is under adsorption, its supply valve is open, and its exhaust valve is closed. Conversely, when a sieve is in the desorption phase, its supply valve is closed, and its exhaust valve is open. The supply and exhaust valves switch every 3 seconds. A custom manifold, engineered by SMC Italy, integrates the sieves, valves, and all connections, enhancing robustness and minimizing potential connection errors during manufacturing and maintenance (Fig. 4).

The oxygen-enriched gas produced by the sieves is stored in a 170 ml reservoir acting as low-pass filter to provide a continuous

Fig. 4. Oxygen concentrator manifold designed and produced by SMC Italy, Milano, Italy.

gas source and delivered to the patient through two Solenoid Valves (SV) arranged in parallel (K8; Camozzi Automation, Brescia, IT). The valves opening is controlled by adjusting the duty cycle of a 50-Hz PWM driving signal, which presents a hysteresis-free linear relationship with the output flow.

The oxygen flow the concentrator needs to produce to achieve the requested fraction of inspired oxygen ($FiO_{2\ TARGET}$) at the airway opening is computed using mass balance equation:

$$FiO_{2\ TARGET} = \frac{O_{2\ CONC} \cdot \dot{V}_{CONC} + 0.21 \cdot \dot{V}_{awo}}{\dot{V}_{CONC} + \dot{V}_{awo}} \quad (4)$$

Where $\dot{V}_{awo}$ is the ventilator flow that reaches the airways opening (3), $\dot{V}_{CONC}$ the concentrator flow, and $O_{2\ CONC}$ the oxygen concentration. Multiple combinations of $\dot{V}_{CONC}$ and $O_{2\ CONC}$ will yield the same $FiO_{2\ TARGET}$. This defines an under-constrained problem or, in other words, a control allocation problem. The controller exploits this degree of freedom to minimize power consumption by solving the following constrained static minimization problem:

$$\min_{CS,SV} P_{CONC}\ (CS, SV) \quad (5)$$

$$\text{s.t.} \frac{O_{2\ CONC} \cdot \dot{V}_{CONC} + 0.21 \cdot \dot{V}_{awo}}{\dot{V}_{CONC} + \dot{V}_{awo}} = FiO_{2\ TARGET} \quad (6)$$

The solution to the above problem requires the knowledge of three characteristic relationships:

$P_{CONC}\ (CS, SV), \dot{V}_{CONC}(CS, SV)$ and $O_{2CONC}(CS, SV)$ i.e., the dependence of the concentrator flow, oxygen concentration and compressor power on the two control variables: the compressor speed (CS) and solenoid valves (SV) duty cycles.

A principle model of these relationships would depend on many physical parameters that are difficult to measure or estimate. Therefore, we used a data-driven modelling approach: a static model was derived by sampling the input space and measuring the resulting oxygen concentration $(O_{2\ CONC})$, flow $(\dot{V}_{CONC}$)and absorbed power. In a series of experiments, the CS

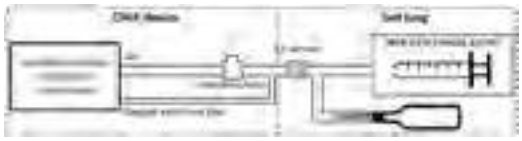

Fig. 5. In vitro validation experimental set-up. The CPAP device is attached to an active test lung with known mechanical properties (R = 60 $cmH_2O{*}s/L$, C = 0.0015 L/cmH_2O). A paramagnetic oxygen sensor is placed at the mouthpiece to measure the oxygen reaching the test lung.

was sampled from 20% to 100% in steps of 10% and the SV from 10% to 100% in steps of 10.

Multiple combinations of CS and SV yield the same ($O_{2\ CONC}$,) flow ($\dot{V}_{CONC}$) confirming the bi-dimensional dependency (see Section III). The CS and SV characteristics were fitted with the following polynomial expressions:

$$CS = p_{00} + p_{10} \cdot \dot{V}_{CONC} + p_{01} \cdot O_{2\ CONC} + p_{20} \cdot \dot{V}^2_{CONC} + p_{11} \cdot \dot{V}_{CONC} \cdot O_{2\ CONC} + p_{02} \cdot {O_{2\ CONC}}^2 \quad (7)$$

$$SV = p_{00} + p_{10} \cdot CS + p_{01} \cdot \dot{V}_{CONC} + p_{20} \cdot CS^2 + p_{11} \cdot \dot{V}_{CONC} \cdot CS + p_{02} \cdot \dot{V}^2_{CONC} \quad (8)$$

Note that for ease of use in the following computation, (7) and (8) describe the inverted $P_{CONC}\ (CS, SV)$, $\dot{V}_{CONC}(CS, SV)$ characteristics. The parameters of the polynomial fitting are shown in Supplementary Table I, the simple one-dimensional monotonic relationship between CS and power consumption in Supplementary Fig. 6.

Based on the three identified functions, the minimization problem (5) is solved with the following algorithm:

1) Compute $\dot{V}_{awo}{=}\dot{V}_{blower}{-}\dot{V}_{leak}$,
2) Solve and sample (4) to find N ($O_{2\ CONC}$, $\dot{V}_{CONC}$) candidates.
3) For each ($O_{2\ CONC}$, $\dot{V}_{CONC}$) solve (7) and (8) to get (CS, SV) within the CS and SV actuation limits.
4) Choose, among the feasible (CS, SV) pairs, the power-minimizing one, i.e., the one with the lowest CS.

The solution to such a static optimization problem is precomputed and stored in a look-up table for a more efficient implementation.

The oxygen-enriched gas injection from the concentrator acts as a disturbance in the bandwidth of the P_{awo} controller. The blower pressure sensor measures this effect, and the PID controller rejects the disturbance.

B. Validation Protocol

The in vitro validation aimed to evaluate the accuracy of the FiO_2 delivered at the airways opening while quantifying the device power drain.

1) Experimental Set-Up: Fig. 5 shows a schematic of the validation set-up:

An active test lung was realized using a mechanical analogue of the respiratory system of either preterm or respiratory distressed infants (R = 60 $cmH_2O{*}s/L$, C = 0.0015 L/cmH_2O) [19] arranged in parallel with a breath simulator driven by volume tracings recorded on human infants to reproduce realistic respiratory patterns. A paramagnetic oxygen sensor (Paracube Sprint Sensor; Hummingbird Sensing Technology, Crowborough, U.K.) measured the FiO_2 at the patient interface. The speed of the oxygen concentrator compressor was recorded for the whole duration of the test and used to compute the overall power drain.

2) Experimental Protocol: The accuracy of the delivered FiO_2 and the corresponding power consumption were evaluated for all combinations of the following settings:

- CPAP at 3, 5, 8 and 10 cmH_2O;
- FiO_2 from 25% to 70% in steps of 5%;
- simulated minute ventilation of 800, 1000, and 1500 ml/min.

3) Data Analysis: We used Bland-Altman analysis to compare the target and measured FiO_2 at the inlet of the breath simulator. We evaluated the power drain at different $FiO_{2\ TARGET}$, comparing it with the maximum power consumption of the oxygen concentrator.

C. Feasibility Study

A field usability study was performed at St. John's XXIII Hospital of Atapara, Aber, Uganda (Supplementary Material). Following a 20-min training, 15 nurses were asked to perform six tasks on a mannequin and to fill the Post-Study System Usability Questionnaire (PSSUQ). For each task, we recorded the number and type of misuses.

III. Results

Oxygen concentrator characterization

The power drain of the concentrator components was:

- supply and exhaust valves: $<$ 1W each;
- solenoid valves delivering oxygen to the patient: 1.9 to 5 W depending on their opening level;
- sensors: 10 W in total;
- compressor: 65 to 146 W, proportional to its speed see Supplementary Material.

Fig. 6 shows the flow and oxygen concentration of the oxygen-enriched gas for each combination of compressor speed and output valves aperture.

The flow and oxygen concentration of the output gas increased as the compressor speed increased. By contrast, as the valves aperture increased, the output flow increased, but oxygen concentration decreased.

We used such results to derive (7) and (8) coefficients.

In vitro validation

We found a strong agreement between the set and delivered FiO_2 (Fig. 7): the mean difference was -1.07 %, and the limits of agreement were -5.56 and 3.83%.

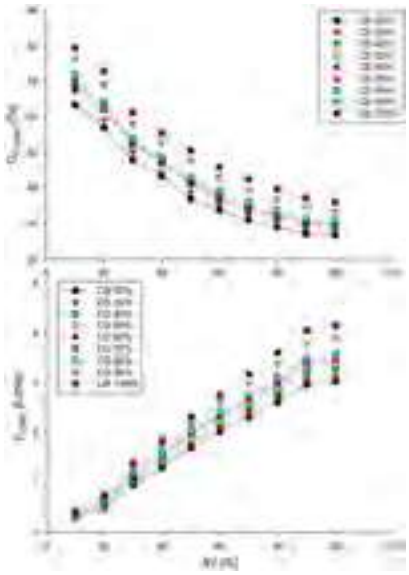

Fig. 6. Results of the oxygen concentrator characterization. [top] Increasing solenoid valves' duty cycle decreases the oxygen concentration of the output gas flow; [bottom] Increasing solenoid valves' duty cycle improves the output gas flow. A higher compressor speed increases both the oxygen concentration (top) and flow (bottom) of the output.

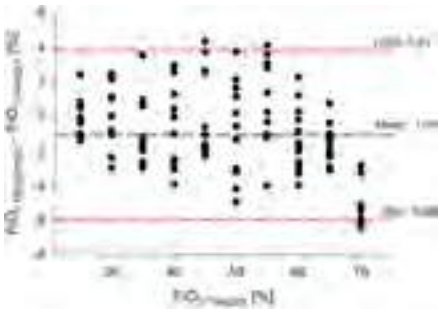

Fig.7. Bland-Altman plot showing the difference between delivered and set FiO_2.

The oxygen concentrator power drain was 130 W in standard mode, producing the maximum achievable oxygen concentration. Thanks to the novel control algorithm, the power consumption decreased with FiO_2, allowing a saving of up to 50% when the set FiO_2 was below 60% (Fig. 8). Moreover, in these optimized conditions the back-up battery duration is more than 60 minutes.

Feasibility study

Participants made a total of 5 mistakes, 3 of which in the start-up phase. The mean±SD PSSUQ score was 1.64 ± 0.49 (worst 7), showing high appreciation.

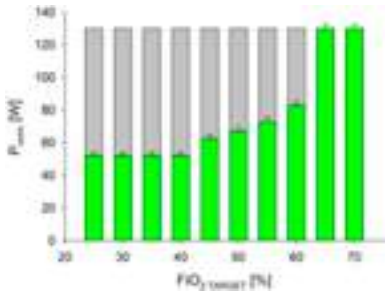

Fig. 8. Power consumption of the compressor at different FiO_2 levels. The automatic algorithm yields a power saving up to 50% when patients are requiring FiO_2 equal or lower than 60%.

IV. Discussion

We described a novel device designed to provide non-invasive respiratory support to neonates in low-resource settings. The device integrates a turbine-operated CPAP module and a portable oxygen concentrator, resulting in independence from external sources of compressed air and oxygen, which are limited in LMICs [9]. The turbine ensures the possibility of providing CPAP at the desired FiO_2, which is crucial to mitigate the risks of oxygen toxicity. For example, the unrestricted use of oxygen in preterm newborns can lead to the development of retinopathy of prematurity, which has a higher incidence in LMICs than in high-income countries[17], [18]. Compressed medical air is even more limited than oxygen in low-resource settings, and air-oxygen blenders are often too expensive [9]. Oxygen concentrators represent the most cost-effective and sustainable oxygen source in LMICs. However, oxygen concentrators usually fail to produce the high oxygen pressures and flow rates required by most standard blenders and respiratory support devices. Since neonatal respiratory support devices work with high bias flows, blending oxygen with air at the inlet of the breathing circuit results in a large waste of oxygen, making the treatment expensive and inefficient. The proposed system delivers an oxygen-enriched gas mixture directly at the airways opening, avoiding oxygen waste through the expiratory pathway. A novel characteristic of this device is that the oxygen concentrator speed is adjusted to achieve the desired FiO_2, minimizing power consumption. Indeed, a major limitation of bedside oxygen concentrators is that they require an uninterrupted energy source and have high power consumption, which can be a bottleneck for their use in settings with unstable electricity. By contrast, thanks to the synergistic operation of the ventilation and oxygen concentrator modules, the proposed device has limited power drain and could potentially work on batteries.

Both the compressor speed and the opening of the output valves influence the oxygen concentration and the output flow. To achieve the desired FiO^2, our algorithm automatically selects the optimal combination of oxygen concentrations and gas flows, minimizing power consumption. Since compressor speed primarily influences power usage, the oxygen concentrator

control system determines the minimum speed required to attain the desired FiO2 and respiratory support settings. Compared to standard operation, the proposed approach decreases power consumption by 40 to 60%.

Devices specifically developed for LMICs are are already used to deliver bCPAP to neonates in resource-limited settings. Specifically, the Pumani (Hadleigh Health Technologies, US) and the Dolphin (MTTS, Vietnam) have an integrated blower but rely on an external oxygen source. The Vayu bCPAP (Vayu Global Health Innovations, US) employ an inexpensive gas entrainment blender but requires a source of compressed oxygen. Finally, the Baby CPAP (Diamedica, U.K.) have integrated sources of oxygen and air but has similar power consumption as bedside oxygen concentrators and, consequently, requires reliable electricity [9], [20].

The in vitro validation showed that the device can generate FiO_2 levels up to 70% with minimal errors at all considered CPAP levels. The inability to achieve FiO_2 close to 100% was deemed acceptable, considering its intended use for treating neonates with mild to moderate respiratory distress in LMICs. We speculate that patients with severe respiratory failure requiring FiO_2 above 70% cannot be cared for in centres with limited facilities and resources because they need high-intensity treatments (e.g., invasive mechanical ventilation) and close monitoring delivered by skilled personnel. Even if the device can function with minimal facilities, its safe and effective use necessitates healthcare professionals' ability to identify patients who may benefit, monitor them, adjust respiratory support settings accordingly, and manage the airway interface. Patients should receive good essential newborn care for the device to be cost-effective. Otherwise, non-respiratory issues might negatively affect the outcome.

The present results are encouraging and justify further development and technology transfer of the device, incorporating the inputs and suggestions of the usability study, thanks to the partnership with a social enterprise with strong expertise in developing technologies for low-resource countries. Clinical studies on neonates are warranted to evaluate the safety and effectiveness of the device, along with its reliability on prolonged use in clinical practice in a relevant environment.

V. Conclusion

We developed a proof-of-concept respiratory support device for treating neonates with mild to moderate respiratory distress in low-resource settings. The device does not need external medical gasses and has limited power consumption. It could accurately deliver CPAP at FiO_2 up to 70% on a test lung mimicking infants up to 10 kg. If such results are confirmed in clinical field studies, after further development, the proposed device can positively impact the respiratory outcomes of infants with respiratory distress in low-resource settings.

Supplementary Materials

See Supplementary materials to find further images which give more details on the proposed device as well as a detailed description of the Guided User Interface and of the performed usability study on field.

Conflict of Interest

The authors declare that they have no competing interests.

Authors contributions

Conceived the study: SP, EZ, MC, RD.

Critically revised the device specifications: GP, JI, PL, MO, SO,

Design of the device: SP, EG, EZ, RD.

In-vitro validation study: SP, EG.

Usability study protocol and data collection: SP, GP, JI, PL, MO, SO, RD.

Data analysis: SP, EZ, EG, MC, RD.

SP, EZ, MC, RD drafted the manuscript. All authors reviewed and revised the manuscript and have read and approved its final version.

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A multicentre neonatal manikin study showed a large heterogeneity in tactile stimulation for apnoea of prematurity

PAPER

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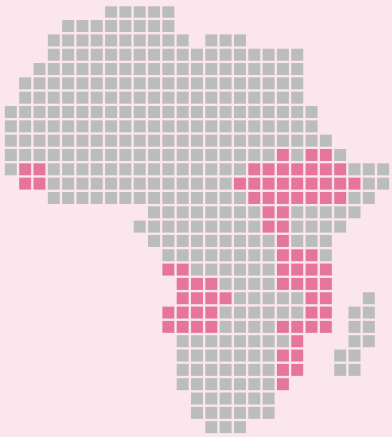

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Parental stress, depression, anxiety and participation to care in neonatal intensive care units: results of a prospective study in Italy, Brazil and Tanzania

PAPER

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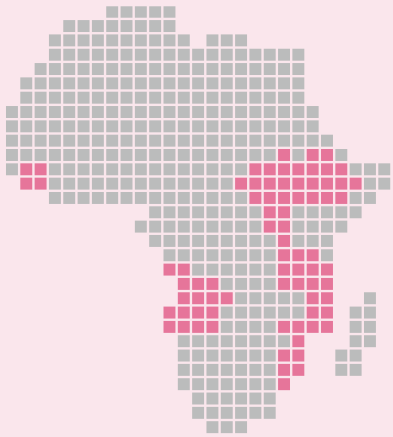

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Parental stress, depression, anxiety and participation to care in neonatal intensive care units: results of a prospective study in Italy, Brazil and Tanzania

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ABSTRACT

Background Studies comparing the frequency of different mental health conditions across different settings and evaluating their association with parental participation in newborn care are lacking. We aimed at evaluating the frequency of parental stress, anxiety and depression, along with the level of participation in newborn care, among parents of newborns in Italy, Brazil and Tanzania.

Methods Parental stress, anxiety, depression and participation in care were assessed prospectively in parents of newborns in eight neonatal intensive care units (NICUs) utilising: the Parental Stressor Scale in NICU (PSS:NICU); the Edinburgh Postnatal Depression Scale (EPDS) and EPDS-Anxiety subscale (EPDS-A); the Index of Parental Participation in NICU (IPP-NICU). Univariate and multivariate analyses were conducted.

Results Study outcomes were assessed on 742 parents (Brazil=327, Italy=191, Tanzania=224). Observed scores suggested a very high frequency of stress, anxiety and depression, with an overall estimated frequency of any of the mental health condition of 65.1%, 52.9% and 58.0% in Brazil, Italy, Tanzania, respectively ($p<0.001$). EPDS scores indicating depression (cut-off: ≥13 for Brazil and Tanzania, ≥12 for Italy) were significantly more frequent in Tanzania (52.3%) when compared with either Brazil (35.8%) and Italy (33.3%) ($p<0.001$). Parental participation in care was also significantly higher in Tanzania (median IPP-NICU=24) than in the other two countries (median=21 for Brazil, 18 for Italy, $p<0.001$). Severe stress (PSS:NICU ≥4) was significantly more frequently reported in Brazil (22.6%), compared with Italy (4.7%) and Tanzania (0%, $p<0.001$). Factors independently associated with either parental stress, anxiety or depression varied by country, and a significant association with parental participation in care was lacking.

Conclusions Study findings suggest that parental stress, anxiety and depression are extremely frequent in NICUs in all countries despite diversity in the setting, and requiring immediate action. Further studies should explore the appropriate level of parental participation in care in different settings.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Existing literature highlighted a high frequency of mental distress among parents of infants in neonatal intensive care units (NICUs), but multicountry studies on multiple mental health outcomes and data from low-income settings are lacking.
⇒ Parents' participation in care is a pillar of family-centred care, yet it has been poorly documented in most NICUs.

WHAT THIS STUDY ADDS

⇒ This study suggests that parental stress, anxiety and depression are extremely frequent in NICUs, both in high-income and low–middle-income countries, without a direct correlation with parental participation in newborn care.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Immediate action should be taken to screen parents in the NICU for depression, anxiety and stress.
⇒ Mechanisms should be put in place to provide rapid access to mental healthcare providers to the parents whose screening for psychological distress was found to be present.
⇒ Further studies should define the most appropriate level of parental participation in care in different settings, as well as support systems for parents, in alignment with the principle of family-centred care.

INTRODUCTION

Every newborn has the right to survive and thrive, yet each year globally 2.3 million die after birth, additionally 1.9 are stillbirths, and nearly all (98%) of these deaths occur in low and middle-income countries (LMIC).[1–3] In addition, several million babies are born either preterm or small for gestational age[4 5] or get sick in the first days of life, and among

these, it is estimated that about 1 million survive with long-term disabilities.[6] Implications of being small and sick often extend beyond the neonatal period.[6] Small or sick newborns and their families are at high risk of long-term psychological and financial problems, which in turn can negatively affect their developmental, social and cognitive growth.[4–8] Substantial human potential for lifelong health and well-being is lost through newborn mortality and morbidity.[5 6]

Babies who are preterm or small for gestational age or those with congenital anomalies or postnatal infections are usually hospitalised for a medium to long-term period in neonatal intensive care units (NICU) or semi-intensive care units. Globally, it is estimated that every year up to 30 million newborns require some level of inpatient care.[9] Ensuring that all newborns receive the best care in NICU is critical and is recognised as a key aspect of human rights.[9 10] Over the last decades, there has been increasing awareness on the importance of quality of care provided in NICU as well as on the stressful nature of the NICU environment, both for infants and for parents.[11–14]

Specific to the parents' side, recent evidence suggests that the frequency of distressing symptoms among parents of infants in NICU is very high.[11–13] A recent systematic review confirmed a high frequency of parental stress related to NICU admission documented by 53 included studies, independently from timing of hospitalisation or newborn characteristics, and with parental role alteration being the greatest source of stress.[11] However, very few studies have been conducted in Asia and South America, and none in Africa.[11]

Other reviews[12 13] looking at a wider range of mental health conditions in parents of newborns in NICU suggested a high frequency of depression and anxiety across diverse ethnocultural groups and countries.[12 13] However, several gaps in existing evidence were noted: inconsistency in the use of measurement instruments and timing of measurement; lack of data on fathers; high risk subgroups.[12–14] Although in the very recent years, a routine screening of mood and anxiety disorders for parents of newborn in NICU has been proposed by several authors,[11–14] yet this is not a reality in most settings, limiting staff awareness on the problem as well as actions to mitigate mental distress in parents of newborn in NICU.

Similarly, although parents' participation in care has been recognised as one of the core pillars of family-centred care and its benefit for parental and newborn health—including newborn weight gain, breastfeeding rate, decreasing length of stay and parental stress and anxiety—have been documented by several randomised controlled trial (RCTs),[15–18] yet in most NICU settings, parental participation in care is not actively promoted nor implemented. Structured programmes, such as the Newborn Individualized Developmental Care and Assessment Program promoting an individualised, relationship-based, family-integrated model of care, by teaching to parents how to interact with their preterm infant[19 20] are difficult to access for most professionals, particularly in LMICs. Little is known on the level of parents' participation in newborn care in many NICU settings, especially in LMICs. Moreover, evidence is lacking on how, in different settings, different levels of participation in care correlates with different levels of mental distress.

This study aimed at documenting the frequency and severity of three mental health conditions—NICU-related stress, depression and anxiety—along with participation in newborn care, among parents of newborns in three different NICU settings: high-income (Italy), upper middle-income (Brazil) and low-income (Tanzania), to identify key differences and communalities. We also explored the association between NICU-related parental stress, depression, anxiety and parental participation to care, when corrected for other variables describing newborns and parental characteristics. This study was conducted within a multicentre project called 'Empowering Parents in NICU' (EPINICU), aiming at developing evidence-informed low-cost setting-specific models of interventions to improve mental health and well-being of parents of newborns admitted in NICU, and, where appropriate, improve parental participation in newborn care in NICU, across different settings.

METHODS

Study design and setting

This was a multicentre cross-sectional study, and it is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.[21] The STROBE Checklist is provided as online supplemental table 1.

The study was conducted in three countries classified in three different income groups: Italy (high income), Brazil (upper middle income) and Tanzania (lower middle income). Data were collected in hospitals participating to the EPINICU project. The project included only referral and/or teaching hospitals. More details on hospital characteristics are provided in online supplemental table 2.

Study participants

Mother, fathers and other caregivers of newborns who were hospitalised in the NICU or semi-intensive care for at least 24 hours in Brazil and Tanzania (where hospitalisation is usually short) and 48 hours in Italy (where hospitalisation last at least 2 days), with an age of at least 18 years, able to understand the local language (Portuguese in Brazil, Italian in Italy and Swahili in Tanzania) were enrolled prospectively. A priori exclusion criteria were parents with previously diagnosed mental disorders or cognitive difficulties which hampered data collection; parents of newborns dead at birth or during hospitalisation or which were hospitalised for less than 24 hours; maternal deaths; parents aged less than 18 years; parents not fluent in the languages in which the questionnaire

Table 1 Key characteristics of questionnaire used for data collection

Outcome	Questionnaire	Number of domains and questions	Recall period	Score range	Cut-offs recommended in literature
Stress	Parental Stressor Scale for NICU (PSS:NICU)	26 questions in three domains ► Sights and Sounds (6 items) ► Infant Behaviour and Appearance (13 items) ► Parental Role Alteration (7 items). ► A final question about overall stress during NICU hospitalisation.	Not specified	1–5 for each question (total: 1–5)	No recommendation in literature
Depression	Edinburgh Postnatal Depression Scale (EPDS)	10 questions	Last 7 days	0–3 for each question (total: 0–30)	For diagnosis of depression: ≥ 12 Italy ≥ 13 Brazil and Tanzania [22–33]
Anxiety	EPDS-Anxiety subscale (EPDS-A)	3 questions	Last 7 days	0 to 3 for each question (total: 0–9)	For diagnosis of anxiety: ≥ 6 [34]
State anxiety	State Anxiety Inventory (STAI Y1)	20 questions	In the last 24/48 hour	1–4 for each question (total 20–80)	For diagnosis of anxiety: >40 Anxiety level 41–50: mild anxiety 51–60: moderate anxiety >60: severe anxiety [35–46]
Trait anxiety	Trait Anxiety Inventory (STAI Y2)	20 questions	Not specified (describe how you generally feel)	1–4 for each question (total 20–80)	For diagnosis of anxiety: >40 Anxiety level 41–50: mild anxiety 51–60: moderate anxiety >60: severe anxiety [35–46]
Participation to care	Index of Parental Participation (IPP-NICU)	30 questions in four domains ► Daily Living (6 items) ► Providing Comfort (7 items) ► Advocating for Newborn Health (7 items); ► Technical Tasks (10 items).	Previous 24 hours	0–1 (yes or no) for each question (total 0–30, different maximum scores for each subdomain)	No recommendation in literature

was provided (fluency was assessed by the clinicians in charge); parents not providing consent to the study.

Study outcomes and data collection tools

We predefined as key outcomes for this study: (1) parental NICU-related stress (our primary outcome); (2) parental depression; (3) parental state and trait anxiety; (4) parental participation in newborns care. In order to collect these outcomes, we seek to select the most appropriate questionnaires, that is, those more widely validated and used, and feasible in our contexts (table 1). Newborns' and parents' characteristics were also collected.

Stress was measured with the Parental Stressor Scale for NICU (PSS:NICU),[22] which is a scale specific to parental stress related to NICU. The scale has been properly validated in Italy[23] and Brazil.[24] Studies on the PSS:NICU are lacking from Africa,[11] therefore for use in our project in Tanzania the PSS:NICU questionnaire was translated and back translated in Swahili by expert mother tongue researchers, according to The Professional Society for Health Economics and Outcomes Research (ISPOR) guidelines.[25] PSS:NICU includes 26 statements divided in three sections: stress due to 'Sights and Sounds' (6 items), to 'Infant Behaviour and Appearance' (13 items) and to 'Parental Role Alteration' (7 items). In PSS:NICU, questions do not refer to a specific time period. Answers for each question are on a Likert scale from 1 point for 'not at all stressful', 2 points for 'mild stress', 3 points for 'fairly moderate stress', 4 points for 'very stressful' and 5 points for 'extreme/severe stress'. Total PSS:NICU scores are calculated according to author instructions,[22] using two methods: (a) the stress occurrence level (SOL) is calculated including only experienced items; (b) the overall stress level (OSL) is calculated scoring 'not applicable items' with one point. According to the author's instructions, SOL should be used when the focus is the

parent as it captures better their experience, while OSL when the focus on the NICU environment.[22]

Parental depression was measured with the Edinburgh Postnatal Depression Scale (EPDS), which is the most widely used instrument for screening postnatal depression. It has been validated in many countries, including in Italy in mothers and fathers,[24 26] and in Brazil[24 27]; it has been translated in Swahili[28] and used in several African countries, including Tanzania.[28–31] The scale includes 10 questions, which evaluate the emotional state of the last 7 days, with four possible answers each (points ranging from 0 to 3), and a total score ranging from 0 to 30. The cut-off values considered more accurate for the diagnosis of depression are: a value ≥12 both for women and men in Italy,[24 26] and a cut-off ≥13 in Brazil[24 27] and Tanzania,[28–32] although other studies from Africa[33] used a lower cut-off (≥12).

Anxiety was measured, as primary analysis, by considering the EPDS-Anxiety subscale (EPDS-A), which allows individuals with high anxiety symptoms to be identified through a subset of EPDS items.[34] The EPDSA-A final score can range from 0 to 9 and a score ≥6 has proved to detected women with symptoms for at least one anxiety disorder, including generalised anxiety disorder, panic disorder or obsessive-compulsive disorder. As secondary additional analysis, in Italy and Brazil, anxiety was also measured by the State-Trait Anxiety Inventory (STAI), which include two complementary subscales: (1) the State Anxiety Scale (STAI State) evaluates the current state of anxiety, asking how respondents feel 'right now', using 20 items each with a scale from 1 (not symptoms) to 4 (very much so); (2) the Trait Anxiety Scale (STAI Trait) evaluates 'anxiety proneness', by assesses frequency of feelings 'in general', including general states of calmness, confidence and security.[35] The Trait Anxiety Scale has been suggested to capture not exclusively trait anxiety but rather a higher order trait such as negative affectivity/neuroticism that characterises both anxiety and depression.[36 37] The STAI has been validated in Italy,[29–39] Brazil[40 41] and widely used in Africa.[42 43] Each scale includes 20 items with a score ranging from 1 (almost never) to 4 (almost always), thus for each scale, the total score can range from 20 to 80. Although slightly different cut-offs for STAI have been used in the literature, in general, scores over 40 are considered indicative of anxiety, scores in between 41 and 50 indicating mild anxiety, 51–60 moderate anxiety and>60 severe anxiety.[44–46]

Parental participation was measured with the Index of Parental Participation (IPP) to paediatric care,[47] which was previously used in context with low resources.[48] For use in the NICU setting, the IPP was adapted by a team of senior neonatologists and epidemiologists. This adapted version of the IPP (IPP-NICU) was approved by Dr Melnik, the author of the original instrument.[47] The IPP-NICU questionnaire was translated and back translated for use in the project in Brazil and Tanzania, following the ISPOR guidelines.[25] The IPP-NICU includes four subdomains: activities related to Daily Living (6 items); Providing Comfort (7 items); Advocating for newborn health (7 items); Technical Tasks (10 items). Questions refer to the previous 24 hours. The total number of items is 30, with a dichotomous (yes/no) answering. The total score ranges from 0 to 30, with different maximum scores for each subdomain, and higher scores indicating higher parental participation in care.

A structured form, developed in dialogue with partners and field tested before use, was used to collect key newborns and parental characteristics, according to predefined case definitions. Data from parents were collected with a structured questionnaire among parents, data on newborns were collected from medical records and from parents.

Data collection procedures

The study and above-described questionnaires were introduced to parents by trained health professionals, either a neonatologist or other NICU staff close to discharge from NICU. The questionnaires were self-administered in Italy and Brazil. In Tanzania, due to the high rate of maternal illiteracy, data were collected with an oral interview, carried forward by ad hoc trained researcher not involved in case management or in data analysis. To reduce the burden of data collection, STAI questionnaires were not performed in Tanzania and performed in a subsample of parents in the other two countries. In Brazil depression, parental state and trait anxiety and participation in care were assessed only in one facility (Instituto de Medicina Integral Professor Fernando Figueira - IMIP), while in the other five hospitals only data on stress were prioritised.

Data collection periods slightly varied due to administrative procedures (project contracts and ethical clearance), and the different impact of the COVID-19 on research activities, and specifically were in Italy from November 2019 to November 2020 (with a gap of 2 months in March and April 2020, due to COVID-19 restrictions); in Tanzania from December 2019 to August 2020; in Brazil from May 2020 to December 2021.

Data analysis

A sample of 166 parents was needed for each country based on an estimated prevalence of stress in parents of newborns in NICU of 50%±10%, based on the existing literature,[11–13] with a confidence level of 99%.

First, we conducted a descriptive analysis, identifying key similarities and key differences across countries. Summary statistics were presented as absolute frequencies and percentages, and as medians and IQRs for continuous non-normally distributed data. Frequency of parental stress, anxiety and depression were assessed using the following cut-offs recommended by the literature (table 1): for EPDS, we assessed prevalence of parents with a score ≥13 in Brazil and Tanzania, and ≥12 in Italy[24 26–32]; for EPDS-A, we used a cut-off ≥6[34]; for the State-Trait STAI, we assessed prevalence of parents with a score cut-off >40.[44–46] For the PSS:NICU, in absence of any

indication in literature, we assessed prevalence of parents with a score ≥3, which identify 'fairly moderate stress'. Anxiety was primarily assessed with EPDS-A, while STAI was used as additional score system in Brazil and Italy, and to assess severity of anxiety. Severe stress and severe anxiety were respectively calculated by considering the frequencies of parents with SOL score ≥4 and STAI state score >60.[44–46] For calculating frequencies of all conditions, we used as a sample the subgroup of parents for whom all the scores of interests were available. To analyse intersections between groups of parents identified with different conditions, the SOL score was used for stress, as for existing recommendations.[22]

Additionally, we conducted univariate and multivariate logistic regression models for each country, considering the presence of mental health conditions under analysis (ie, depression, stress, anxiety, any of them) as binary outcome variables and parental participation to care as well as parental (ie, age, marital status, residence, financial situation, working status, role, education, participation to care) and newborn characteristics (gestational age, weight at birth, malformation, surgery, intubation, COVID-19, length of stay, unit of stay) as explanatory variables. For these analyses, we used the same cut-off descripted above for the mental health conditions, while we categorised the independent continuous variables according to their overall distribution in each country. The SOL score was used for stress, as for existing recommendations.[22] Frequencies, ORs and adjusted ORs (adjOR) were calculated, with 95% CIs and p values of significance.

To assess differences between two values, we employed the two proportions, z test (for proportions) and the Mood's median test (for medians). When comparing three proportions, we conducted multiple comparisons using the z test. For three or more medians, we used the Asymptotic K-sample Brown-Mood median test. All the tests were two tailed. Statistical analyses were performed using Stata V.14 and R V.4.1.2. For all tests performed, a p value of less than 0.05 was considered statistically significant.

Patient and public involvement in research

Patients were involved as responders of the questionnaire of data collection. In each of the countries, patients are being involved in designing actions on how to improve care in NICUs, based on the results of this study.

RESULTS

Population characteristics

Of the 2536 newborns admitted to the eight NICUs during the study period, 1511 (59.6%) meet the inclusion criteria. Among these, 837 (55.4%) were not enrolled due to several reasons related to their parents, including COVID-19, while only a minority (5.6%) refused consent (figure 1). Overall, we included 674 newborns and 742 parents/caregivers (Brazil=327, Italy=191, Tanzania=224). Fathers were mostly represented in the Italian sample (19, 79 and 4 fathers in Brazil, Italy and Tanzania, respectively).

Both parental (online supplemental table 3) and newborn (online supplemental table 4) characteristics significantly differed among the three countries.

- Differences among parents included caregiver age, working status, marital status, educational level (all p values <0.001) and women parity (p=0.003).
- Most of newborns' characteristics, such as Apgar score at 5th minute and frequency of associated medical conditions and related treatments (ie, surgery, ventilation support at birth), were significantly different across countries (p values <0.05). Out of the total sample, 400 (59.3%) newborns were preterm (gestational age at birth <37 weeks), with a higher frequency in Brazil (78.6%) and Italy (61.7%) when compared with Tanzania (29.9%, p<0.001). The median length of stay in NICU for Brazil (29 days) was significantly higher than the one recorded in Italy (14 days, p<0.001) and Tanzania (7 days, p<0.001).

Detected frequency of stress, depression and anxiety

Key similarities across countries:

- The detected frequencies of depression, anxiety and stress—calculated based on the pre-defined cut-off for each indicators—were high in all facilities (figure 2, online supplemental table 5A), with an overall frequency of any of the conditions of 65.1%, 52.9% and 58.0% in Brazil, Italy, Tanzania, respectively (all p values of multiple comparisons >0.05, in particular: Brazil vs Italy=0.06, Italy vs Tanzania=0.34, Brazil vs Tanzania=0.27). Results calculated using STAI were quite similar: 69.8% in Brazil and 63.1% in Italy (online supplemental table 5B, figure 3).

Key differences across countries:

- EPDS scores suggestive of depression were significantly more frequent in Tanzania (52.3%) when compared with both Brazil (35.8%) and Italy (33.3%)—(both p values <0.001).
- The three countries had different patterns of intersections across populations identified with different conditions (figure 2, online supplemental table 6.
- The frequency of all three conditions simultaneously was higher in Brazil (16.0%) and Italy (11.5%) compared with Tanzania (1.8%) (both p values for one-sided comparisons <0.001). Results calculated using STAI were quite similar: 10.4% in Brazile and 13.1% in Italy (online supplemental table 5A,B, figure 3).

Severity of stress, depression and anxiety

Key similarities across countries:

- In all countries, the scores of stress, depression and anxiety had a wide variability (figure 4) and reached values near to the maximum: the EPDS maximum score was 24 in Italy and 26 in Brazil and Tanzania;

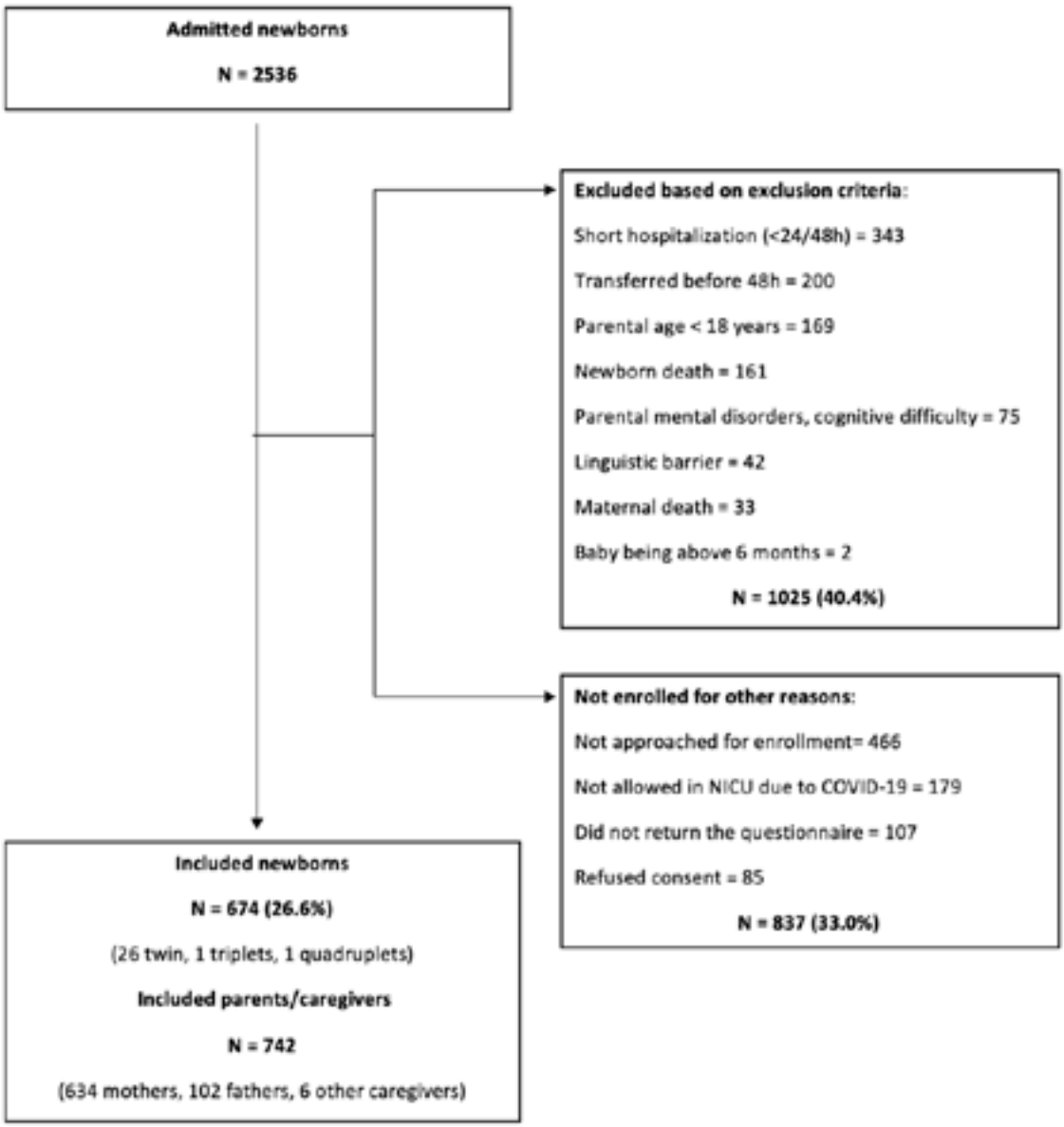

Figure 1 Study flow diagram. NICU, neonatal intensive care unit.

the PSS:NICU SOL maximum score was 5 in Italy and 4 in Brazil and Tanzania; EPDS-A reached the maximum value (score of 9) in each country, while STAI state maximum score was 70 in Italy and 69 in Brazil.

- Severe anxiety (defined as STAI State >60) had similar frequencies in Brazil (5%) and Italy (4%), p value=0.998 (online supplemental table 6B).

Key differences across countries:

- Parents in Tanzania had significantly higher median scores for depression (EPDS median equal to 13, IQR[9;16]) when compared with other countries (p value <0.001) (figure 4).
- Parents in Brazil had higher median scores for anxiety and stress (STAI state median equal to 45 and SOL median equal to 3.4) than the other countries under analysis (p value=0.002 for STAI state, p value <0.001 for SOL); frequency of severe stress (PSS:NICU—SOL≥4) was also significantly higher in Brazil (22.6%) compared with Italy (4.69%, p value <0.001) and Tanzania (0%, p value <0.001) (figure 4, online supplemental tables 6B and 7).

Figure 2 Frequency of detected parental depression, anxiety, stress and intersections among identified populations. For anxiety, the EPDS-A score was used. For PSS:NICU, the SOL score was used. Depression cut-offs: EPDS≥12 for Italy and≥13 for Brazil and Tanzania. EPDS, Edinburgh Postnatal Depression Scale; NICU, neonatal intensive care unit; PSS:NICU, Parental Stressor Scale in NICU; SOL, stress occurrence level.

Stress scores by domains

Key similarities across countries:

- Among the different domains of the PSS Score, 'Sights and sounds' was the one perceived as least stressful, when compared with the other domains, in all three countries under analysis (figure 5).

Key differences across countries:

- For both Italian and Brazilian parents, the domains where the higher scores of parental stress were reported was the paternal role alteration (SOL median 3.4 for Italy and 4.5 for Brazil), while for Tanzanian parents, it was the infant behaviour and appearance (SOL median 2.38) (figure 5).

Parental participation in care

Key similarities across countries:

- In no country parental participation in care score reached its possible maximum value, with the largest gap in all countries being on 'technical tasks' (figure 6).

Key differences across countries:

- In general, Tanzanian parents had the highest participation scores (median IPP-NICU score equal to 24, IQR [21; 26]), even in the domain of technical task (median 8 out of 10, IQR [7; 9] vs Brazil (median 6, IQR [4;8]) and Italy (median 4, IQR [2;7])—p value <0.001). Italian parents reported the lowest scores

Figure 3 Frequency of parental depression, anxiety (STAI score) and stress and intersections among identified populations. For PSS:NICU, the SOL score was used. For STAI, the STAI State score was used. Depression cut-offs: EPDS≥12 for Italy and≥13 for Brazil. In Tanzania, the STAI score was not collected. EPDS, Edinburgh Postnatal Depression Scale; NICU, neonatal intensive care unit; PSS:NICU, Parental Stressor Scale in NICU; SOL, stress occurrence level; STAI, State-Trait Anxiety Inventory.

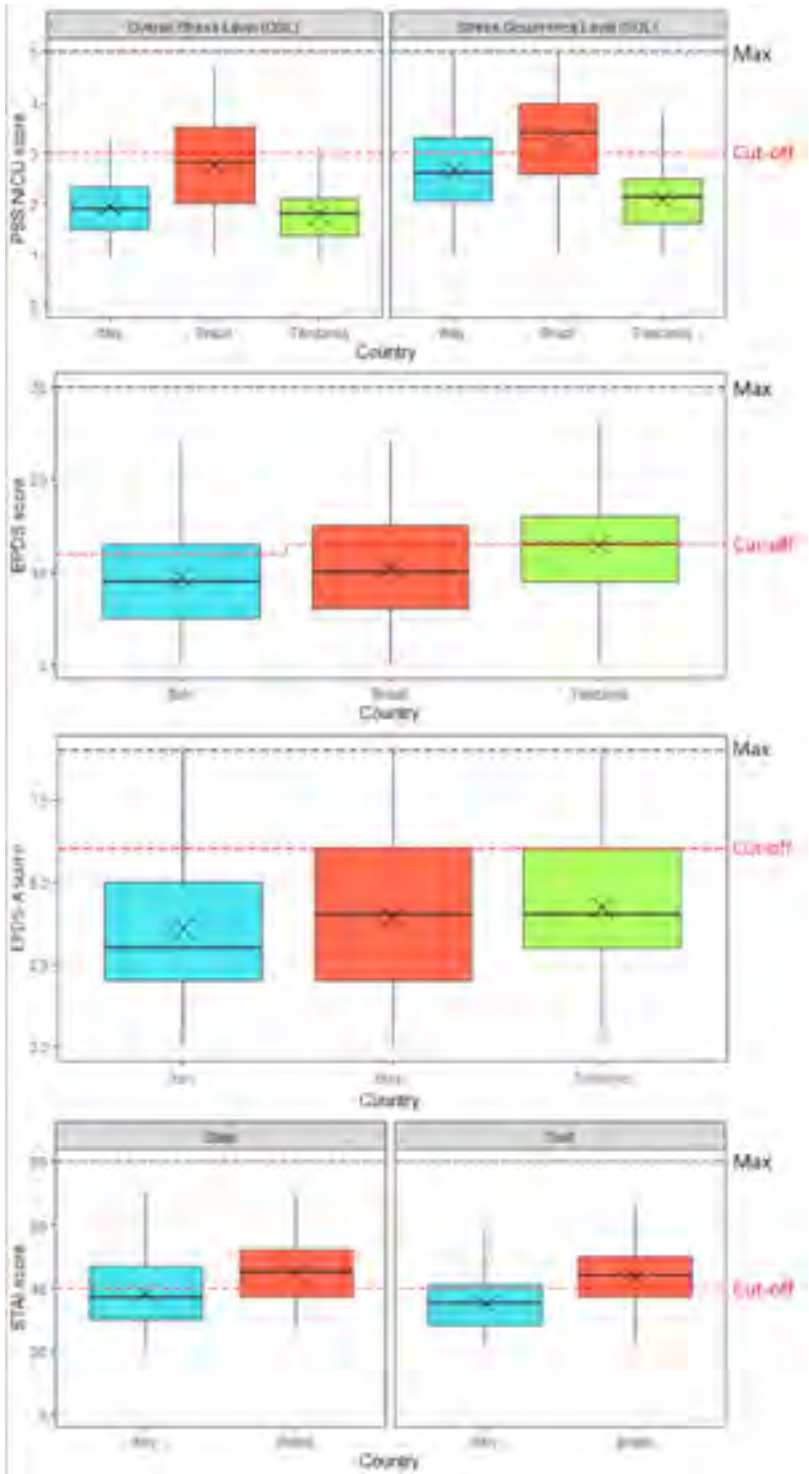

Figure 4 Severity of stress, depression and anxiety (median scores). The figure shows the median, the mean (represented by a 'X') and the IQR of each score. EPDS, Edinburgh Postnatal Depression Scale; NICU, neonatal intensive care unit; PSS:NICU, Parental Stressor Scale in NICU; STAI, State-Trait Anxiety Inventory.

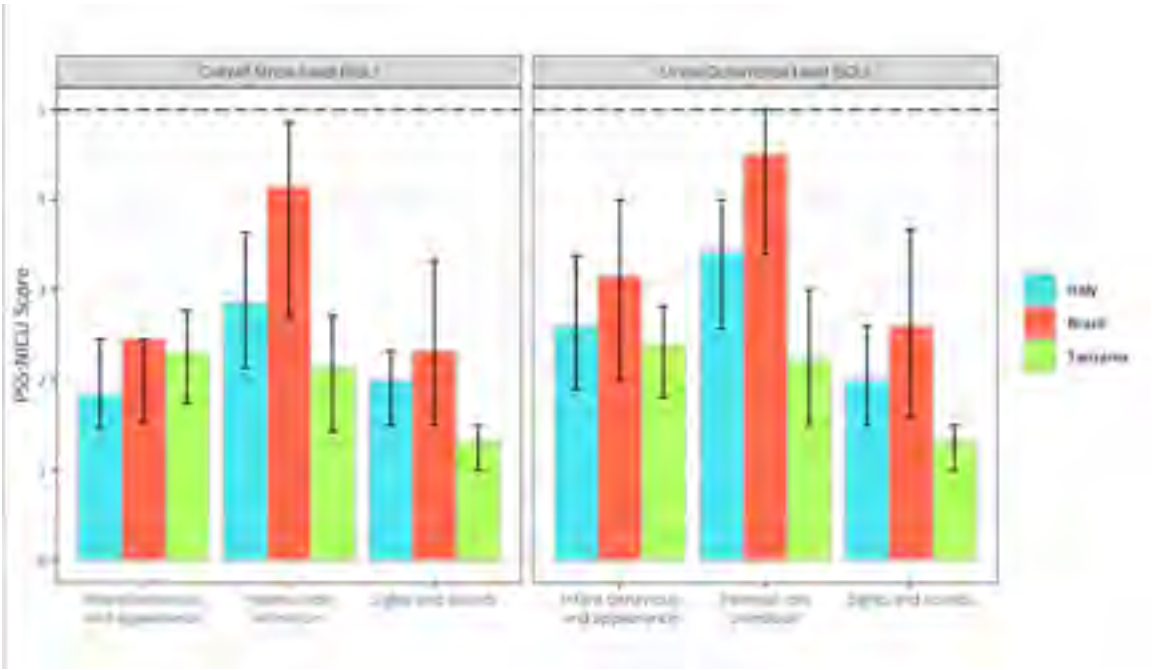

Figure 5 Stress by domain (median scores). The figure shows the median and the IQR of the PSS:NICU. NICU, neonatal intensive care unit; PSS:NICU, Parental Stressor Scale in NICU.

(median IPP-NICU score equal to 18, IQR [12; 22]). In Brazil, there was a medium–high level of participation (median 21, IQR [15; 24.8]) (figure 6, online supplemental table 8).

Multivariate analyses

Results of multivariate analyses varied by country, with, in general, few factors significantly associated with mental health outcomes, when corrected for all other factors.

In Italy, (online supplemental tables 9–11), stress significantly negatively associated with being a parent of twin newborns (adjOR 0.24, 95% CI 0.06 to 0.71, p value=0.018), while both depression and anxiety significantly associated with being a mother (adjOR 2.93, 95% CI 1.35 to 6.65, p value=0.008; adjOR 3.03, 95% CI 1.27 to 7.83, p value=0.016).

In Brazil (online supplemental tables 12–14), mothers from the interior/rural area had significantly lower odds for stress than those from the city (adjOR 0.33, 95% CI 0.13 to 0.84, p value=0.023); all other variables had non-significant associations with any of the mental health outcomes of interest, when corrected for the other variables.

In Tanzania (online supplemental tables 15–17), parental age higher than 25 years old associated with higher odds of parental anxiety (adjOR 2.04, 95% CI 1.04 to 4.09, p value=0.040), while being the parent of a newborns with length of stay higher than 7 days associated with lower odds of parental anxiety (adjOR 0.43, 95% CI 0.21 to 0.84, p value=0.016); all other variables had non-significant associations with any of the mental health outcomes of interest, when corrected for the other variables.

DISCUSSION

This study detected as a key communality across Italy, Brazil and Tanzania a very high frequency in of NICU-related stress, depression and anxiety, without a direct correlation with parental participation in newborn care. Key differences included a higher frequency of maternal depression in Tanzania, and stress in Brazil. Previously existing studies did not directly compare three major outcomes related to mental health—NICU-related stress, depression and anxiety (both state and trait)—along with participation in newborn care, and in this sense, this study is filling a research gap.

Study findings strongly support previous recommendations[11–14 49 50] on the need of routine screening for mood, anxiety disorders and stress in parents of newborn in NICU. The feasibility of screening for mood and anxiety disorder has been positively evaluated by a recent systematic review.[51] Common facilitators included engaging multidisciplinary staff in programme development and implementation, partnering with experienced facilities (champions), and incorporating parents screening into routine newborn clinical practice, while constraint in accessing mental health support was the most significant barrier.[51]

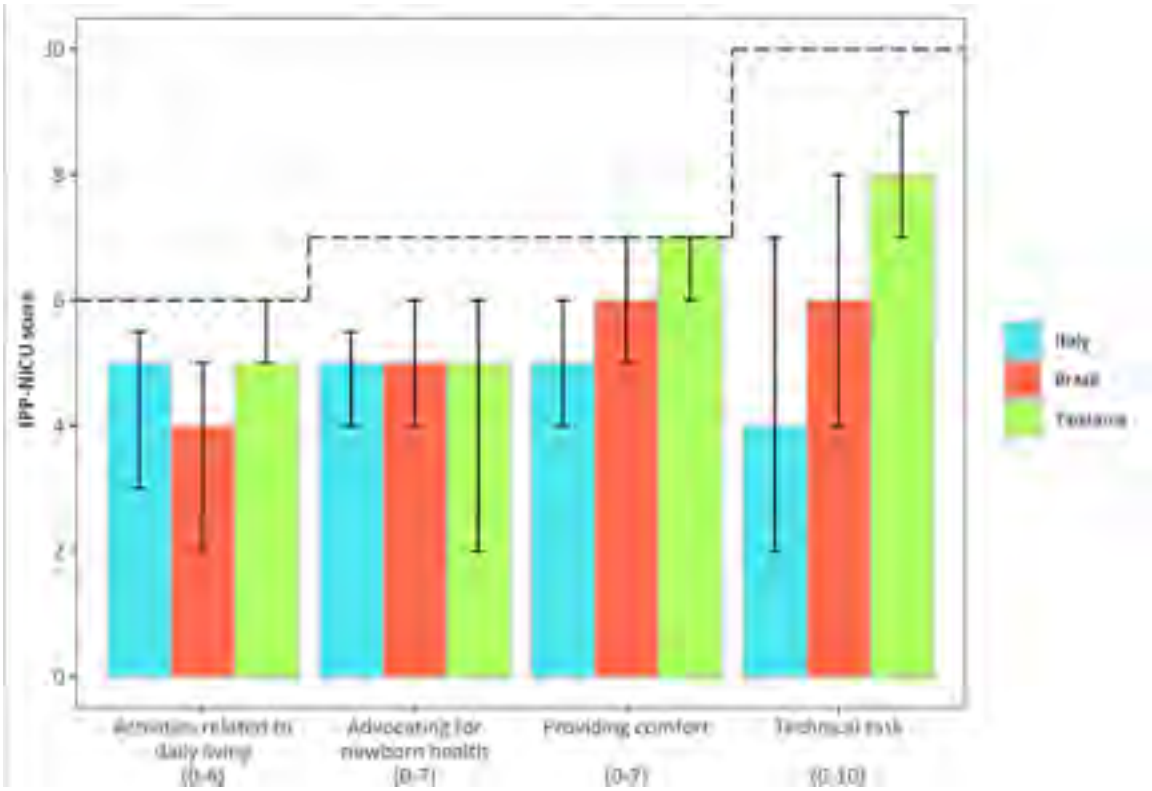

Figure 6 Parental participation, by domain (median scores). The figure shows the median and the IQR of the IPP-NICU. NICU, neonatal intensive care unit; IPP-NICU, Index of Parental Participation in NICU.

Prevention and support/treatment to parents with mental distress can be provided not only through psychological and social services but also through many other innovative ways. Existing systematic reviews of interventions to reduce parental depressive and anxiety symptoms identified many effective interventions, including, beside cognitive behavioural therapy[52]: educational interventions on a wide range of topics such as newborn attachment, newborn growth and development, NICU environment, how to manipulate and nurture the baby, how to observe infant's behaviours and provide positive stimulation and relaxation, newborn home care, training on problemsolving strategies, and on how to deal with own emotions, plus information on existing related resources[52–54]; parent's-centred support communication[54]; parents' groups[53]; fathers involvement in care[53]; parents dairy to process emotions and experiences[53]; music[53]; emotional support[54]; relaxation techniques (breathing, muscle relaxation, guided imagery)[53 54]; massage[53]; environmental interventions such as family rooms,[54] noise reduction,[52] bright light therapy.[52]

Such interventions clearly require involvement of NICU staff, including nurses, as highlighted by a recent systematic review.[53] Therefore, as a first step, there is the need to increase staff awareness—which cannot be given for granted—on the very high frequency of mental distress among parents of newborns in NICU. Second, based on the observed prevalence of mental distress among parents of newborn in NICU, related competences should be incorporated in the core curriculum of all NICU key staff. Evidence suggests that gaps in communication are one of the key areas reported by mothers as substandard[55 56]; therefore, competences to effectively establish, on a routine basis, effective communication and a collaborative relationship between staff and parents, even those with severe mental distress, appear to be one of the key core competencies needed for staff working in NICU. All these changes require a culture of family-centred developmental care, where both family and staff needs are considered comprehensively (including psychological needs), in a proactive manner (taking action).

Study findings, with Tanzanian mothers compared with Italian and Brazilian parents reporting higher frequency of depression, despite higher participation to newborn care, are not in contradiction with existing RCTs, summarised by a recent systematic review,[15] showing the many benefits of participation to care, including a reduction in maternal mental health distress and depression.[15] Postpartum depression, as shown by a recent metanalysis,[57] is frequent in African mothers and it is

associated with a wide range of risk factors, which our study did not aim at exploring—such as poor obstetric condition, history of adverse birth and infant health outcomes, a previous history of mental health disorders, low economic status, poor social support and intimate partner violence. Higher participation in care in Tanzania may be explained by staff shortage. Plausibly, when participation in care is promoted in the right environment and through parents' empowerment, it brings a benefit, while when mothers are left alone with their children without support, it may be not associated with good mental outcomes. The most appropriate level of parental participation in newborn care in different settings has not been established yet. We believe that such an evaluation should take into consideration, beside the context readiness (eg, existing resources, risk of infection, etc), both views of parents and staff, their level of empowerment, their cultural expectations and the existence of other existing support systems (eg, staff and parental training, policies.

Findings of the multivariate analyses suggest that risk factors for different mental health conditions may differ significantly across countries and settings, and calls for more in-depth studies. Other results of the multivariate analyses, such as the finding of stress negatively associated with twin birth or longer duration of stay, contradicts previous research and will need to be further confirmed.

We acknowledge limitations of this study. First, the observational nature of the study did not aim at testing any causal relationships among different study variables. In the lack of other previous multicountry assessments, this study was conceived as descriptive. However, it had the merit of documenting key mental health conditions together with participation in care, allowing comparison across countries, and providing data critical to develop context-specific interventions, as expected for the subsequent phases of the EPINICU project. Subgroup analyses looking at differences in study outcomes by sex of parents have been reported elsewhere.[58]

Second, data collection, occurring mostly during the COVID-19 pandemic, may have overestimated the frequency of mental distress, and slightly different time periods of data collection across the three countries may have affected results. However, detected frequency of stress, anxiety and depression aligns with those reported in studies in the prepandemic period,[11–13] while the COVID-19 diseases per se mostly cause mild disease in children.[59] An analysis of the Italian dataset across different time periods (prepandemic, low and high COVID-19 incidence) showed that prevalence of stress, anxiety and depression did not change significantly over time.[60] Future studies shall document to which extent parental mental distress in NICU persists beyond COVID-19.

Third, this study was conducted in one single referral facility per country, except for Brazil. More studies (or even better, data from screening programmes) should aim at documenting the prevalence of parental mental distress in different settings.

Fourth, while previous studies suggested that the severity of parental mental distress may change during the course of hospitalisation,[61] our study did not aim at documenting how such changes occurred. More evidence on this topic shall be derived from a desirable routine practice of screening mental distress in parents of newborn in NICU.

Fifth, the exclusion of parents with previously diagnosed mental health condition may have underestimated the frequency of our outcomes. Oral interview data collection procedure in Tanzania may reduce comparability of the results and biased results.

Finally, the questionnaire used may have their intrinsic limitations: they collect data that are based on a self-assessment and on different time periods (table 1); cultural appropriateness of EPDS in Africa is still debated[32] and the same may apply to the concept of stress; IPP-NICU questionnaire does not capture parental satisfaction with participation to newborn care. With these limitations, the questionnaires used in this study are the most widely validated and used in literature.[22–43]

CONCLUSION

This study suggests that parental stress, anxiety and depression can be extremely frequent in NICUs, both in high-income and low–middle-income countries, without a direct correlation with parental participation in newborn care. Immediate action should be taken to screen parents in the NICU for depression, anxiety and stress, and to refer them to appropriate care. Further studies should define the most appropriate level of parental participation in care in different settings, as well as support systems for parents, in alignment with the principle of family-centred care.

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Caesarean sections, indications and outcomes: a cross-sectional study using the Robson classification in a tertiary hospital in Sierra Leone

PAPER

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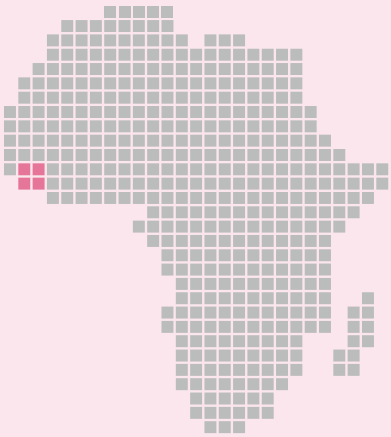

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Caesarean sections, indications and outcomes: a cross-sectional study using the Robson classification in a tertiary hospital in Sierra Leone

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ABSTRACT

Objective WHO recommends the use of the Robson's 'Ten Groups Classification' for monitoring and assessing caesarean section (CS) rates. The aim of this study was to investigate the rates, indications and outcomes of CS using Robson classification in a tertiary hospital in Sierra Leone.

Design Cross-sectional study.

Setting Princess Christian Maternity Hospital (PCMH), Freetown, Sierra Leone.

Participants All women who gave birth in PCMH from 1 October 2020 to 31 January 2021.

Primary and secondary outcome measures Primary outcome: CS rate by Robson group. Secondary outcomes: indications for CS and the newborn outcomes for each Robson group.

Results 1998 women gave birth during the study period and 992 CS were performed, with a CS rate of 49.6%. Perinatal mortality was 7.8% and maternal mortality accounted for 0.5%. Two-thirds of the women entered labour spontaneously and were considered at low risk (groups 1 and 3). CS rates in these groups were very high (43% group 1 and 33% group 3) with adverse outcomes (perinatal mortality, respectively, 4.1% and 6%). Dystocia was the leading indication for CS accounting for about two-thirds of the CS in groups 1 and 3. Almost all women with a previous CS underwent CS again (95%). The group of women who give birth before term (group 10) represents 5% of the population with high CS rate (50%) mainly because of emergency conditions.

Conclusion Our data reveals a notably high CS rate, particularly among low-risk groups according to the Robson classification. Interpretation must consider PCMH as a referral hospital within an extremely low-resourced healthcare system, centralising all the complicated deliveries from a vast catchment area. Further research is required to assess the impact of referred obstetrical complications on the CS rate and the feasibility of implementing measures to improve the management of women with dystocia and previous CS.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Indications for caesarean section (CS), outcomes of newborns and women were investigated within each Robson group for a better understanding of practices and possible needs.
⇒ Birth registries did not report referral status, preventing in-depth analysis of the contribution of referral cases, accounting for almost one-third of admissions, to the CS rate.
⇒ Only the type of health professional who conducted the CS was recorded. Information about the staff responsible for the decision for CSs was not reported, limiting further analysis and understanding of decision-making processes.
⇒ Maternal and neonatal deaths occurring after discharge were not recorded.

INTRODUCTION

Caesarean section (CS) is a key surgical intervention to improve the outcome for the mother and fetus. The appropriate use of CS during childbirth is crucial: high rates may indicate unnecessary use of the intervention, while low rates may indicate unmet obstetrical needs and inadequate access to care.[1–3]

CS is not without risks so when a CS is performed without medical indication, it exposes women to unnecessarily increased risk of complications in the short-term (eg, blood loss, infections, visceral injury, thromboembolism, anaesthesia-related complications), in the long-term (pelvic adhesion, chronic pain, sexual dysfunction, subfertility) and for future pregnancies (eg, placental problems, uterine rupture, stillbirth and preterm birth).[4–8] These risks are exacerbated in women in low-resource settings where lack of medical equipment, inadequately trained personnel or limited access to health facilities can lead to suboptimal management of complications.[1 4]

In 1985, the WHO suggested the appropriate CS rate to be 10–15% at the population level.[9] Since then, CS rates have increased globally to unprecedented levels[3 10] raising

concern about the consequences of this increase. Since 2015, the WHO has not endorsed an 'ideal' CS rate but rather emphasises the need to monitor CS rates in a meaningful, reliable and action-oriented manner at the healthcare facility level.[11] For this purpose, WHO recommends the Ten Group Classification, also known as Robson classification[12] as a global standard for assessing, monitoring and comparing CS rates.[11]

The Robson classification can be used to study and assess CS rates in more uniform groups of women and in relation to other perinatal outcomes and processes. More targeted interventions can be designed and implemented in each group independently and subsequently evaluated. The classification has been successfully used to identify both overuse and underuse in high-, low- and middle-income countries, thus showing value across a variety of resource levels.[13]

Sierra Leone has one of the highest maternal mortality ratio, stillbirth and neonatal death rate worldwide. Strategies implemented by the governments and partners in the country to reduce mortality have aimed to increase access to skilled attendants at birth and emergency obstetrical care, including CS.[14] In Sierra Leone, the CS rate at the national level remains low, although the country has witnessed a rapid increase in the last two decades, from 1.5% (2003–2008) to 3% (2012–2017).[3] The quality of care for surgery remains suboptimal, with a high perioperative mortality rate of 1.5% and haemorrhage, hypertensive disorders and sepsis being the most important causes of death in women undergoing a CS.[15 16] Nevertheless, the use of CS varies widely between districts[15] showing that disparities in the healthcare assistance coexist.

The aim of this study was to investigate the rate of CS, the indications, as well as maternal and newborns' outcomes at Princess Christian Maternal Hospital in Freetown, Sierra Leone, using the Robson classification. An additional objective was to identify substandard practices and recommend strategies aimed at improving maternity care.

METHODS

Study design

We conducted a cross-sectional study at the Princess Christian Maternity Hospital, in Freetown (Western Area Urban District), Sierra Leone. Our study population consisted of all women who gave birth in this hospital during a 4-month period between 1 October 2020 and 31 January 2021.

We used the Robson classification system to study women. The Robson system classifies all women admitted for birth in the facility on the basis of essential obstetrical characteristics which are routinely collected in all maternities for the clinical care of the women (parity, gestational age, number of fetuses, previous CS, on-set of labour and fetal presentation and lie). We used the WHO Implementation Manual on the Robson classification system as the main guide for the analysis and interpretation.[17]

Context

The Princess Christian Maternity Hospital (PCMH) is a tertiary-level government hospital located in Sierra Leone's capital city, Freetown. It is the main referral hospital for maternal care in the capital's Western Area district, with a catchment area of about 1 million inhabitants.

Healthcare for mothers and newborns in Sierra Leone is provided free of charge according to the Ministry of Health and Sanitation (MoHS) national 'Free Health Care Initiative'.[18 19] However, the availability of drugs and consumables is irregular and additional financial support such as donations, is essential. Doctors with Africa CUAMM is a non-governmental organisation collaborating with the MoHS and supporting PCMH since 2016 as the main technical partner.

Every year, the hospital admits about 9000 patients to the maternity ward, attends more than 6000 births, provides more than 20 000 antenatal visits and 18 000 outpatient visits for women and children, as well as comprehensive care services for obstetrical emergencies.[20] The hospital has 119 beds and includes various wards and units: general maternity, eclamptic, puerperium, postoperative, antenatal and gynaecology. The hospital employs nurses, midwives and four teams each consisting of one obstetrician/gynaecologist, one medical officer (licensed non-specialist physician), some junior doctors in quarterly rotation and one surgical community health officer, who is a staff trained to perform surgical practices such as CS, under MoHS regulation.

Variables, data collection and analysis

PCMH does not have a digitalised system for medical records. The presence of two dedicated volunteer doctors facilitated data collection during the study period. Data were obtained from patient's paper charts, labour ward and operating theatre registers, and were entered by members of the research team in a Microsoft Excel database specifically designed for this study.

Variables collected included maternal age, obstetrical history (parity, previous CS, fetal presentation), mode of birth (ie, spontaneous vaginal birth, operative vaginal birth or CS), the onset of labour (spontaneous, induced, pre-labour CS), staff who performed the CS (ie, obstetrician or surgical technicians) and the indication for CS. Moreover, we collected maternal and neonatal outcomes: maternal death, live birth, fresh stillbirth, macerated stillbirth, early neonatal death, Apgar score at 5 min.

For each woman who underwent a CS, a single indication was reported from the hospital registry. Diagnosis and definition of all pathological conditions were derived from the National Protocol and Guidelines for Emergency and Newborn Care.[21] The accuracy of the indications assigned in relation to the definitions was not verified by the data collectors. When more than one indication was recorded, we selected only one for the analysis, according to a predefined hierarchy devised for this study based on earlier proposals in the literature:[22–25] (1)

Urgent or emergency CS (severe hypertensive disorder including severe pre-eclampsia, eclampsia, antepartum haemorrhage due to abruptio placentae or placenta previa, laparotomy for uterine rupture), (2) previous CS, (3) mechanical or dynamic dystocia (obstructed and prolonged labour, cephalopelvic disproportion, transverse lie, failed induction), (4) intrapartum acute fetal distress (including cord prolapse), (5) breech presentation, (6) maternal medical causes (severe anaemia, sickle cell disease, severe malaria) (7) fetal causes other than fetal distress (macrosomia, idrocefalo, twins, intrauterine fetal death) and (8) others (elective CS, unknown, postdate, prolonged premature rupture of membranes).

For multiple pregnancies, data were registered only for the twin born first. We used birth weight >2500 g as a proxy for gestational age >37 weeks in the Robson classification. This adaptation has been suggested and previously used for the Robson classification in settings where the accurate assessment of gestational age is a challenge.[23 26]

The maternal mortality rate was defined as the number of maternal deaths over the total number of live births. Stillbirth was defined as a baby born with no signs of life after 28 weeks of gestation or weighing more than 1000 g. We defined early neonatal death as the death of a liveborn neonate, by discharge or day 7 of life whichever occurs first. Perinatal mortality was defined as the sum of stillbirths and early neonatal deaths among all deliveries.[27] The CS rate was defined as the total number of caesarean deliveries among women divided by the total number of deliveries.[3] The onset of labour was defined as regular contractions of at least three every 10 min, 100% effaced cervix and at least 4 cm dilatation.[28]

For the Robson classification, we calculated the total number and rate of CS in each of the 10 groups and both the absolute and relative contribution of each group to the total CS rate, maternal death and newborn outcomes (ie, live births, stillbirths, early neonatal deaths and newborns with an Apgar score <7 at 5 min discharged alive). We reported the indications for CS in each Robson group as the percentage of the total CS conducted in each group.[17] We also report women with incomplete information on any obstetrical variables that prevented classification within one of the Robson groups. We used the threshold for fetal viability at a birth weight <1000 g and <28 weeks' gestational age. Below this threshold, women were not included.

Patient and public involvement

No patients/members of the public were involved in the definition of the research question or outcome measures, nor in the design and implementation of the study. We have no plans to involve patients/members of the public in the dissemination of the study's results.

RESULTS

From 1 October 2020 to 31 January 2021, 1998 women delivered at the PCMH and 23 were unclassifiable in the Robson groups due to missing data. The characteristics of women and newborns are summarised in table 1.

Table 1 Characteristics of mothers and newborns, 1 October 2020 to 31 January 2021, Princess Christian Maternity Hospital, Sierra Leone (n=1998)

Maternal characteristics (n=1998)		
Age	Range	12–45
	Media	26
Parity	Parity=0	746 (37.4%)
	Parity=1	630 (31.5%)
	Parity ≥2	618 (30.9%)
	Missing	4 (0.2%)
Onset of labour	Spontaneous	1680 (84.1%)
	Induced	62 (3.1%)
	Pre-labour CS	242 (12.1%)
	Missing	14 (0.7%)
Previous CS	Yes	198 (10%)
	No	1792 (89.7%)
	Missing	8 (0.4%)
Number of fetuses	Single	1894 (94.8%)
	Multiple	101 (5%)
	Missing	3 (0.2%)
Presentation/lie	Cephalic	1849 (92.5%)
	Breech	124 (6.2%)
	Oblique/transverse	22 (1.1%)
	Missing	3 (0.2%)
Final mode of birth	Vaginal	990 (49.6%)
	Assisted vaginal*	12 (0.6%)
	Caesarean section	992 (49.6%)
	Missing	4 (0.2%)
CS operator (n=992)	Obstetrician/ gynaecologist	287 (28.9%)
	Surgical technicians	705 (71.1%)
Maternal death		9 (0.5%)
Newborn characteristics		
Birth weight	<2.5 kg	155 (7.8%)
	≥2.5 kg	1837 (91.9%)
	Missing	6 (0.3%)
Newborns outcome	Live births	1838 (92.0%)
	Stillbirths	148 (7.4%)
	Early neonatal death	8 (0.4%)
	Missing	4 (0.2%)
Apgar score at 5 min among live births	<7	294 (16.0%)
	≥7	1544 (83.8%)
	Missing	4 (0.2%)

*Forceps or vacuum.
CS, caesarean section.

The average age of the study population was 26 years and about half of women (n. 992) gave birth by CS during

Table 2 The Robson reporting table and neonatal outcomes by Robson group, Princess Christian Maternity Hospital, Sierra Leone, October 2020 to January 2021 (n=1998)

Group*	Of women in the group	Number of CS in the group	Group size (%)	Group CS rate (%)	Absolute group contribution to overall CS rate (%)	Relative contribution of group to overall CS rate (%)
1	559	238	28.0	42.6	11.9	24.0
2	71	58	3.6	81.7	2.9	5.9
2a	19	6	1.0	31.6	0.3	0.6
2b	52	52	2.6	100	2.6	5.2
3	763	249	38.2	32.6	12.5	25.1
4	80	63	4.0	78.8	3.2	6.4
4a	24	7	1.2	29.2	0.4	0.7
4b	56	56	2.8	100	2.8	5.6
5	171	163	8.6	95.3	8.2	16.4
6	46	33	2.3	71.7	1.7	3.3
7	58	40	2.9	69.0	2.0	4.0
8	99	66	4.9	66.7	3.3	6.7
9	21	20	1.0	95.2	1.0	2.0
10	107	54	5.4	50.5	2.7	5.4
Unclassifiable	23	8	1.1	34.8	0.4	0.8
Total	**1998**	**992**	**100**	**49.6**	**49.6**	**100**

Group size (%)=n of women in the group/total N women delivered in the hospital×100.
Group CS rate (%)=n of CS in the group/total N of women in the group×100.
Absolute contribution (%)=n of CS in the group/total N of women delivered in the hospital×100.
Relative contribution (%)=n of CS in the group/total N of CS in the hospital×100.
*Birth weight ≥2500 g was used as a proxy for gestational age >37 weeks.
CS, caesarean section.

the study period. More than 60% of women had one or more births previously, only 10% had a previous CS. The majority of the births (1849; 92.5%) were cephalic presentations. Onset of labour was spontaneous in 84.1% (1680) of women while only 3.1% (62) were induced. Surgical technicians performed 71.1% (705) of all CS. Regarding neonatal outcomes, 148 (7.4%) stillbirths and 8 (0.4%) early neonatal deaths have been reported with a perinatal mortality rate of 7.8%. Forceps or vacuum was used to assist birth in 12 (0.6%) women.

Table 2 shows the Robson classification including outcomes by group. Most women were in group 3, comprising multiparous women with a single-term pregnancy in spontaneous labour (38.6% of the study population) and group 1, consisting of nulliparous women with a single-term pregnancy in spontaneous labour (28.3%). Group 5 included 8.6% of the population. Groups 1 and 3, which are normally considered to be at low risk of CS, presented a CS rates of 42.6% and 32.6% while the CS rate in group 5 was 95.3%. Groups 2 and 4 had higher CS rates due to the significant contribution of the subgroups 2b and 4b (nulliparous and multiparous women, single cephalic at term who underwent CS section before labour started). About 70% if the breeches (groups 6 and 7) had a CS. In group 10, delivery was by CS in 50.5% of the cases. Group 3 was the most important contributor to the total number of CS with 25.3%, followed by group 1 with 24.2% and group 5 with 16.5%.

There were nine cases of maternal death in the study population with an overall maternal mortality rate of 0.5%. Severe neonatal outcomes accounted for: 147 (7.4%) stillbirths and eight early neonatal deaths (0.3%) with a perinatal mortality of 7.8%. Of the 1820 live births, 293 (16.1%) reported an Apgar score <7 at 5 min. The outcomes for mothers and newborns, categorised by Robson classes, are provided in the online supplemental material.

Overall, the most frequent indication for CS was dystocia with 384 (39.0%) cases, followed by urgent or emergency indications (163; 16.6%), previous CS (141; 14.3%) and intrapartum acute fetal distress (128; 13.0%). More than half of the emergencies were related to severe pre-eclampsia and eclampsia (92/163; 56.4%). Figure 1 shows the distribution of CS indications in specific Robson groups: low-risk groups 1 and 3, group 5 as women with a previous CS, group 10 as women with preterm births.

In groups 1 and 3, the major indication for CS was dystocia followed by intrapartum acute fetal distress. In group 5, about 80% of the CS had previous CS as the indication, while in high-risk group 10, emergencies were the most frequently reported indications followed by dystocia.

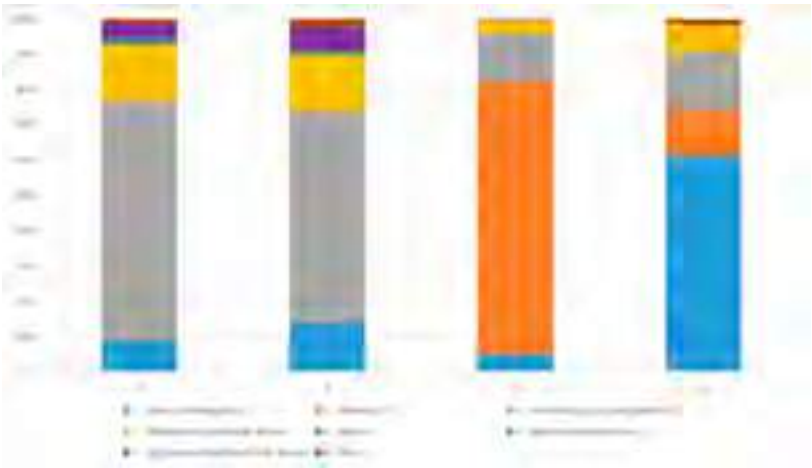

Figure 1 CS Indication among representative Robson groups, 1 October 2020 to 31 January 2021, Princess Christian Maternity Hospital, Sierra Leone (n.984). CS, caesarean section.

DISCUSSION

The Robson classification has proven to be easily applicable even in settings with high organisational complexity and a large number of births, such as PCMH. In fact, only 1.2% of the records of women who gave birth during the study period lacked the necessary information to allow its application. However, the need for volunteer intervention for dedicated data collection indicates that, for now, such evaluations are only being captured for research purposes and the conditions are not yet in place for them to be performed routinely and continuously as recommended.[29 30] During the study period, the overall CS rate at the PCMH was 49.6%, consistent with the rapid increase previously observed from 29.6% in 2016 to 47.6% in 2020.[20] The maternal and perinatal mortality in the study were, respectively, 0.5% (9 maternal deaths) and 7.8% (148 stillbirths and 8 early neonatal death). Robson groups 1 and 3 were the largest (two-thirds of the women giving birth in PCMH) showing that most women enter labour spontaneously. Robson groups 1, 3 and 5 cumulatively contributed more than 65% of the total of CS (24%, 25.1% and 16.4%, respectively), consistent with other analysis reported from Africa.[23 26 31] The CS rates in group 1 and 3 were very high, 42.6% and 32.6%, respectively,[17] with poor neonatal outcomes, with 4.1% of perinatal mortality and 15% of newborns with Apgar scores below 7 at 5 min in group 1, and 5.8% of perinatal mortality and 13.2% of newborns with Apgar scores below 7 at 5 min in group 3. In-depth analysis of these groups are warranted.

The WHO Robson Implementation Manual suggests that the ratio between spontaneous and induced women (group 1: group 2) should be 2:1 or higher. In PCMH, the ratio is 7:1 which is extremely high and may suggest that an increase in the rate of inductions is expected to be beneficial. The overall rate of births with induction in our population was 3.1%. Although it is a value similar to the average of 4.4% observed in other African countries,[32] it may be insufficient considering the suboptimal outcomes. As in many low-resource settings, many factors hinder the appropriate use of induction of labour in PMCH, such as delayed access of pregnant women to health facilities due to transport difficulties and socioeconomic barriers, scarcity or unavailability of drugs, poor antenatal care attendance, poor training of health personnel and traditional beliefs.[33 34]

As a tertiary level and referral hospital for a large catchment area, PCMH receives many high-risk cases and obstetrical complications. Despite the high CS rate registered at the hospital level, the CS rate at the population level remains very low at less than 5%.[35] In many low-resourced setting, the referral status and therefore the emergencies received, contribute substantially to the CS rate.[36] In PCMH, referred women accounted for more than 30% of total admissions in 2020,[20] and are likely to contribute substantially to the high CS rate within the hospital. Because birth registries did not report referral status, we could not report the referral rate among the women who underwent CS in the study.

Dystocia was the indication in 19% of the CS, similar to that found in a multicentre study in sub-Saharan Africa of 18%.[37] Dystocia was the most frequent indication for CS in groups 1 and 3, responsible for approximately 50% of CS for both groups, similar to what was observed in other studies in Tanzania[23] and Uganda.[38] Dystocia is the major indication for primary CS[39–41] especially among nulliparous women[40 41] and our findings support this evidence (24% CS for dystocia in nulliparous vs 16% CS for dystocia in multiparous in our study). This warrants an in-depth analysis to assess the management of women with dystocia. Improving the access and quality of antenatal care[41 42] as well as the appropriate utilisation of partograph and intrapartum fetal monitoring are known as crucial strategies to prevent CS in women

with dystocia.[43] However, in PCMH, referrals of complicated deliveries from birth centres without the capacity to perform CS contribute significantly to the dystocia diagnosis.[36] The dramatic discrepancy between the CS rate in PCMH versus the population-based CS rate is consistent with this observation.[15] We endorse the previous evidence calling for a nationwide effort aimed at increasing the availability of this life-saving procedure.[15]

In our study, over 70% of CSs were performed by surgical technicians. However, unfortunately, it was not possible to record who made the decision to perform the CS, and consequently, we are unable to investigate the decision-making process underlying the different indications for CS. This aspect warrants further investigation, especially considering that the PCMH has transitioned into a University Teaching Hospital and can now rely on mentors and residents who can guide less skilled personnel. Furthermore, the introduction of a mandatory second opinion for CS indication has been recommended to reduce CS births in settings with adequate resources.[4] However, considering the low-resource, understaffed healthcare system in Sierra Leone, we recognise that this intervention may be difficult to implement in this context.

The low proportion of operative vaginal deliveries (0.6%) also is likely to contribute to the high number of CS, as also observed in a study conducted in Ethiopia.[44] This aspect can be addressed by improving staff training in the identification of women suitable for the procedure and in the use of forceps and vacuum extractor.[45]

The CS rate in women with a previous CS (group 5) was 95%. Although guidelines suggest that rates of 50–60% are appropriate, much higher rates are observed particularly in low and middle income countries.[26] This finding also suggests a great difficulty in attempting a trial of labour after caesarean section (TOLAC). In PCMH, TOLAC was rarely proposed to eligible women which would be subject to the skills of the medical team on duty. The scarcity of equipment for monitoring the woman in labour, the unavailability of cardiotocographic monitoring and the absence of accurate data regarding fetal biometry, make it very difficult to ensure the proper management of TOLAC on eligible women, as other studies in Africa suggest.[46–48]

Robson groups 2 and 4 recorded disproportionate CS values (81.6% and 78.7%, respectively) when compared with the reference values of 25–30% and 15%.[17] The low number of inductions (groups 2a and 4a; 6 and 7 women, respectively) compared with the higher numbers of prelabour CS (groups 2b and 4b; 52 and 56 women, respectively) explained the resulting high CS rate in groups 2 and 4. Among the CS in group 2b, 21 (40.3%) were urgent or emergency CS, 17 (32.7%) had indication of intrapartum acute fetal distress. Similarly, in group 4b, 26 (46.4%) had an emergency indication, while 11 (19.6%) were performed for intrapartum fetal distress.

Robson group 10 (premature fetuses) represented about 5% of the women in PCMH and had a CS rate of 50.4%. This high CS rate is usually related to numerous cases of high-risk pregnancies, as fetal growth restriction or eclampsia,[17] requiring to terminate the pregnancy despite prematurity. Excessive recourse to CS in these cases could be explained by the fear of providers to potential peripartum or intrapartum complications.[11] In sub-Saharan Africa, the prevalence of hypertensive disorders in pregnancy is high, up to 8%.[49] At PCMH, 11% of women were diagnosed with hypertensive disorders in 2020, and for 16 women it was the cause of peripartum maternal death, contributing 17% to the total maternal deaths in the year (n=48). In our study, almost one-third of the eclampsia cases occurred in group 10 ([16]; 29.3%), which could explain the high CS rate of the group. On the other hand, dystocia accounted for more than 18% of the CS in group 10, which is counterintuitive to the characteristics of the group itself. This suggests that there may be misreporting of indications, misdiagnosis or misclassification of women (term women classified in this group incorrectly). In-depth analyses of this group, including assessment of gestational age are warranted. The development of protocols for standardised classification of indications reinforcing diagnostic pathways for obstetrical complications should be considered.

Our study has some limitations. The indications for CS were extracted retrospectively from the patients' medical records at face value and when multiple indications were reported, we used a hierarchy to assign the indication.[24] The low reproducibility of classifying indications is well-recognised in the literature.[22] This is exacerbated in PCMH by the absence of guidelines for reporting and classifying CS indications. For twin pregnancies, only outcomes for the first baby were recorded, which may have underestimated the proportion of adverse neonatal outcomes. Maternal and neonatal deaths occurring after discharge were not captured, therefore maternal and perinatal mortality may have been under-reported. In the absence of reliable data on gestational age, we used birth weight as a proxy, an approximation that has been used in earlier studies implemented in low-resource settings. Lastly, data collection took place during the COVID-19 pandemic, which may have impacted hospital access, deliveries, obstetrical complications and CSs. Further studies could be conducted to investigate the role of the pandemic on CS rates in these settings.

CONCLUSION

Our study showed that half of the women who give birth at PCMH underwent CS. Analysis using the Robson classification depicts that groups 1 and 3 constitute two-thirds of the obstetrical population and present very high CS rates (43% and 33%, respectively) with poor newborn outcomes despite being usually considered at low risk. While dystocia was the leading indication for CS in these groups (about 60%), induction of labour may be underused, contributing to suboptimal outcomes. Almost all women with a previous CS underwent CS again (95%), showing rare recourse to TOLAC.

The more appropriate use of labour induction, careful monitoring of obstetrical complications and intrapartum maternal-fetal status, effective training to conduct operative deliveries and TOLAC could be key strategies to improve the appropriate use of CS and the quality of obstetrical care. However, the interpretation of the high number of CSs should take into account that PCMH centralises complicated cases from a very wide catchment area, and the population CS rate remains insufficient according to WHO recommendations. The evaluation of CS according to the Robson classification should be routinely and prospectively introduced into clinical practice to improve the quality of the information collected and enable the monitoring of quality improvement interventions. Further research should be carried out to investigate the contribution of cases referred from other facilities to the CS rate at the hospital level, and an in-depth analysis of the management of women with dystocia and with a previous CS.

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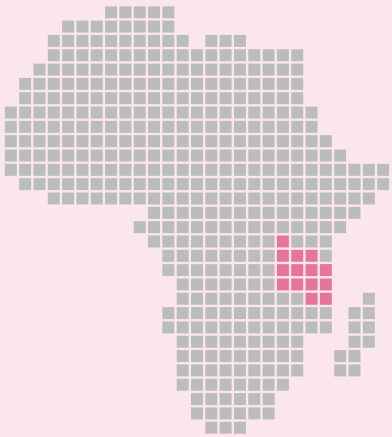

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Factors associated with mortality and neurodevelopmental impairment at 12 months in asphyxiated newborns: a retrospective cohort study in rural Tanzania from January 2019 to June 2022

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Abstract

Background Worldwide about 2.3 million newborns still die in the neonatal period and the majority occurs in low- and middle-income countries (LMICs). Intrapartum-related events account for 24% of neonatal mortality. Of these events, intrapartum birth asphyxia with subsequent neonatal encephalopathy is the main cause of child disabilities in LMICs. Data on neurodevelopmental outcome and early risk factors are still missing in LMICs. This study aimed at investigating the factors associated with mortality, risk of neurodevelopmental impairment and adherence to follow-up among asphyxiated newborns in rural Tanzania.

Methods This retrospective observational cohort study investigated mortality, neurodevelopmental risk and adherence to follow-up among asphyxiated newborns who were admitted to Tosamaganga Hospital (Tanzania) from January 2019 to June 2022. Neurodevelopmental impairment was assessed using standardized Hammersmith neurologic examination. Admission criteria were Apgar score < 7 at 5 min of life and birth weight > 1500 g. Babies with clinically visible congenital malformations were excluded. Comparisons between groups were performed using the Mann-Whitney test, the Chi-square test, and the Fisher test.

Results Mortality was 19.1% (57/298 newborns) and was associated with outborn ($p < 0.0001$), age at admission ($p = 0.02$), lower Apgar score at 5 min ($p = 0.003$), convulsions ($p < 0.0001$) and intravenous fluids (IV) ($p = 0.003$). Most patients (85.6%) were lost to follow-up after a median of 1 visit (IQR 0–2). Low adherence to follow-up was associated with female sex ($p = 0.005$). The risk of neurodevelopmental impairment at the last visit was associated with longer travel time between household and hospital ($p = 0.03$), female sex ($p = 0.04$), convulsions ($p = 0.007$), respiratory distress ($p = 0.01$), administration of IV fluids ($p = 0.04$), prolonged oxygen therapy ($p = 0.004$), prolonged hospital stay ($p = 0.0007$) and inappropriate growth during follow-up ($p = 0.0002$).

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Conclusions Our findings demonstrated that mortality among asphyxiated newborns in a rural hospital in Tanzania remains high. Additionally, distance from home to hospital and sex of the newborn correlated to higher risks of neurodevelopmental impairment. Educational interventions among the population about the importance of regular health assessment are needed to improve adherence to follow-up and for preventive purposes. Future studies should investigate the role of factors affecting the adherence to follow-up.

Keywords Neonatal asphyxia, Low- and middle-income countries, Mortality, Risk factors, Post-discharge follow up, Neurodevelopmental impairment

Background

Worldwide, the mortality rate of children under five years has been dramatically reduced in the last 20 years, while neonatal mortality now accounts for the majority of such deaths [1]. Around 7,000 neonates die every day and 99% of these deaths occur in low- and middle-income countries (LMICs) [1–3].

Intrapartum-related events account for 24% of all neonatal deaths and represent the second cause of neonatal mortality after complications due to prematurity [4, 5]. Of note, the neonatal mortality rate is nine times higher in LMICs with respect to high-income countries (HICs) [4].

Within the intrapartum related events, birth asphyxia represents an acute insult to the fetus or newborn which is characterized mainly by tissue hypoxia that may be associated with ischemia [6].

In HICs, hypoxic-ischemic injury (HII) is defined based on clinical appearance and biochemical markers. HII may lead to various degrees of acute illness such as metabolic derangements, poor muscle tone, breathing problems, alteration in consciousness and seizures which may ultimately result in early neonatal death. Long term morbidities and chronic conditions are mostly represented by neurodevelopmental disorders such as disability (learning and behavioral), poor feeding and cerebral palsy [6].

The standard care for neonates with birth asphyxia in LMICs should remain normothermia, avoiding both hyper- and hypothermia [7, 8]. Every deviation from euthermia (36.5°-37.5°) at admission in the neonatal unit has been associated with an increased risk of mortality [9]. A recent study in Tanzania suggested that deviations from euthermia at admission may also be associated with an increased risk of developing cerebral palsy in survivors at one month of life [10].

In LMICs, the diagnosis of perinatal asphyxia is usually performed according to clinical assessments such as the Apgar score and the neurological evaluation by Sarnat&Sarnat [11]. This neurological evaluation assesses level of consciousness, motility, posture, tone, reflexes and the pupil, leading to the classification in different stages of HII (mild, moderate and severe) that have been associated with early neurological status and short-term prognosis [11].

Early recognition of risk for neurodevelopmental impairment is highly desirable in the first period of life because of the prognostic role of early interventions in the period of greatest brain development and neuroplasticity. However, a detailed neurologic examination may be insufficient when used as the only diagnostic tool and a more comprehensive assessment should ideally encompass brain imaging such as functional Magnetic Resonance Imaging (fMRI) or cranial ultrasound, tools that are mostly not available in LMICs [12].

Before five months of corrected age, the most predictive tools to detect risk of neurodevelopmental impairment are magnetic resonance imaging (86–89% sensitivity), the Prechtl Qualitative Assessment of General Movements (98% sensitivity), and the Hammersmith Infant Neurological Examination (90% sensitivity). After five months of corrected age, the most predictive tools for detecting risk are magnetic resonance imaging (86–89% sensitivity) (where safe and feasible), the Hammersmith Infant Neurological Examination (90% sensitivity), and the Developmental Assessment of Young Children (83% C index) [13].

In LMICs, the most used clinical evaluation in the first year of life is the Hammersmith Infant Neurological Examination performed by skilled personnel according to different stages of life [14].

Child disability is still a serious problem worldwide with 1.3 million newborns surviving each year with major disabilities and 1 million with long-term moderate or mild disability, such as learning and behavior difficulties. In LMICs almost 80% of child disabilities are related to a perinatal brain injury, of which neonatal encephalopathy is the most prevalent cause leading to a substantial burden of preventable childhood neurodisabilities such as cerebral palsy, epilepsy, deafness, and blindness. Limited high quality evidence is available on prevention and management of neonatal encephalopathy in these settings [15].

Simiyu et al. analyzed a similar cohort of asphyxiated newborns in a tertiary hospital in northern Tanzania. Severity of HII was classified according to the Sarnat and Sarnat scoring at birth and at seventh day of life. Mortality among asphyxiated newborns was 12.3%. Newborns with mild and moderate HII showed improvement at Sarnat and Sarnat scoring at 1 week of life [16].

In low-resource countries, data about long term disabilities of babies surviving intrapartum complications are mostly not even available and rehabilitation services are very limited [17–21]. In HICs, two in three individuals with cerebral palsy will walk, three in four will talk, and one in two will have normal intelligence [13].

The objective of this study was to investigate the risk factors for mortality among asphyxiated newborns in a Neonatal Intensive Care Unit (NICU) in rural Tanzania. Furthermore, this study aimed at analysing the risk factors for neurodevelopmental impairment at follow-up and the factors associated to adherence to follow-up.

Methods

Study design

This was a retrospective observational cohort study on the risk factors formortality, neurodevelopmental impairment, and adherence to follow-up among asphyxiated newborns in rural Tanzania.

Institutional context and institutional background

The study was performed at the Tosamaganga Regional Referral Hospital (Tosamaganga Hospital), which is a non-profit, faith-based secondary-level hospital located in the Iringa District Council (IDC), Iringa region in Tanzania. IDC is a rural district in South-Western Tanzania that covers approximately 320,000 people [22]. In 2023, Tosamaganga Hospital registered 3,503 deliveries and 715 admissions to the NICU unit.

Doctors with Africa CUAMM (University College of Aspiring Medical Missionaries) is an Italian Non-Governmental Organization (NGO) supporting health service delivery in Africa for more than 70 years. In the region of Iringa, Doctors with Africa CUAMM has implemented several projects to strengthen the local health system, particularly in the field of maternal and child health.

Patients

All neonates admitted to the NICU of Tosamaganga Hospital between 1st January 2019 and 30st June 2022 with a diagnosis of asphyxia and birth weight > 1500 g were retrospectively evaluated for inclusion in the study. According to Tanzanian guidelines [23], neonatal asphyxia was diagnosed if the Apgar score at 5 min of life was minor than 7. Babies with clinically visible congenital malformations were excluded.

Data collection

All data were extrapolated from the Health Information Management System (HMIS) currently in use at Tosamaganga Hospital and collected in a dedicated electronic spreadsheet after being anonymised. This process involved clinical staff employed by both Tosamaganga Hospital and CUAMM. All analyses were performed in the second semester of 2023.

The analysis of risk factors for mortality included discharge status, mode of delivery, being outborn or inborn, age at admission in NICU, sex, birth weight, twin pregnancy, Apgar score at 5 min of life, presence of meconium at delivery, body temperature at admission, presence of respiratory distress, convulsions, administration of IV fluids, antibiotic therapy, oxygen therapy and length of hospital stay.

Follow-up information included number of follow-up visits, age and weight at last visit, inappropriate growth, and risk of neurodevelopmental impairment at first and last visits. Inappropriate growth at follow-up was assessed by comparing weight at discharge and at last follow-up visit using growth percentiles according to the World Health Organization (WHO) growth charts. The neurological status was assessed during a 12-month follow-up using the Hammersmith neonatal or infant neurologic examination charts according to age [14]. Infants were classified as at risk of neurodevelopmental impairment if two or more abnormal items were found.

The analysis of factors associated with neurodevelopmental impairment risk at follow-up included travel distance and time from household to hospital, delivery information (mode of delivery, outborn/inborn), neonatal data (age at admission, sex, birth weight, twin pregnancy, Apgar score at 5 min of life, presence of meconium at delivery, body temperature at admission, presence of respiratory distress and convulsions), information during hospital stay (administration of IV fluids, antibiotic therapy, oxygen therapy and length of stay) and inappropriate growth at follow up.

The analysis of factors associated with adherence to follow-up included travel distance and time from household to hospital, sex, and birth weight.

Statistical analysis

Numerical data were summarized as median and interquartile range (IQR), while categorical data as absolute and relative frequency (percentage). Comparisons between groups were performed using the Mann-Whitney test, the Chi-square test, and the Fisher test, as appropriate. Multivariable analyses were not performed due to the small number of events compared to the candidate risk factors of interest. All tests were two-sided and a p-value less than 0.05 was considered statistically significant. The statistical analysis was carried out with R 4.3 (R Foundation for Statistical Computing, Vienna, Austria) [24].

Results

The analysis included 298 children who were hospitalized during the study period and met the inclusion criteria. Patient characteristics are summarized in Table 1. Additionally, we reported the study's patient flow chart in Fig. 1.

Overall, 61.1% of babies were born through vaginal delivery (45.1% from spontaneous delivery and 16% assisted via vacuum extraction) and 38.9% through a C-section (almost all emergency C-sections). Only 5.7% of babies were outborn and referred to the study hospital for birth complications. Median birth weight was 2,995 g (IQR 1,670-3,290). Of note, 47.6% of the births in 2020–2022 presented meconium-stained fluid at delivery, while such information was not available in the records of infants born in 2019. Median temperature at admission was 35.4 °C (IQR 34.7–36.0). Clinical diagnosis of convulsion was present in 32.2% of babies. As per local protocol, almost all babies (95%) received antibiotic treatment at admission, while IV fluids were administered to 64.4% of babies.

Median length of hospital stay was 7 days (IQR 5–10). Overall, 57 patients died (19.1%) while 241 were alive at discharge (80.9%). Alive patients included 236 discharged at home by a doctor, two self-discharged, and three transferred patients. Mortality was associated with outborn ($p<0.0001$), older age at admission ($p=0.02$), lower Apgar score at 5 min ($p=0.003$), convulsions ($p<0.0001$), and administration of IV fluids ($p=0.003$) (Table 1).

Figure 1 reports follow-up adherence in 236 improved patients. After discharge, most patients (202/236, 85.6%) were lost to follow-up after a median of 1 visit (IQR 0–2), and 33.2% of them (67/202) did not even attend the first follow-up visit. Thirty patients attended a regular follow-up with a median of 5 visits (IQR 5–6), while four patients were readmitted after a median of 3 visits (IQR 2–3). No follow-up information was available for self-discharged ($n=2$) and transferred ($n=3$) patients.

Follow-up information in 169 improved patients who attended at least one follow-up visit is reported in the Supplementary Material. In 30 closed patients (those who completed the 12 months follow-up), inappropriate growth was found in 50% and the risk of neurodevelopmental impairment decreased from 50% at first visit to 13.3% at last visit. In 135 defaulted patients (those who were lost to follow-up), inappropriate growth was found in 34.6% and the risk of neurodevelopmental impairment was around 30%. Four patients were readmitted at median 2 months of age with half of them showing inappropriate growth and were at risk of neurodevelopmental delay.

The factors associated with the risk of neurodevelopmental impairment at the last visit are reported in Table 2. The risk of neurodevelopmental impairment at the last visit was associated with longer travel time between household and hospital ($p=0.03$), female sex ($p=0.04$), convulsions ($p=0.007$), respiratory distress ($p=0.01$), administration of IV fluids ($p=0.04$), prolonged oxygen therapy ($p=0.004$), prolonged hospital stay ($p=0.0007$) and inappropriate growth during follow-up ($p=0.0002$).

Mode of delivery (either spontaneous, assisted via vacuum, or cesarean section) was not found to be statistically associated with increased mortality (Table 1) nor with increased risk for developmental impairment during follow-up (Table 2).

Table 1 Patient characteristics in the whole sample and stratified by mortality outcome

	All patients ($n=298$)	Discharged/transferred ($n=241$)	Deceased ($n=57$)	*p*-value
Delivery:	124/275 (45.1%)	105/223 (47.1%)	19/52 (36.5%)	0.32
Spontaneous vaginal	44/275 (16.0%)	33/223 (14.8%)	11/52 (21.2%)	
Assisted vaginal	107/275 (38.9%)	85/223 (38.1%)	22/52 (42.3%)	
C-section				
Outborn	17/297 (5.7%)	7/240 (2.9%)	10 (17.5%)	< 0.0001
Age at admission, days	1 (1–1)	1 (1–1)	1 (1–2)	0.02
Males	179/297 (60.3%)	143/240 (59.6%)	36 (63.2%)	0.73
Twins	8 (2.7%)	8 (3.3%)	0 (0.0%)	0.36
Apgar score at 5 min	5 (4–6)	5 (4–6)	5 (3–5)	0.003
Birth weight, gr	2995 (1670–3290)	3000 (2660–3300)	2950 (2670–3270)	0.75
Temperature at admission, °C	35.4 (34.7–36.0)	35.4 (34.7–36.0)	35.3 (34.7–36.2)	0.87
Convulsions	96 (32.2%)	64 (26.6%)	32 (56.1%)	< 0.0001
Meconium-stained amniotic fluid (not available in 2019)	89/187 (47.6%)	74/151 (49.0%)	25/36 (41.7%)	0.54
IV fluids	192 (64.4%)	145 (60.2%)	47 (82.5%)	0.003
Antibiotic therapy	283 (95.0%)	228 (94.6%)	55 (96.5%)	0.74
Respiratory distress	202 (67.8%)	160 (66.4%)	42 (73.7%)	0.35
Oxygen therapy, days	2 (1–5)	2 (1–7)	2 (1–3)	0.87

Data summarized as n/N (%) or median (IQR)

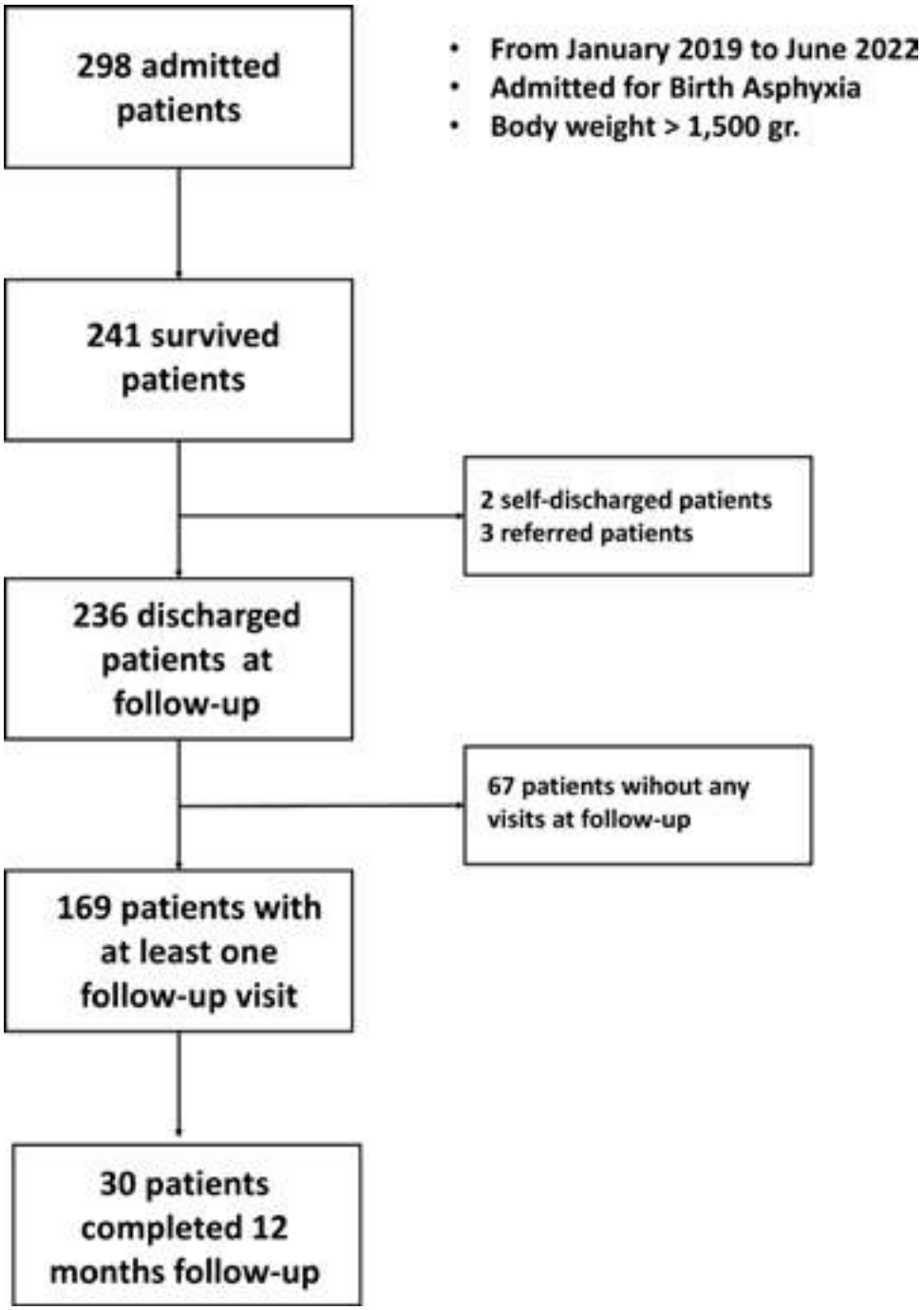

Fig. 1 Patient Flow Chart of the study

Table 2 Factors associated with the risk of neurodevelopmental impairment at the last visit

	Patients without neurodevelopmental risk at the last visit (*n* = 122)	Patients with neurodevelopmental risk at the last visit (*n* = 45)	*p*-value
Distance between household and hospital, km	29 (12–40)	35 (20–52)	0.07
Travel time between household and hospital, min	41 (20–55)	46 (31–72)	0.03
Delivery: Spontaneous vaginal Assisted vaginal C-section	48/112 (42.9%) 20/112 (17.8%) 44/112 (39.3%)	26 (57.8%) 3 (6.7%) 16 (35.5%)	0.11
Outborn	3/121 (2.5%)	3 (6.7%)	0.35
Age at admission, days	1 (1–1)	1 (1–1)	0.82
Males	69/121 (43.0%)	11 (24.4%)	0.04
Twins	5 (4.1%)	0 (0.0%)	0.33
Apgar score at 5 min	5 (4–6)	5 (4–6)	0.24
Birth weight, gr	2995 (2662–3308)	3100 (2730–3300)	0.47
Body temperature at admission, °C	35.4 (34.7–36.0)	35.3 (34.8–35.9)	0.85
Convulsions	29 (23.8%)	21 (46.7%)	0.007
Meconium (not available in 2019)	37/82 (45.1%)	16/28 (57.1%)	0.38
IV fluids	70 (57.4%)	34 (75.6%)	0.04
Antibiotic therapy	117 (95.9%)	42 (93.3%)	0.78
Respiratory distress	80 (65.6%)	39 (86.7%)	0.01
Oxygen therapy, days	2 (1–6)	5 (2–13)	0.004
Length of hospital stay, days	8 (7–11)	12 (8–17)	0.0007
Inappropriate growth	35 (28.7%)	28 (62.2%)	0.0002

Data summarised as n (%) or median (IQR)

Table 3 Factors associated with adherence to follow-up

	Discharged patients:		
	Closed patients* (*n* = 30)	Defaulted patients** (*n* = 202)	*p*-value
Distance between household and hospital, km	22 (14–36)	35 (20–54)	0.07
Distance between household and hospital, min	34 (20–53)	46 (30–69)	0.07
Males	20 (66.7%)	76/201 (37.8%)	0.005
Birth weight < 2500 gr	6 (16.7%)	32 (15.8%)	0.99

Data summarised as n (%) or median (IQR)

*Closed = patients who completed 12 months' follow-up

** Defaulted = patients lost to follow-up

Low adherence to follow-up was associated with female sex ($p = 0.005$) but not with the other factors considered (Table 3).

Discussion

Our findings confirmed that neonatal mortality in LMICs remains a significant burden and is associated with preventable and treatable conditions, underlying the importance of improving prenatal and perinatal care among asphyxiated newborns in such settings [9, 25].

In our cohort, around one out of five newborns died after a few days of life, in agreement with previous studies showing that most deaths due to intrapartum-related complications occur in the first week of life [26, 27]. In addition, perinatal complications, such as meconium-stained amniotic fluid at birth and respiratory distress, convulsions and hypothermia were common among asphyxiated newborns. Our findings suggested the association of higher mortality risk with being outborn, older age at admission, lower Apgar score at 5 min, convulsions and administration of IV fluids. Differently from HICs, neonatal mortality in LMICs usually occurs from preventable and treatable conditions [6, 28]. Previous investigations indicated being outborn, low 5-minutes Apgar score, depressed clinical status at NICU admission, occurrence of infection or seizures within 24 h from admission and receiving aminophylline during hospital stay as risk factors for mortality [25]. The prognosis of aspyxiated newborn born outside the hospital was strictly related to the availability of a referral system [29]. Ambulances connecting health centers and Tosamaganga Hospital are often not running due to a lack of maintenance or fuel shortage. Strengthening the referral system is a central issue in the secondary prevention of birth asphyxia [30]. Moreover, adequate neonatal resuscitation skills and equipment are fundamental in the prevention

of perinatal asphyxia [30]. In particular, frequent retraining of the health personnel attending women during delivery could be a strategy to maintain a good quality of service [31]. Finally, interventions of primary prevention for birth asphyxia (i.e. improving antenatal care services, developing coverage, equity and quality of the obstetric supply, women's education, and empowerment) generally have the greatest impact in improving health outcomes [30].

Unfortunately, we were unable to differentiate the primary cause of death (such as meconium aspiration syndrome and persistent pulmonary hypertension as causes of respiratory insufficiency, level of metabolic derangement, confirmation of infection, birth trauma or intracranial hemorrhage) due to the limited availability of diagnostic instruments in the study setting. Thus, the primary diagnosis was based on the clinical evaluation by the attending clinician, while more information about the neonatal neurological status using validated scoring systems, such us Sarnat and Sarnat score, may provide important clues to short- and long-term prognosis [32].

International literature offers scarce information on the follow-up of neonates with perinatal complications in LMICs [13, 33]. In the study setting, neonatal follow-up of discharged patients started in 2019 and, to our knowledge, this is the first study evaluating long-term follow-up characteristics of asphyxiated newborns in Tanzania. Our data highlighted that one of the most important barriers to the study of long-term neurodevelopmental outcomes in LMICs was the low adherence to follow-up after discharge from NICU. Most patients in the present study lost to follow-up after a median of one visit and a considerable proportion never attended any follow-up visits at all.

We analysed the factors associated with low adherence to follow-up and found that male patients were more likely to attend follow-up visits. Thes results agreed with data reported in a systematic review showing that care-seeking rates were lower for female vs. male neonates in south Asia, especially in households with older female children [34]. The authors argued that parents were prone to pay more and seek high-quality care for males than females, and such difference in care-seeking behavior might partially explain the higher mortality among female neonates in South Asia. The promotion of policies supporting gender equality and context-specific strategies with local partners may challenge the socio-economic and cultural norms that led to such inequality [35]. Moreover, further investigations should consider the role of travel distance from the household to the hospital, which may affect the adherence to follow-up [35].

Unfortunately, the limited sample size prevented us from drawing strong conclusions on this matter. Of course, we also acknowledge that other socio-economic and cultural factors may be involved in the low adherence to follow-up.

Results in the small group of those attending the follow-up clinic suggested the association of neurodevelopmental impairment with longer travel time between household and hospital, female sex, convulsions, respiratory distress, administration of IV fluids, prolonged oxygen therapy and hospital stay, and inappropriate growth during follow-up. Of note, these factors may be prevented or reduced by improving antenatal and peripartum care, thus reducing the neonatal burden of morbidity and mortality [30].

Low-income settings suffer from constraints in terms of preventive, diagnostic, and therapeutic strategies, as well as access to adequate health care structures. [34] Most of the population of the sub-Saharan area still live in the rural countryside, where proper and safe means of transportation are often unavailable or unaffordable [29]. From a cultural point of view, educating the population about the importance of health assessment by healthcare personnel for preventive purposes and not only for acute health issues still represents a challenge. This consideration is consistent with the relevant proportion of neonates who were considered at risk of neurodevelopmental impairment at the first follow-up visit. In addition, we found a high proportion of inappropriate growth during follow-up, suggesting that many survivors from perinatal asphyxia may suffer from eating difficulties probably due to neurological compromise [36].

Further evaluations may assess how many of these patients will be affected by malnutrition in their childhood. Overall, we agreed that interventions aiming at improving the comprehensive care of the newborn should focus on strengthening the continuum of care including fetal, intrapartum, postnatal and early childhood period [37].

This study suffers from some limitations that pave the way for further research opportunities. Firstly, the retrospective data collection limited data availability and precluded any causal associations. Seconddly, the single-center design restricted the generalizability of the findings to similar settings. Thirdly, the low adherence to follow-up visits reduced the sample size for the investigation of risk factors for of neurodevelopmental impairment, suggesting caution in the interpretation of such findings.

Conclusions

Our findings confirmed that neonatal mortality in LMICs remains a significant burden and is associated with preventable and treatable conditions, underlying the importance of improving prenatal and perinatal care in such settings. The low adherence to follow-up after discharge, and the magnitude of inappropriate growth and

neurodevelopmental impairment found, highlighted the urgent need for educational interventions among the population about the importance of regular health assessment for preventive purposes. Future studies should investigate the role of travel distance from household to hospital on the adherence to follow-up, and evaluate appropriate interventions to improve post-discharge care of neonates who suffered from perinatal complications in LMICs.

Abbreviations

[LMIC]	Low and middle-income country
[IV]	Intravenous fluids
[HIC]	High-income countries
[HII]	Hypoxic-ischemic injury
[IDC]	Iringa District Council
[FMRI]	Functional Magnetic Resonance Image
[NICU]	Neonatal Intensive Care Unit
[IDC]	Iringa District Council
[CUAMM]	University College of Aspiring Medical Missionaries
[NGO]	Non-Governmental Organization
[WHO]	World Health Organization
[IQR]	Interquartile range

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-024-06837-w.

Supplementary Material 1

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Author contributions
EM1, MB and DT designed the study. EK, EM2, CM collected the data. FC, EM1, MB analyzed the data. EM1 wrote the first original draft and MB, BP, FC, DT, and AS contributed to the final version. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All data were retrieved from hospital records by hospital staff and were collected in an anonymized dataset. The study was approved by the Review Board of Tosamaganga Hospital (protocol number DOIRA/TVAH/VOL/56/02), which waived the need for written informed consent given the retrospective nature of the study and the use of anonymized data from hospital records.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Publisher's note

Nursing and midwifery simulation training with a newly developed low-cost high-fidelity placenta simulator: a collaboration between Italy and Ethiopia

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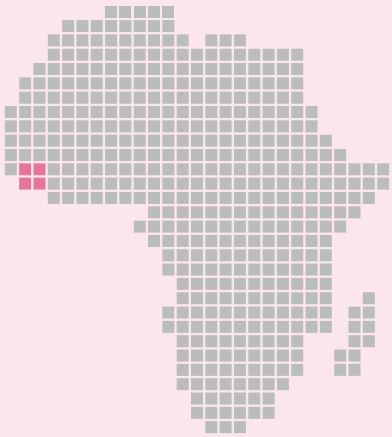

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RESEARCH Open Access

Nursing and midwifery simulation training with a newly developed low-cost high-fidelity placenta simulator: a collaboration between Italy and Ethiopia

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Abstract

Background Simulation training provides safe environment for skill acquisition and retention. This study addresses a critical challenge in Africa – umbilical cord and placenta management after childbirth – aiming to bridge theoretical learning with practical experiences through simulation. We realized a new low-cost high-fidelity simulator of placenta and umbilical cord. We conducted a needs-based training course for nursing and midwifery students at St. Luke Hospital of Wolisso, Ethiopia, to validate our new simulator and compare its acceptability and teaching effectiveness with other two simulators (conventional low-fidelity model and human placenta).

Methods We surveyed St. Luke Hospital medical experts to obtain their feedback on the new simulator's face, content, and usability. We carried out a simulation training course for 67 students who received theoretical lectures and simulation courses being divided into three groups according to the simulator used. We assessed the simulators' user acceptability using the Technology Acceptance Model (TAM) and compared the final objective evaluations by tutors between groups.

Results Experts confirmed the new simulator's fidelity, material quality, and usability. Students training on the new simulator demonstrated higher objective scores and perceived it as more useful and user-friendly compared to human placenta, while there was no difference between conventional simulator and human placenta in the TAM items.

Conclusion We validated a new high-fidelity simulator developed by the Sant'Anna School of Advanced Studies in Pisa, Italy, using the TAM scale and robust statistical methods, thanks to a successful collaboration with St. Luke's Hospital in a simulation training course where students achieved higher objective scores and perceived the simulator

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as more useful and easier to use than a real human placenta, suggesting significant educational benefits and potential for future research.

Keywords Placenta, Umbilical cord, Simulation, Training, Midwifery, Nursing, Ethiopia

Introduction

Simulation training is a valuable tool in healthcare education, enabling safe skill acquisition, practice, and knowledge retention [1, 2]. Recent advances in African higher education have seen the successful implementation of physical simulation [3], boosting confidence and satisfaction among medical students [4, 5]. This study addresses a crucial aspect of healthcare, i.e. the management of the umbilical cord and placenta after childbirth.

Umbilical cord care and placenta management after childbirth are crucial for preventing infections, promoting healing, and ensuring the well-being of both the mother and newborn. Proper management reduces the risk of complications like hemorrhage and infection, which are significant causes of maternal and neonatal mortality. However, many healthcare providers, especially in low-resource settings, lack adequate training in these areas, leading to inconsistent practices and poor outcomes. Improved education and training are essential to standardize care, enhance safety, and reduce preventable deaths related to childbirth [6, 7].

Umbilical cord care and placenta management after childbirth are a matter of particular significance in the African context, especially due to a substantial lack of related education. Recent research confirmed the relevance of this issue, highlighting the prevalence of unsafe cord-care practices and low maternal knowledge of interventions such as chlorhexidine gel in Africa, which contribute to neonatal sepsis and mortality [8, 9].

Simulation training bridges classroom learning and real-world clinical experiences, offering benefits such as enhanced patient safety, error prevention, replicable case scenarios, increased confidence, and collaborative team training [10–12]. Simulation training in Africa offers valuable opportunities for improving healthcare skills and emergency response through realistic practice. It can adapt to various resource levels, from basic to advanced models. However, challenges include financial constraints, inadequate infrastructure, and a shortage of trained personnel. Effective implementation requires culturally relevant scenarios and integration with existing education systems. Despite these obstacles, simulation training holds promise for significantly enhancing healthcare education and worker preparedness across the continent [13].

In fact, while questions have arisen about the feasibility of integrating medical simulation into African healthcare systems, pioneering efforts have yielded positive outcomes among medical students and trainers [4, 14, 15]. The establishment of a simulation center in Rwanda exemplifies the untapped potential of medical simulations in Africa [16–18].

Financial constraints, personnel shortages, and technological limitations, such as inadequate power supply and limited Internet access, have hindered the growth of healthcare simulation. Addressing these challenges necessitates the development of methodologies that actively engage local resources and technologies to ensure the sustainability of training initiatives [15]. Additionally, effective training must align with a patient-centered and realistic approach [14], thereby requiring careful consideration of socio-cultural factors and their influence on the learning and teaching process.

Therefore, this work was designed to organize and implement a needs-based training course on umbilical cord care and placenta management after childbirth at the St. Luke Catholic Hospital and College of Wolisso, Ethiopia. This study involved both permanent staff and students, offering insights into the integration of such training into future educational curricula. The initiative underscored the importance of aligning training efforts with local context and resources while harnessing the transformative potential of simulation training to address critical healthcare challenges in Africa.

Prior literature has already demonstrated successful outcomes using low-fidelity manikins in various African settings, despite recognizing low-cost high-fidelity models as the most promising technical solution [12, 14, 17]. Low-fidelity simulators are simple, low-cost tools used to teach basic skills or procedures, offering a simplified view of real-world situations while lacking dynamic interaction. They are ideal for beginners. In contrast, high-fidelity simulators are devices that present a faithful replication of the anatomy, tissues biomechanical properties, and physiological behavior in relation to the clinical task it is intended to teach [19]. A low-cost high-fidelity simulator is a device possibly able to retain all the features of the high-fidelity simulators while keeping the final selling price affordable even for low resources setting.

Currently, the market provides low fidelity-simulators of the umbilical cord and placenta, which offer a poor replication of the anatomy and biomechanical properties of real tissues. The materials and design solutions adopted result in devices with limited abilities in providing comprehensive and quality training. Additionally, only part of clinical procedures can be effectively trained with them [20]. Recent literature solutions solved the low-fidelity issue with biohybrid simulators. These

devices combine commercial simulators with pieces of the real umbilical cord [21, 22]. They provide higher fidelity though their applicability is limited by the risk of biological contamination and availability of the human tissue.

For these reasons, the development of a new synthetic simulator at high-fidelity and low-cost of umbilical cord and placenta was deemed necessary. After validating the new simulator's face, content, and usability by conducting expert surveys, we carried out the abovementioned training course to investigate and compare the acceptability and teaching effectiveness of our new high-fidelity simulator with a commercial low-fidelity simulator and the actual human placenta.

Methods

Validation of the new high-fidelity simulator

The development of the new low-cost, high-fidelity simulator began with an initial collaboration between Sant'Anna School researchers and healthcare professionals from St. Luke's Hospital. This collaboration led to the creation and local validation of a preliminary low-fidelity simulator of the placenta and umbilical cord at St. Luke's Hospital, as discussed in a prior short communication [23]. These early findings, along with subsequent online meetings, informed the design and realization of the new simulator presented here. To validate the newly developed high-fidelity simulator, expert surveys were conducted prior to the simulation-based training course. Anonymous paper surveys were administered to experts in nursing, gynecology, midwifery, and neonatology at St. Luke's Hospital, assessing the simulator's face validity, content validity, and usability. The surveys utilized modified face, content, and usability measures, with responses recorded on a 1-to-5 Likert scale (from "strongly disagree" to "strongly agree"). Only the experts' specialties were collected, with their informed consent. Results are presented descriptively, highlighting the new simulator's key features (Supplementary Appendix S1).

Characteristics of the newly developed high-fidelity simulator

The new high-fidelity simulator (Fig. 1) accurately reproduces the anatomical structures necessary to teach and train umbilical cord care and placenta management. The replicated umbilical cord consisted of two structures: a disposable and a reusable part. The disposable part was made of uncolored Ecoflex 0010 silicone (Ecoflex series, Smooth-On, USA) in a cylindrical shape with three through-holes aligned with the symmetry axis replicating

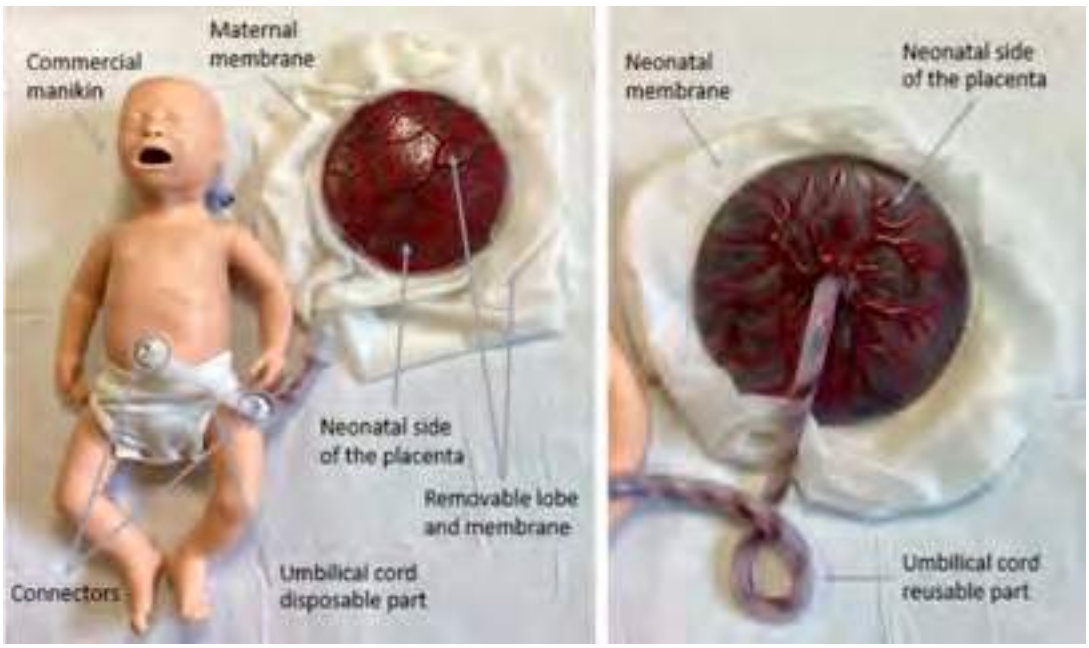

Fig. 1 High fidelity umbilical cord and placenta simulator realized by the BioRobotics Institute of the Sant'Anna School. *Legend*. On the left: the simulator main components and maternal side of the placenta are visible. During the training, the simulator was connected to a commercial neonatal manikin (Newborn Anne, Laerdal, Norway) commonly used by St. Luke College that better resembled an Ethiopian neonate improving the suspension of disbelief. On the right: a portion of the reusable part of the umbilical cord and the neonatal side of the placenta are visible

the umbilical vein and two umbilical arteries. This part is cut during the procedure and can be used a maximum of five times. The disposable part was connected to a commercial neonatal manikin and the reusable part through two ad hoc connectors 3D printed in PETG material (RS PRO, RS Components, UK). The reusable part, made of colored Ecoflex 0010, reproduces the umbilical vessels arranged helically as in the healthy real umbilical cord, and it ends with the placenta. The disposable part of the umbilical cord was wrapped with white soft tulle fabric, while the vessels in the reusable part were made from shoelaces coated in colored silicone.

The placenta replicates the superficial vessels on the neonatal side and the 20 lobes on the maternal side and is made by colored Ecoflex 0010 silicone. Neonatal and maternal membranes were fabricated by coating a white soft tulle fabric with Ecoflex 0010 silicone and then, glued to the placental main body. One lobe and the maternal membrane can be easily detached and attached to simulate different pathological scenarios thanks to multiple hook-and-loop fasteners. The colors, materials, and sizes were carefully selected by means of literature data and real umbilical cord pictures to accurately reflect the visual and biomechanical properties of real tissues.

Acceptability and teaching effectiveness of the new high-fidelity simulator

Study setting

The study was conducted at St. Luke Catholic Hospital and College of Nursing and Midwifery, Wolisso, Ethiopia. Ethiopia has made significant strides in improving healthcare access and outcomes over recent decades, but it still faces substantial hurdles. The national healthcare infrastructure is primarily public, with the government playing a central role in providing services, particularly in rural areas where most of the population resides. Key challenges include a shortage of healthcare professionals, limited infrastructure, and insufficient resources. Many rural areas lack adequate health facilities, and the ratio of healthcare workers to the population is low, which affects service delivery. Maternal and child health, infectious diseases like malaria and tuberculosis, and malnutrition remain major public health concerns [24, 25].

St. Luke Hospital is a non-profit referral facility located in Wolisso, the capital of southwestern Shoa in the Oromiya region [26, 27]. It is run by the Ethiopian Government, the Ethiopian Catholic Church, and the NGO CUAMM - Doctors for Africa. It serves a population of approximately 1.25 million residents, in conjunction with 80 other healthcare facilities [28]. This private institution, accredited by the Oromiya public health system, functions as the referral center for three primary hospitals in the Southwest Shoa Zone – Ameya, Bantu, and Tullu Bolo [29]. The hospital is equipped with a maternity waiting home to accommodate pregnant women from distant areas with potentially high-risk pregnancies. The hospital plays a vital role in maternal and neonatal care as testified by the high number of deliveries performed every year (around 4,300 in 2017).

Study design

We prospectively collected data during the simulation-based training course. Two researchers from Sant'Anna School of Advanced Studies, Pisa, Italy (specifically, the authors S. M. and A. F.) visited St. Luke Hospital and College to organize this training course with nursing and midwifery college students. The researchers brought with them the new high-fidelity simulator of the umbilical cord and placenta, previously described. A research collaboration agreement was signed between the two Institutions to implement the training course.

The training course

On Day 1, the St. Luke college teachers (namely, the authors S. T., M. T., and M. W.) gave face-to-face theoretical lectures on umbilical cord management and placenta care to their nursing and midwifery students ($n=67$). The teaching materials normally used by university teachers during lectures were employed. A first questionnaire was administered to the students, to collect their baseline characteristics (Supplementary Appendix S2). Considering the high number of attendees, we split them into two subgroups of equal numerosity, one in the morning and one in the afternoon.

On Day 2, hands-on training activities were carried out by using three different simulators: group (A) a standard low-fidelity commercial simulator owned by the St. Luke College (GHDE&MD company); group (B) the new high-fidelity simulator developed by Sant'Anna School; and group (C) a real placenta with still attached the maternal portion of the umbilical cord (Supplementary Appendix S3). Accordingly, attendees were randomly divided into three homogeneous groups of 22 (group A), 23 (group B), and 22 (group C) students, respectively. The randomization process was carried out by making each student pick a number from 1 to 67 from a closed box. Each group was given simulation lessons separately using the assigned simulator and in the same fashion by all three college teachers who were always present throughout the course. The college teachers showed to the attendees how to manage three different clinical scenarios: regular placenta and umbilical cord; placenta with a missing lobe and regular umbilical cord and placenta membranes; placenta with a missing membrane and regular umbilical cord and placenta lobes. Then, each student performed a practical simulation by replicating the three scenarios.

On Days 3–4, participants were involved in evaluation sessions to test the effectiveness of the training.

The attendees were divided into small subgroups of 2–3 people (21 of 3 people, 2 of 2 people). All the students in the same group did the practical session with the same simulator. One of the three scenarios was assigned randomly to each subgroup. All subgroup members had to work together and recognize the scenario, perform the actions they had learned during the training, and explain what they were doing. The attendees' performance was objectively evaluated by the teachers through a quantitative evaluation sheet (Supplementary Appendix S4). This evaluation sheet filled by the teachers aimed to quantitatively assess the skills acquired by the students during the hands-on sessions and provide a comparison between groups A, B and C, and thus, define which simulator brought to the best learning outcomes. The Mann-Whitney *U* test was used to explore between-group differences in the final scores given by tutors.

The evaluation session lasted a maximum of 20 min. After the simulation, the attendees were required to fill out in 10 minutes a second questionnaire, which included the items of the TAM scale (Technology Acceptance Model, Supplementary Appendix S5), as well as a pre/post evaluation test about the topics taught during the course (Supplementary Appendix S6). This pre/post evaluation test was designed to assess the proficiency gained by the students during the entire training course using true/false questions. The same Pre/post evaluation test was filled by the students both before starting the simulation training course and at the end of it. Then, the final scores were compared using the Student's *t* test for paired samples to verify that the scores in the *post* questionnaire were significantly higher than those in the *pre* questionnaire.

Throughout the course, breaks and refreshments were scheduled, to give the students time to rest.

Participants and ethics

The participants of this study were the 2nd year students enrolled in the College's Nursing and Midwifery Training program, with no previous experience in the topics taught during the training course. The course participation was on voluntary basis, free of charge and there was no economical compensation for attendants. No exclusion criteria were applied, but data from students who did not complete the course were not considered. No respondents' details or contact data that might allow tracing back the participant's identity (e.g., name, surname, date of birth, place of birth, email address, etc.) were collected. All survey data were anonymized using a unique identification numeric code (a number from 1 to 67) for each respondent that allowed the responses to the first and second questionnaires to be jointly analyzed.

The study was carried out in compliance with the Declaration of Helsinki and the Italian law on privacy 101/2018, which is aligned with the European GDPR 2016/679. Participants were fully informed of all possible risks they might face during the study, could opt out of the study at any time, and enrolled only after providing informed consent. The study protocol was approved by the Ethics Committees of both St. Luke College Hospital (resolution n. 0469/2023) and Sant'Anna School of Advanced Studies (resolution n. 14/2023).

Assessment

Using the validated TAM as the main theoretical framework, we developed the second questionnaire exploring these four dimensions: Perceived Usefulness (PU), Perceived Ease-of-Use (PEU), Behavioural Intention (BI), and Fidelity of the Simulator (FS) [30, 31]. The questionnaire was administered on Days 3–4 at the end of the evaluation sessions. The items were modified according to the characteristics of Sant'Anna simulators and were categorized as 1-to-7 Likert scales (from "extremely disagree" to "extremely agree").

First, we used Mann-Whitney's U test to investigate the differences in the scores of TAM items for placenta vs. standard simulator, standard simulator vs. new simulator, and placenta vs. new simulator. We also analyzed the between-group differences in the objective quantitative scores provided by teachers at the end of the evaluation session. Then, we ran a partial least squares structural equation model [32, 33] (PLS-SEM) to test both the associations between the TAM items and the respective dimensions considered as latent variables (measurement model) and the following cause-effect relationships (structural model): H_1) FS has a positive effect on PU; H_2) PEU has a positive effect on PU; H_3) PU has a positive effect on BI; H_4) FS has a positive effect on PEU.

We also performed a PLS-SEM-based multigroup analysis to understand whether the associations between the items and dimensions, as well as the cause-effect association paths, differed significantly among the three study groups. Then, using the latent variables created by the model for all dimensions (PU, PEU, BI, FS), we ran quantile regression models adjusted for participants' baseline characteristics to test the difference in each dimension for groups A and B as compared with group C taken as reference.

Statistical analyses were performed using Stata Software version 17.0 (Stata-Corp, LLC, College Station, Texas, USA). Statistical significance was set at a p-value < 0.05.

Results

Validation of the new high-fidelity simulator

Expert surveys involved 37 health professionals, specifically 12 midwives, 15 nurses, 1 gynecologist, 1 neonatologist, and 8 other professionals (Supplementary Table

Table 1 Baseline characteristics of the study population

Baseline characteristics	Total (*n* = 67)	A) Standard simulator (*n* = 22)	B) New simulator (*n* = 23)	C) Human placenta (*n* = 22)	*p*-value
Age, median (IQR)	21.0 (20.0, 22.0)	20.5 (20.0, 22.0)	21.0 (20.0, 22.0)	21.0 (20.0, 22.0)	0.83
Sex, n (%)					0.57
Male	18 (26.9%)	5 (22.7%)	8 (day34.8%)	5 (22.7%)	
Female	49 (73.1%)	17 (77.3%)	15 (65.2%)	17 (77.3%)	
Civil status, n (%)					0.37
With partner	3 (4.5%)	1 (4.5%)	2 (8.7%)	0 (0.0%)	
Without partner	64 (95.5%)	21 (95.5%)	21 (91.3%)	22 (100.0%)	
University faculty, n (%)					0.53
Midwifery	34 (50.7%)	12 (54.5%)	13 (56.5%)	9 (40.9%)	
Nursing	33 (49.3%)	10 (45.5%)	10 (43.5%)	13 (59.1%)	
Previous hands-on activities, n (%)					0.25
Yes	16 (23.9%)	4 (18.2%)	4 (17.4%)	8 (36.4%)	
No	51 (76.1%)	18 (81.8%)	19 (82.6%)	14 (63.6%)	
Economic status, n (%)					0.53
Very good	3 (4.5%)	0 (0.0%)	1 (4.3%)	2 (9.1%)	
Good	25 (37.3%)	9 (40.9%)	10 (43.5%)	6 (27.3%)	
Not good	39 (58.2%)	13 (59.1%)	12 (52.2%)	14 (63.6%)	
Previous work activities, n (%)					0.24
Yes	5 (7.5%)	0 (0.0%)	3 (13.0%)	2 (9.1%)	
No	62 (92.5%)	22 (100.0%)	20 (87.0%)	20 (90.9%)	
Previous university studies, n (%)					0.35
Yes	4 (6.0%)	2 (9.1%)	2 (8.7%)	0 (0.0%)	
No	63 (94.0%)	20 (90.9%)	21 (91.3%)	22 (100.0%)	
Interest in participating in the course, n (%)					0.35
Yes	66 (98.5%)	22 (100.0%)	23 (100.0%)	21 (95.5%)	
No	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	
Satisfaction with face-to-face lessons, n (%)					0.37
Very satisfied	64 (95.5%)	21 (95.5%)	21 (91.3%)	22 (100.0%)	
Quite satisfied	3 (4.5%)	1 (4.5%)	2 (8.7%)	0 (0.0%)	

To describe the participant baseline characteristics obtained from the first questionnaire, we reported continuous variables as median and interquartile range (IQR), and categorical variables as counts and proportions (%). To test the non-significant difference between the three study groups in the sociodemographic data, we used the Kruskal-Wallis and the $\chi 2$ tests, respectively.

S1). Results from surveys indicated that, on 1-to-5 Likert scales, the overall impression of the simulator was good (mean score 4.38), with high fidelity of the anatomic structures (4.38), materials (4.24), and visual appearance (4.43). Experts agreed that all the simulation steps could be performed using the new simulator (4.24), which was also perceived as useful for teaching purposes (4.59) and easy to be used (4.59).

Acceptability and teaching effectiveness of the new high-fidelity simulator

We enrolled 67 participant students. As shown in Table 1, the median age was 21 years, and the predominant sex was female (73%). 95% of the participants lived without a partner, and 58% of them declared not to have a good economic status. Half of the participants were midwifery students, and half were nursing students. Most students had been involved in no previous hands-on activities, work activities, or other university studies. Most students were interested in participating in the course and satisfied with the face-to-face lectures. There was no difference in the baseline characteristics between the three study groups.

Table 2 Pre-post difference in the Pre/post evaluation test scores

Score true/false	Mean	95% CI
Pre (Day 1)	4,7	4,4 to 4,9
Post (Days 3–4)	8,4	8,2 to 8,6
Difference pre-post	-3,7	-4 to -3,5
Student's t test *p*-value	< 0.001	

The Pre/post evaluation test scores were significantly higher after the simulation training course (Table 2). In the pre-evaluation test, the mean score was 4.7 over a total of 10 points. In the post-evaluation test, the mean score almost doubled reaching 8.4/10. Furthermore, The TAM item scores PU1, PU2, PU4, PEU2, and PEU3 were significantly higher in the group B than in the group C (Table 3). The item score PEU3 was also higher in the group B than in the group A, while there was no

Table 3 Difference in TAM (Technology Acceptance Model) items between the new simulator (group B) and the real human placenta (group C)

TAM items	Human placenta (*n* = 22)	New simulator (*n* = 23)	*p*-value (Mann-Whitney test)
PU1, median (IQR)	6.0 (5.0, 6.0)	7.0 (6.0, 7.0)	**0.006**
PU2, median (IQR)	6.0 (6.0, 7.0)	7.0 (6.0, 7.0)	**0.038**
PU3, median (IQR)	6.0 (6.0, 7.0)	7.0 (6.0, 7.0)	0.130
PU4, median (IQR)	6.0 (6.0, 6.0)	7.0 (6.0, 7.0)	**0.026**
PU5, median (IQR)	7.0 (6.0, 7.0)	7.0 (6.0, 7.0)	0.880
PEU1, median (IQR)	6.0 (6.0, 7.0)	7.0 (6.0, 7.0)	0.058
PEU2, median (IQR)	6.0 (5.0, 6.0)	6.0 (6.0, 7.0)	**0.006**
PEU3, median (IQR)	6.0 (6.0, 6.0)	7.0 (6.0, 7.0)	**< 0.001**
PEU4, median (IQR)	6.0 (6.0, 6.0)	6.0 (6.0, 7.0)	0.200
PEU5, median (IQR)	6.0 (5.0, 7.0)	7.0 (6.0, 7.0)	0.053
BI1, median (IQR)	7.0 (6.0, 7.0)	7.0 (7.0, 7.0)	0.130
BI2, median (IQR)	6.0 (6.0, 7.0)	6.0 (6.0, 7.0)	0.380
FS1, median (IQR)	6.0 (6.0, 7.0)	6.0 (6.0, 7.0)	0.260
FS2, median (IQR)	6.0 (6.0, 7.0)	7.0 (6.0, 7.0)	0.080
FS3, median (IQR)	6.0 (5.0, 7.0)	6.0 (6.0, 7.0)	0.170

The median scores of each item of the TAM scale belonging to the four dimensions (Perceived Usefulness, Perceived Ease of Use, Behavioral Intention, Fidelity of the Simulator) were compared between the human placenta simulation group and the new simulator group by using the Mann-Whitney *U* test. Bold values indicate statistically significant *p*-values.

Table 4 Between-group differences in the objective final scores given by tutors

	C) Human placenta	A) Standard simulator	*p*-value
	n = 22	*n* = 22	
Final score by tutors, median (IQR)	7.0 (6.0, 9.0)	8.5 (3.0, 10.0)	0.94
	C) Human placenta	**B) New simulator**	***p*-value**
	n = 22	*n* = 23	
Final score by tutors, median (IQR)	7.0 (6.0, 9.0)	11.0 (8.0, 11.5)	< 0.001
	A) Standard simulator	**B) New simulator**	***p*-value**
	n = 22	*n* = 23	
Final score by tutors, median (IQR)	8.5 (3.0, 10.0)	11.0 (8.0, 11.5)	< 0.001

The Mann-Whitney *U* test was used to explore between-group differences in the final scores given by tutors. Please, see Supplementary Appendix S4 for further information on sheet used for the objective evaluation by tutors

significant difference between the group A and the group C (Supplementary Tables S2-S3).

The median final objective scores given by college teachers were statistically higher in group B compared to the scores obtained by group A and C (Table 4). On the contrary, there was no statistically significant difference between the scores obtained by groups A and C. Specifically, the group who worked with the standard simulator (A) got a mean final score of 8.5, the group that used the real placenta (C) received a mean final score of 7, while the group using the new simulator (B) reached a mean final score of 11.

The measurement model showed that the loadings of all TAM items (except PU1 and PEU1) were above the recommended value of 0.7 (Table 5). All values of composite reliability and Cronbach's alpha were higher than 0.7, and rho_A values were between composite reliability and Cronbach's alpha. The average variance extracted (AVE) values exceeded the recommended threshold (0.5). We also assessed discriminant validity using the Fornell-Larcker criterion (Supplementary Table S5). Multigroup analysis showed no significant differences in factor loadings of TAM items between the three study groups.

The association paths were tested in the structural model (Fig. 2, Supplementary Table S6) by using a bootstrapping procedure. All hypothesized positive paths were significantly supported by the model's results (p-value < 0.05). Multigroup analysis revealed no significant differences between the study groups in the association paths. Furthermore, adjusted quantile regression models showed that the two latent variables PU and PEU (computed by the PLS-SEM) were significantly higher in the group B than in the group C, while there was no difference between the group A and the group C (Fig. 3, Supplementary Tables S7-S8).

Discussion

Main findings

Our study describes the realization and validation with Ethiopian experts of a new low-cost high-fidelity simulator together with the implementation of a simulation course on placenta and umbilical cord management delivered to midwifery and nursing students at St. Luke's College, Ethiopia. Experts confirmed the new high-fidelity simulator's fidelity, material quality, and usability. The simulation course ensured adequate preparation of the attendees, as evidenced by the results obtained in the evaluation session. The course enabled students to comprehensively train all the steps of umbilical cord care and placenta management in an immersive setting. Attendees had the opportunity to appraise placental and umbilical weight, encumbrance, and consistency, and to thoroughly examine their main features to understand how to distinguish between a healthy and a pathological placenta.

Furthermore, the final objective evaluation given by the tutor, along with the results from the pre/post training questionnaires, demonstrated the educational effectiveness of the simulation and the teaching methods employed. All students successfully completed the training course and passed the final exam. The new simulator outperformed the other two, highlighting the value of a low-cost, high-fidelity simulator in resource-limited settings, as previously demonstrated in the literature [23,

Table 5 Measurement model: factor loadings

Latent variable	Indicator variable	Loading	Cronbach's alpha (CA)	Composite reliability (CR)	rho_A	Average variance extracted	Std simulator vs. placenta (*p*) *	New simulator vs. placenta (*p*) *
Usefulness	PU1	0.581					0.454	0.293
	PU2	0.866					0.338	0.345
	PU3	0.741	0.798	0.862	0.820	0.560	0.171	0.612
	PU4	0.824					0.157	0.404
	PU5	0.695					0.247	0.128
Ease-of-Use	PEU1	0.531					0.612	0.097
	PEU2	0.802					0.728	0.169
	PEU3	0.702	0.773	0.844	0.822	0.528	0.418	0.602
	PEU4	0.777					0.323	0.138
	PEU5	0.866					0.902	0.316
Behavioural Intention	BI1	0.833	0.583	0.827	0.583	0.705	0.393	0.704
	BI2	0.846					0.222	0.153
Fidelity of the Simulator	FS1	0.851					0.300	0.497
	FS2	0.819	0.792	0.878	0.796	0.706	0.179	0.317
	FS3	0.851					0.261	0.443
Reference values for validity		> 0.7	> 0.7	> 0.7	CA < rho_A < CR	> 0.5	* *p*-values from multigroup analysis	

Average R-squared = 52.1%
Absolute Goodness-of-Fit = 55.8%
Relative Goodness-of-Fit = 93.5%

The loadings of all TAM items (except PU1 and PEU1) were > 0.7 confirming that all items successfully linked to the corresponding latent dimension. The model fitting was confirmed by all values of composite reliability and Cronbach's alpha > 0.7, and by rho_A values between composite reliability and Cronbach's alpha. The average variance extracted (AVE) values exceeded the recommended threshold (0.5). Multigroup analysis showed no between-group significant differences in factor loadings of TAM items

34]. Employing local facilitators and hands-on activities allowed all the student to acquire and retain new knowledge and be able to obtain positive results in the pre/post questionnaire. This result is particularly significant and was achieved through the combined approach of introducing new concepts using teaching strategies already familiar to the students, along with the use of simulators. The students' familiarity with the tutors and teaching methods fostered a comfortable and engaging learning environment, encouraging active participation and facilitating the internalization of new knowledge. In addition, the simulator-based training, conducted individually and in small groups, required students to immediately apply theoretical concepts to practical skills in a safe, non-judgmental setting.

At the same time, our study sought to compare the acceptability of a new technology, that is the new high-fidelity simulator developed by Scuola Sant'Anna, with a standard low-cost simulator and a real human placenta. The results of the PLS-SEM model validated the use of the TAM scale to assess the user acceptability of the three analyzed simulators. The association paths did not differ among the three study groups, making our results consistent across the entire study population. In addition, the results of the TAM scale showed that the new high-fidelity simulator was perceived by students as more useful and easier to be used than the real human placenta. The behavioral intention variable did not differ between the new simulator and the real placenta. In contrast, there were no significant differences between the standard simulator and placenta for the four items of the TAM scale.

Limitations

This study has some limitations. First, our results are not generalizable because the study was conducted in a single center. Second, our results may have been influenced by confounding factors that we did not consider. For example, although there were no differences among the three groups, the randomization process may have led to the formation of groups that differed in characteristics that we did not consider, partly because the sample size did not allow more than 6–7 variables to be included in the regression models. Third, the evaluation session was conducted by all three groups with the new high-fidelity simulator; therefore, students who had done the training with that simulator may have been advantaged. However, this choice was dictated by the need to use a simulator that would allow to perform several times all the required steps and tasks without lacking fidelity and avoiding the important issues related to the use of biological tissues such as the real placenta.

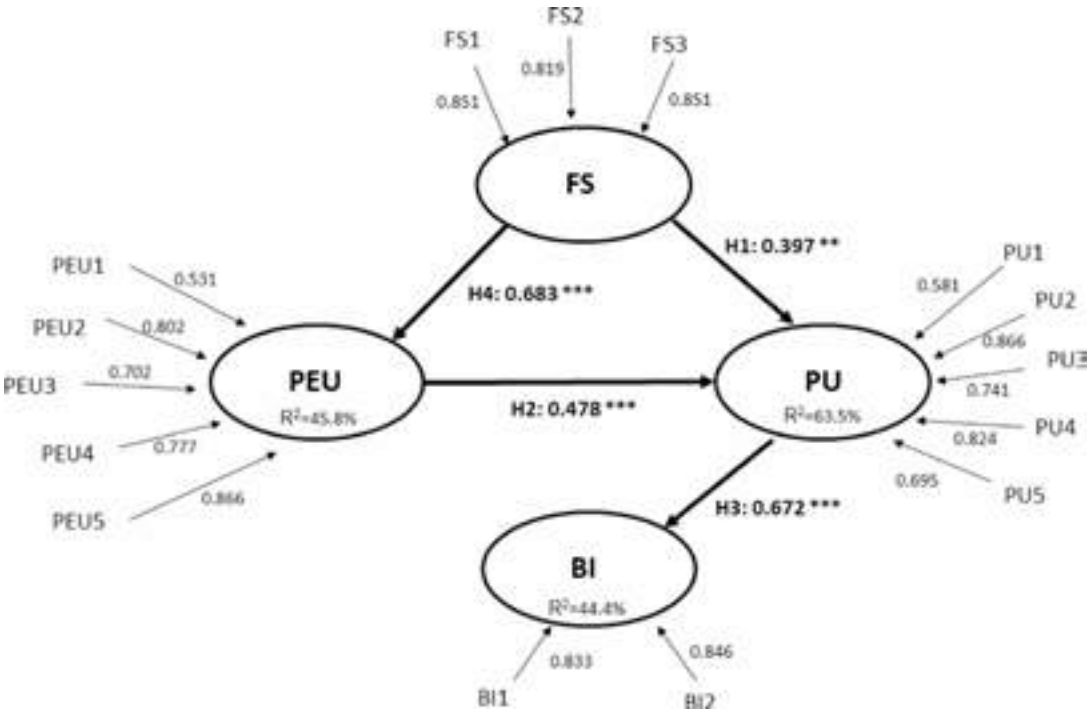

Fig. 2 Testing the hypotheses of the structural model. *Legend*. PU: Perceived Usefulness; PEU: Perceived Ease of Use; BI: Behavioral Intention; FS: Fidelity of the Simulator; R2: R-squared; H1-H2-H3: hypotheses 1-2-3. Note: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

The new simulator is primarily composed of silicone, an unexpensive and sustainable material derived from silica. This material is highly stable and does not undergo degradation. It is also non-toxic to aquatic or soil organisms and can be recycled, making it an environmentally friendly option. As a result of these considerations, the reusable part of the simulator may be utilized for an extended period, whereas the disposable part can be easily disposed without contributing to a significant environmental impact. Despite its capacity to be exploited up to five times prior to depletion, the utilization of a disposable component diminishes the long-term sustainability of the entire simulator. The scarcity of silicone in African countries necessitates a supply chain from a developed country, which can result in expensive products. This phenomenon, already documented by relevant literature, underlines the need to explore alternative solutions using local resources and sustainable by the African market. Moreover, in many parts of Africa, high temperatures and limited access to clean water pose significant challenges for maintaining and properly cleaning medical equipment. These environmental factors can impact the effectiveness of sanitation procedures, potentially leading to equipment contamination and increased risk of infections. Addressing these challenges requires innovative solutions and adaptations to ensure the safe and effective use of medical tools and simulation devices in such conditions.

Implications

Sant'Anna new simulator is the first example in the literature of a high-fidelity simulator of the umbilical cord and placenta, which enables to teach and repeat all the steps necessary for the management of these organs after delivery. To date, the current market offers only low-fidelity umbilical cord and placenta simulators, which, albeit inexpensive and reusable, do not allow all the required steps and tasks to be performed. Also, they present a poor replication of the anatomy and biomechanical properties of the human organs. On the other hand, the high-quality teaching ensured during the course was previously achievable only through direct exposure of the students to real human organs, which inevitably entailed biological risk.

The implementation of the Sant'Anna new high-fidelity simulator allowed for the teaching and training to be conducted in a biohazard and chemical-risk free environment, as the device boasts a high level of fidelity and the utilized materials classified as safe for skin contact. High-fidelity low-cost simulators are considered a valuable

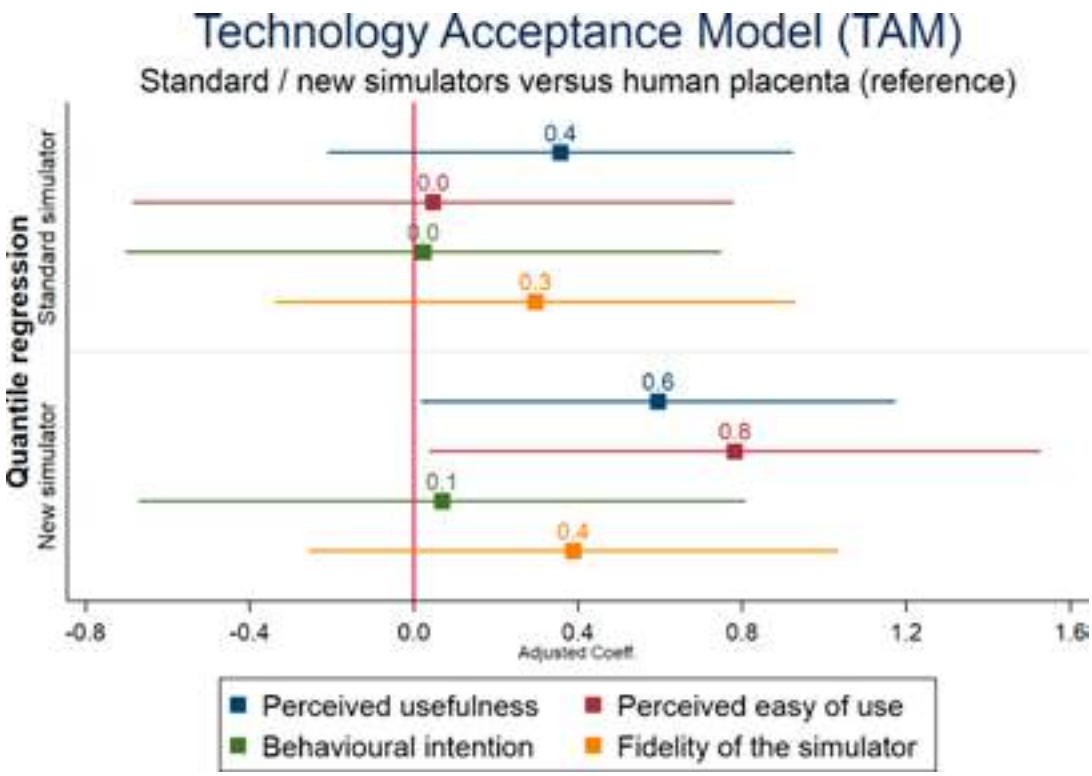

Fig. 3 Quantile regression models for the TAM items. *Legend*. The latent variables for the four dimensions generated by the partial least squares structural equation model (PLS-SEM) were used as dependent variables. The models were adjusted by age, sex, faculty, reported economic status, and previous involvement in hands-on training activities (see Supplementary Tables S7-S8)

option for medical training in low-income countries. These simulators guide quality teaching and training, which are essential for the development of critical skills that can enhance patient outcomes and healthcare level.

The production costs of the disposable part of the new Sant'Anna simulator are not low. In principle, this is a challenge inherent with the sustainability of such equipment, and substantially questions if it can be of general interest. On the other hand, its reusable part can ensure long-term use and can be easily interfaced with low cost and local solutions, e.g., rubber tubes. Indeed, the simulator was left at St. Luke College to teach future students as per the collaboration agreement signed with Sant'Anna School. This experience should encourage collaborations between institutions that can produce high-fidelity, long-term reusable simulators, with or without replaceable parts, and institutions in low-income countries that could benefit from them. As a matter of facts, our study demonstrated that the new simulator provided at least comparable preparedness to that provided by the other two simulators, while also being perceived as more useful and easier to use by students. Preparedness, in the context of simulation-based training, refers to the degree to which an individual or group is equipped with the knowledge, skills, and confidence necessary to perform tasks or face real-world challenges [35]. In training environments, simulators play a critical role in fostering preparedness by replicating real-world conditions in a controlled, risk-free setting, as already described in the literature [36]. In our study, the new simulator, which was shown to provide at least comparable preparedness to that of the other two simulators, likely achieved this by offering realistic scenarios that allowed students to practice and refine their skills in a way that closely mirrors real-world conditions.

At the same time, we must recognize that the new simulator, while providing higher final scores in the objective evaluation by tutors, did not demonstrate higher acceptability than the standard low-cost simulator. Probably, in similar contexts, students perceive a commercial and a high-fidelity simulators as equally useful and easy-of-use. However, Sant'Anna simulator offers the advantage of performing cord clamping and cutting via a replaceable part. It also shows students the correct anatomy of the placenta in a risk-free environment and two different

pathological conditions, differently from other simulators. Training with this simulator could provide students with greater efficiency and lower risks when they first encounter a real clinical situation.

Conclusion

We successfully tested the new high-fidelity simulator for umbilical cord care and afterbirth placenta management, developed by the Sant'Anna School team, employing the tool described by Maglio et al. [23] and the TAM scale alongside robust statistical methods. The validation process not only confirmed the effectiveness of the simulator but also highlighted the fruitful collaboration between Sant'Anna School and St. Luke's College in organizing a comprehensive simulation training course for local students. The course was designed to align with the rigorous teaching standards of St. Luke's College, ensuring that the training provided met the highest educational benchmarks.

Our findings revealed that students who trained with the new simulator achieved significantly higher objective scores during the evaluation sessions compared to those who practiced with the real human placenta. Furthermore, the students reported that the simulator was both more useful and easier to use than the real placenta, underscoring the simulator's practical value in an educational setting. These results suggest that integrating high-fidelity simulators into medical training can substantially enhance learning outcomes, offering a more effective and accessible alternative to traditional methods.

The success of this initiative highlights the potential for further research and development in simulation-based education, particularly in medical and healthcare training. The positive student feedback and improved performance metrics indicate that such simulators could play a crucial role in advancing medical education, ultimately contributing to better-prepared healthcare professionals. Our study lays the groundwork for future exploration into the broader applications of high-fidelity simulators, advocating for their adoption in various educational contexts to improve training efficacy and student engagement. Finally, yet importantly, it would be interesting to replicate this study within the framework of Basic Emergency Obstetric and Newborn Care (BEmONC) as integrated into Ethiopian healthcare education. BEmONC programs are crucial for improving maternal and neonatal health outcomes in low-resource settings by providing essential emergency care for pregnant women and newborns. Exploring the effectiveness of high-fidelity simulators in this context could offer valuable insights into how advanced simulation tools impact the training and preparedness of healthcare professionals dealing with obstetric and neonatal emergencies.

Abbreviations

TAM	Technology Acceptance Model
NGO	Non-governative organization
CUAMM	Collegio Universitario Aspiranti Medici Missionari
MeS	Management and Health
PU	Perceived Usefulness
PEU	Perceived Ease-of-Use
BI	Behavioural Intention
FS	And Fidelity of the Simulator
PLS-SEM	Partial least squares structural equation model
BEmONC	Basic Emergency Obstetric and Newborn Care

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12909-024-06152-0.

Supplementary Material 1

Author contributions

A.F. and S.M. equally contributed as first authors to conceptualizing and designing the study; collecting and managing data and performing statistical analyses; writing the first draft of the manuscript; reading, reviewing and editing the manuscript. S.Ta., M.T., and M.W. contributed to designing the study; collecting data; reading, reviewing and editing the manuscript. I.C. contributed to conceptualizing and designing the study; interpreting data; reading, reviewing and editing the manuscript. F.M. and E.F. contributed to conceptualizing the study; interpreting data; reading, reviewing and editing the manuscript. S.To., M.V., A.M. equally contributed to conceptualizing and designing the study; interpreting data; reading, reviewing and editing the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Participants were fully informed of all possible risks they might face during the study, could opt out of the study at any time, and enrolled only after providing informed consent. The study protocol was approved by the Ethics Committees of both St. Luke College Hospital (resolution n. 0469/2023) and Sant'Anna School of Advanced Studies (resolution n. 14/2023).

Consent for publication

Consent for publication was obtained from the study participants, who provided their consent for publication when they signed the informed consent for participation in the study.

Competing interests

The authors declare no competing interests.

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Publisher's note

Doctors with Africa Cuamm data and activities in Princess Christiana Maternity Hospital (PCMH) and Pujehu district

POSTER AND ORAL PRESENTATION

Conference
National Institute for Health and Care Research and Sierra Leone University Maternal Health Conference

Location
Freetown, Sierra Leone

Presentation date
January 2024

Authors
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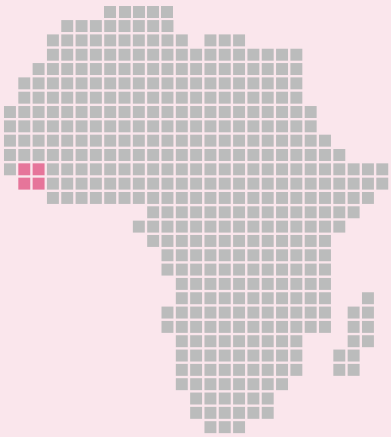
Focus country
Sierra Leone



Risk Factors related to neurodevelopmental delay and adherence to follow up in a population of asphyxiated newborns in Tosamaganga Hospital - Tanzania: a retrospective study

POSTER AND ORAL PRESENTATION

Conference
East Africa ECD conference

Location
Dar es Salaam, Tanzania

Presentation date
March 2024

Authors
R. Itambu and R. Lazzaro

Focus country
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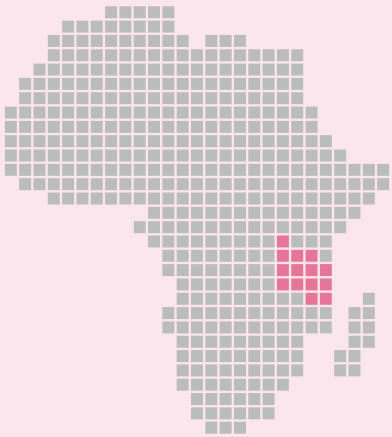

The pilot experience of the Malawi Development Assessment Tool (MDAT) of Doctors with Africa CUAMM in Mozambique

POSTER AND ORAL PRESENTATION

Conference
ECDAN Network, Eastern African Regional Early Childhood Conference on ECD

Location
Dar es Salaam, Tanzania

Presentation date
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Authors
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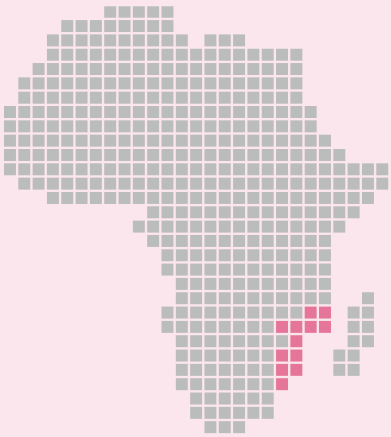
Focus country
Mozambique



The pilot experience of the Malawi Development Assessment Tool (MDAT) of Doctors with Africa CUAMM in Mozambique

POSTER AND ORAL PRESENTATION

Conference
UNICEF: Building brighter futures: Evidence for children

Location
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Authors
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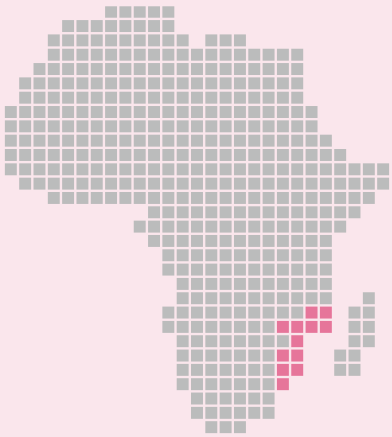
Focus country
Mozambique



Parental stress, depression, anxiety and participation to care in neonatal intensive care units: results of a prospective study in Italy, Brazil and Tanzania

POSTER AND ORAL PRESENTATION

Conference
Tini feet, best steps

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Authors
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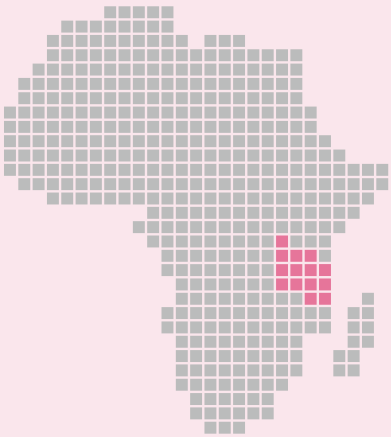
Tanzania



Bambini con altri nomi

POSTER AND ORAL PRESENTATION

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Confronti in Pediatria

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Focus country
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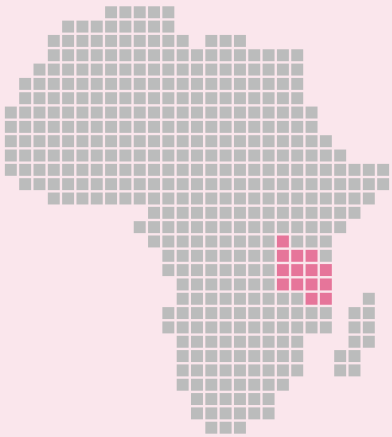

Public health and universal coverage

ICU registries: From tracking to fostering better outcomes

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A Cost-Effectiveness Assessment of an Ambulance-Based Referral System for Emergencies: The Case of Beira, Mozambique

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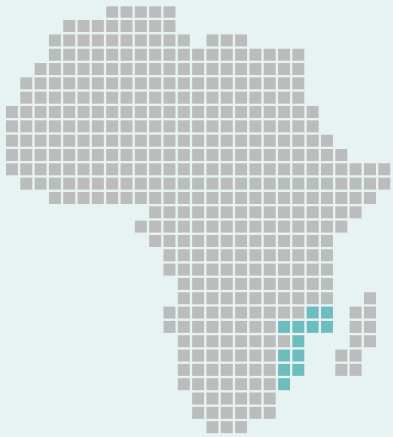

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A cost-effectiveness assessment of an Ambulance-based referral system for emergencies: The case of Beira, Mozambique

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A cost-effectiveness assessment of an Ambulance-based referral system for emergencies: The case of Beira, Mozambique

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Abstract

We set out to estimate the cost-effectiveness of an ambulance-based referral system for emergencies, connecting primary care health centres to a central hospital in a sub-Saharan low-income context. We adopted an observational retrospective study design in the setting of the Beira District (Sofala Region, Mozambique) and classified effective referrals based on the triage emergency codes assigned during transfer. We focused solely on referral running costs required to run the ambulance and complete safe and effective transfer, including staff (nurses and drivers) and communication costs between health centres, ambulance operators and the central hospital. A total of 7849 referrals were included in the analysis, 6295 of which were deemed effective. The total running cost of the intervention (11 months) was $172.071. The cost-per-effective referral was $27,33, which is below the acceptability benchmarks that can be considered "very attractive" ($58,20) and that we defined as 1/10 of the national GDP per capita of Mozambique ($582). Sensitivity analysis corroborates our findings, which confirm and extend previous evidence on the high cost-effectiveness of ambulance-based referral systems for emergencies in sub-Saharan low-income countries.

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1. Introduction and Background

Emergency healthcare services play a fundamental role in improving healthcare outcomes, especially in low-income countries (LICs) (Kobusingye et al., 2005). Access to real-time emergency care is often limited in such regions, posing significant challenges to proper healthcare delivery (Werner et al., 2020; World Health Organization, 2018). In low-resource settings, delays in receiving adequate assistance at healthcare facilities persist as a significant concern for various emergency conditions (Shah et al., 2020). Globally, an estimated 24–28 million lives are lost each year due to conditions necessitating emergency care, comprising 51% of mortality and 42% of the total global disease burden (Hsia et al., 2015). This burden is 4.4 times greater in low and middle-income countries (Chipendo et al., 2021). Delayed requests for assistance by healthcare professionals and inadequate transportation for referrals are among the principal factors hampering timely and effective emergency care (MINISTÉRIO DA SAÚDE Moçambique - Relatório Anual, 2020). Ambulance-based referral systems for emergencies (AbRSEs) emerge as key interventions addressing these challenges, facilitating timely access to emergency care (Mucunguzi et al., 2014.; Ragazzoni et al., 2021).

AbRSEs are particularly beneficial for addressing different types of emergency conditions in LICs, including medical emergencies, surgical emergencies, obstetric complications, and pediatric emergencies stemming from endemic communicable and non-communicable diseases (Shah et al., 2020). They play a crucial role in reducing morbidity and mortality rates by enhancing access to - and quality of - emergency healthcare services, thereby addressing preventable deaths (WHO, OECD & The World Bank, 2018). Skilled management of emergencies, including timely access to specialized care and interventions, is essential to improve outcomes across all emergency types. Many elements of effective emergency care are globally applicable and feasible to implement, often requiring minimal investments (WHO, OECD & The World Bank, 2018). Consequently, numerous non-governmental organizations (NGOs), in collaboration with governmental bodies, are implementing AbRSEs to address a wide range of emergency conditions at various levels (Conti et al., 2022).

However, ensuring the long-term sustainability of AbRSEs necessitates assessing their affordability and cost-effectiveness, especially as initial support often comes from programs whose funding reaches an end across a few years. Consequently, upon cessation of external funding, local and national health bodies must allocate scarce resources appropriately to sustain these services (WHO, 1996). Inadequate allocation may lead to loss of life that would be avoidable instead (Groppi et al., 2015; Somigliana et al., 2011).

Despite evidence supporting the efficacy of AbRSEs, their cost-effectiveness remains underexplored. Moreover, evidence-based advocacy remains crucial to ensure ongoing investments and improvements in their implementation across LICs (Werner et al., 2020; World Health Organization, 2018).

While some economic analyses highlight the cost-effectiveness of comprehensive emergency interventions, studies specifically examining the economic profiles of AbRSEs are limited. Recent studies have started to address this gap, with findings suggesting that AbRSEs can be highly cost-effective in LICs. However, these findings come from AbRSEs mainly dedicated to obstetric and pediatric emergencies (e.g., Accorsi et al., 2017).

The present study assesses the cost-effectiveness of an AbRSE designed to address different emergencies. We assess it by analyzing 7849 referrals throughout an 11-month period in 2022. Our setting is the district of Beira, Mozambique. The AbRSE studied is implemented by the NGO *CUAMM – Doctors with Africa* (from now on, CUAMM) connecting 15 minor Health Centres to the Hospital Central da Beira. Our results suggest a high cost-effectiveness of the intervention.
By generating science-based evidence on the effectiveness and affordability of AbRSEs, stakeholders can advocate for their scaling up and integration into national healthcare systems. This is essential for liberating countries in the Global South from dependency on external aid and fostering self-reliance in addressing their healthcare needs. Therefore, estimating the cost-effectiveness of AbRSEs is not only a scientific endeavour but also a means to empower local governments and ministries to make informed decisions that can positively impact the health and well-being of their populations.

2. Methods

2.1 Study Setting

Mozambique is classified as a LIC with a GDP per capita equal to 582 USD (World Bank, 2022), and as one of the least developed nations globally according to the UNDP Human Development Index (185 out of 191). It has a population of 33’244’414 people, with a life expectancy at birth of 56.1 years (Instituto Nacional De Estatística – Moçambique, 2022; 2024). Its demographic configuration is constituted by a prevalently rural distribution of the population (67.49% as of 2016), a young age structure (45.2% under age 15) and high fertility rates (5.24 births per woman as of 2016) (Yaya et al., 2020). Poverty in the country remains pervasive, with over half the population struggling to meet basic needs, including access to healthcare (Yaya et al., 2020).
Indeed, Mozambique's healthcare indicators do reflect these developmental challenges: despite efforts to improve living standards and continued economic growth following the end of the civil war (1977–1992), as of today, significant challenges persist in the healthcare landscape. Among the main issues afflicting the national healthcare system (NHS) effectiveness, chronic shortage of skilled personnel, poor financial management, and inadequate planning are reported. Accessing essential healthcare for a considerable portion of the population remains very difficult. Not surprisingly, Mozambique scores among the lowest worldwide in terms of coverage rates of basic public health services (22%) and physicians per 1000 inhabitant’s ratio (0.1%) (Vera Cruz & Dlamini, 2021). As of 2022, there are 10.4 health professionals per 1000 inhabitants (Instituto Nacional De Estatística – Moçambique, 2022).
According to the Mozambican Ministry of Health (MISAU), which oversees healthcare governance, the latest investigation on maternal and neonatal mortality - the “III- Relatório Annual de Auditoria de Mortes Maternas e Neonatais – 2018” (MINISTÉRIO DA SAÚDE Moçambique - Relatório Anual, 2020) - shows that Mozambique presents an Institutional Maternal Mortality Ratio (IMMR, deaths occurring within healthcare facilities) of 82 over 100,000 live births in 2018. As of 2020, the WHO estimates an Overall Maternal Mortality Rate (OMMR, TEGEGNE et al., 2023) of 127 over 100,000 live births, quite above the sustainable development goal (target 3.1) objective, i.e., 70 over 100,000 live births (*United Nations - Agenda for Sustainable Development*, 2015). Moreover, the

UNICEF global databases (Unicef, 2014)) indicate 54.8% of institutional deliveries, i.e., deliveries under safe procedures by professional (TEGEGNE et al., 2023), meaning that a bit less than half of deliveries happen in less safe conditions the latest figure shows. Indeed, the WHO (2020) reports that neonatal mortality is at 4 over 1,000 live births whereas infant mortality is at 51 over 1000 live births. Mozambique's epidemiological profile is "pre-transitional", with widely spread communicable diseases (e.g, malaria, HIV/AIDS, tuberculosis, acute respiratory infections and diarrheal diseases) alongside non-communicable ones (e.g., cancers, cardiovascular diseases and injuries) (dos Anjos Luis & Cabral, 2016), ranking globally among the top five countries with the highest tuberculosis prevalence and within the top ten countries with the highest AIDS prevalence (Garrido & UNU-WIDER, 2020)

2.1.1 The Beira District and the AbRSE

Beira is the capital of Sofala Province and the second most populous city in Mozambique, with 719,506 inhabitants as of 2022 (Instituto Nacional De Estatística – Moçambique, 2023). The city covers an area of 633 km2 and is in the Indian Ocean coastal area of Mozambique, making it vulnerable to climate disasters such as cyclones and floods (Macamo, 2021). The Hospital Central da Beira (HCB) is the second largest in Mozambique with 640 beds. It serves as the main hub for emergency referrals in Beira District the Sofala Province. In addition to the central hospital, there are 17 Health Units (HCs) in Beira distributed across the whole area, each dedicated to serving a part of the district and its population (Instituto Nacional De Estatística – Moçambique, 2023). Health services are generally delivered without a direct cost burden for the patient, whereas medicines are provided at a fixed price. Each HC has at least one medical doctor, but larger ones may employ up to four (Lokotola et al., 2022). Alongside doctors, every HC personnel is comprised of a minimum of 15/20 staff, generally composed of nurses, community health workers and technical officers (Lokotola et al., 2022). The HCB is a central hospital at the quaternary level[1], while the 17 HCs mostly deliver primary care services. These basic ambulatory services include general adult and pediatric examination, basic laboratory tests, and drug administration, and may be followed by a short observational stay. However, they cannot provide long-term patient hospitalization, specialized consultation, surgery procedures, or advanced emergency care. Therefore, they refer patients to the HCB for more complex and urgent services (World Bank, 2004). In this context, referrals are managed by the Italian NGO CUAMM through an AbRSE implemented in 2019, as a response to the Cyclone Idai disaster. The AbRSE is constantly strengthened through International Cooperation for Development funding to make it independent and economically sustainable. To this purpose, starting in February 2022, the Italian Agency for Cooperation and Development (AICS) has funded a 36-

[1] The Mozambican NHS is structured into four different levels of care, with each level providing progressively more complex services. Primary care is delivered at the first level and is provided at local health units. These facilities offer basic maternal and child health services. The second level functions at the whole district level, serving as the referral point for the first level. Services offered at the second level might include surgery (e.g, for cesareans). The tertiary level is located at provincial hospitals and functions as a referral level. Finally, the quaternary level is located at central hospitals and represent the main hub for regional referrals (Augusto et al., 2018)

month project led by the Veneto Region, and operationalized by CUAMM with the support of other international and local institutions[2]. The goal of the initiative is to strengthen and manage medical emergencies and urgencies with a focus on obstetric and pediatric emergencies. The interventions aim at improving patient transfers from 15 served peripheral HCs to the city to HCB using an AbRSE. The project provides new ambulances, staff training and effective implementation and management of a coordinated system for referrals. The ambulance fleet is distributed in different HCs according to the patients they treat per day and their location in the area. Each ambulance serves 3 to 4 designated HCs. The number and the location of ambulances vary according to referral flows and resource availability. HC's location spans from a 1,5 km distance to 33 km from the HCB.
See Table 1 for a comprehensive description of ambulance stations, distance from HCB, HCs served by each ambulance and patient flows for every HC. Table 2 reports how ambulance fleet spatial allocation, staff numbers and HCs served by the referral system changed throughout 2022.
Patients cannot directly call for an ambulance and use their means to reach the closest HC. It is the HC staff that can possibly ask for the ambulance through a mobile phone call. After receiving the call, the ambulance staff – a CUAMM-trained nurse and a driver – calls the HCB asking for authorization to transfer the referral. Once at the HC, CUAMM-trained nurses prioritize emergency cases using a triage system (see. Conti et al., 2022 for a detailed explanation of the triage system used in this case). Only yellow, orange, and red emergencies should be transported to the HCB, while green and blue emergencies represent minor conditions that can be treated at the HC.

Table 1. Ambulance location, patient flows per HCs and distance in km to HCB (in parenthesis)

Ambulance Station	HCs served
Chingussura (16km) 1071	• Inhamizua (22km) 812 • Ceramica (33km) 40 • Matadouro (21km) 25 • Chamba (17km) 13
Nhaconjo (14km) 1502	• Manga Loforte (12km) 450 • Nhangau (27km) 242
Munhava (8km) 1043	• Mascarenhas (9km) 505 • Marrocanhe (15km) 165 • Chota (6km) 4
Ponta-Gea (4km) 1101	• Macurungo (3km) 864 • Sao Lucas (1,5km) 2

[2] Ca 'Foscari University of Venice, Green Cross Padova, Beira District Health, Women and Social Action (Serviço Distrital de Saúde, Mulher e Acção Social di Beira (SDSMAS)), Mozambique Emergency Medical Service (Serviço de Emergência Medica em Moçambique (SEMMO)) and Beira Central Hospital. The project is being funded by grants for Government and municipal initiatives for the "Promotion of Territorial Partnerships and Territorial Implementation of the 2030 Agenda," published by Italian Agency for Cooperation and Development (AICS) The project aims to contribute to the reduction of morbidity and mortality rates in the region.

Table 2. Relevant event timeline for ambulances and staff variations throughout 2022

Date	Event
Until April 2022	One ambulance and two minibuses adapted to work as ambulance rented.
April 1, 2022	Two ambulances were purchased; two minibuses were decommissioned. Ambulances are operational at Ponta-Gea, Chingussura, and Nhaconjo, covering 12 health centres.
15th March 2022	Six drivers and three nurses were recruited, joining existing teams. A total of 9 drivers and 9 nurses were distributed among operational ambulances.
October 1, 2022	An additional three drivers and three nurses were recruited. A total of 12 drivers and 12 nurses were assigned, with four drivers and four nurses per ambulance. The number of health centres covered increased from 12 to 15.

2.2 Study Design and Data Collection

Our study retrospectively examines ambulance callouts and transfers from the HCs to the HCB from February 1st, 2022, to December 31st, 2022, spanning 11 months. We used various data sources, including databases and logbooks from CUAMM, to gather information on ambulance referrals, vehicles, fuel consumption records, and financial records. Ambulance referral data are the electronic transcription of patient referral charts recorded by CUAMM-trained nurses during emergency transfers. CUAMM staff regularly collects all the paper-made patient referral charts at the HCB so that trained dedicated local data-entry personnel digitize them into an electronic spreadsheet. CUAMM supervises and monitors the accuracy of the process weekly. For our analysis, we extracted the following variables: sex, age, disease category (medical, surgical/trauma, pediatric, obstetric/gynaecological), nurse-assigned triage priority codes (green, yellow, orange, red) and department allocation of the referrals when hospitalised. Data were anonymized upon variable extraction and only complete records were included in the cost-effectiveness analysis. The study was conducted according to the ethical guidelines of the Declaration of Helsinki.

We retrospectively evaluated all cases referred to the HCB by ambulance as effective and non-effective, based on the emergency code assigned by the CUAMM nurses after triaging the patients. We classified green and blue referrals as ineffective, whereas yellow, orange, and red codes as effective. The purpose of this classification is to create indicators to measure the effectiveness of the referral system. It gives us a proxy to determine whether the system is performing its primary functions of assisting and transferring yellow, orange, and red emergencies that cannot be treated at the HCs. However, we understand that in LICs, ambulances have additional social responsibilities. For instance, they transport patients who are not in life-threatening conditions but have no other means of reaching the HCB (Conti et al., 2022). Thus, we also performed a complementary analysis to evaluate the cost-effectiveness of the intervention with a different outcome variable (*number of years saved*) and focusing more specifically on obstetric and neonatal emergencies. This analysis is available in the Annex section of this paper.

3. Cost-effectiveness Analysis

Our analysis aims to determine the cost-effectiveness ratio of the intervention, which in our case is the cost per effective referral. Cost-effectiveness analysis is a comparative method to assess the costs and health outcomes of different interventions. It is generally performed by comparing the costs and health outcomes between different interventions or against the status quo (e.g., intervention vs no intervention). The analysis estimates the cost required to gain a unit of health outcome. By providing a way to assess the costs and benefits of alternative health interventions, cost-effectiveness analysis can be used to prioritize resource allocation and identify projects that can produce the greatest health improvement in locations with limited resources (WHO, 2022).
Cost-effectiveness analysis plays two key roles in the global health landscape. Firstly, it can be used to assess the efficiency of the current and future health systems. It helps in prioritizing processes, resource management insights and planning to achieve the greatest health benefits. Secondly, it can be used to support decision-making by national authorities when evaluating if new interventions should enter a "health benefit package", i.e., to be adopted more broadly within the country. By combining these applications, cost-effectiveness analysis ensures optimal utilisation of financial resources in the health sector, resulting in the greatest possible health gain with the available health budget (Bertram et al., 2016).

Our analysis develops along the lines of previous studies (Accorsi et al., 2017; Breman & Britan 2011) and considers the perspective of the governmental health provider who would be responsible for financing the AbRSE once external aid funds are no longer available. The purpose of our research is to provide a means to assist LICs health authorities in making evidence-based, rational, and effective choices. Hence, we evaluated the cost-effectiveness of the system in everyday clinical operations, excluding its setup and initiation, presupposing that all expenses would need backing from the designated governmental health provider to sustain the AbRSE's operation once external international aid is terminated.
We excluded the additional costs required for starting the service, such as supervision, training, health education advertisement and advocacy. Our focus was on the running costs of the AbRSE, and we considered only the costs falling within the referral service, excluding those of the primary care delivered by the HCs and those falling onto the HCB for further care. As such, pre- and post-referral costs were not included in this analysis. We included only the costs of pick-up, transfers, assistance during transfer, and delivery to HCB of the patients referred. Thus, considered costs are ambulance operational costs associated with transportation, such as ambulance amortization, maintenance, fuel, personnel costs for ambulance staff like nurses and drivers solely employed for the referral service, and medical equipment costs. We also considered costs for communication among ambulance staff, HCs, and the HCB, which encompasses expenses related to cellular devices, computers, and communication credit.
We estimated benefits considering the number of emergencies correctly referred (yellow, orange, red) assuming that without immediate transfer, those cases would have resulted in patient death or disability. This measure serves as a robust proxy for the number of lives saved, an indicator used in previous cost-effectiveness research (e.g., Pinto et al., 2016).

To determine whether an intervention is cost-effective the ratio resulting from the comparison of costs and benefits is then compared with an acceptability threshold. Only cost-effectiveness ratios falling below the threshold are considered favourable and attractive. There is an everlasting academic debate regarding the choice of the most adequate acceptability threshold (e.g, Leech et al., 2018; Bertram et al., 2016). However, most research uses the WHO's (2001) Commission on Macroeconomics and Health's GDP-based thresholds based on 1 to 3 times the national GDP per capita values. As such, similar to Accorsi et al. (2017), we set the acceptability threshold for the cost-per-referral below the GDP per person per year in the country, which is 582 US dollars (World Bank, 2022). Additionally, we included two more levels. It was attractive if the cost was below half of Mozambique's GDP per person per year, i.e., 291 US dollars, and very attractive if it was below one-tenth of it, i.e., 58.20 US dollars (see Table 3 for a detailed explanation of the threshold chosen).

Table 3. Acceptability threshold for the Cost-Effectiveness Analysis

Ratio Level	Acceptable	Attractive	Very Attractive
$/effective referral	< $582	< $291	< $58.20
	GDP per capita in Mozambique (World Bank, 2022)	*50% GDP per capita*	*10% GDP per capita*

4. Results

A total of 7849 ambulance referrals from the 15 served HCs to the HCB were recorded during the 11-month study period. Nhaconjo was the centre with the highest flow of referrals (n = 1502). The ambulance average scene time from HC staff call to arrival at the hospital was 46 minutes. Table 4 reports the referral breakdown per type of emergency. Obstetric emergencies (n = 3151, 40%) were the most numerous, whereas surgical the less frequent (n = 720, 9%).

Out of the total referrals, 20% were classified as ineffective (n =1554) as CUAMM-trained nurses assigned green and blue codes to the transfer. We excluded ineffective referrals from our analysis and focused on the 6295 effective referrals completed. See Table 5 for a complete breakdown of effective referrals into emergency codes.

Table 4. Referrals breakdown per emergency type

Type of Emergency	N	%
Obstetrical	3151	40
Neonatal/pediatric	1903	24
Medical	2075	27
Surgical	720	9
Total Emergencies	7849	

Table 5. Referrals classification into ineffective (green and blue code) vs effective (red, orange, yellow codes).

Referrals Evaluation	N	%
Ineffective referrals (green or blue codes)	1554	20
Effective Referrals	**6295**	**80**
Red	802	13
Orange	2387	38
Yellow	3106	49

The extrapolated cost of the AbRSE for the 11 months, based on the cost of one full year (2022) is displayed in Table 6. We considered a 4-year ambulance utilization (Accorsi et al., 2017) for cost imputation and used 7 years (Tsegaye et al., 2016) for sensitivity analysis. In the 11 months, the total running costs of the AbRSE were $172.070,82. Ambulance rental was the most expensive cost ($62.059,64), followed by CUAMM proprietary ambulance amortization quotas for the 11 months ($39.998,42).

Table 6. Running costs 11 months (February-December 2022) with 4 and 7-year proprietary ambulance amortization.

Item	4-Year Amortization (Accorsi et al., 2017)	7-Year Amortization (Tsegaye et al., 2016)
N. 12 Nurses (3 for each of the 4 ambulances)	$28.838,55	$28.838,55
N. 12 Drivers (3 for each of the 4 ambulances)	$22.037,10	$22.037,10

Item	4-Year Amortization (Accorsi et al., 2017)	7-Year Amortization (Tsegaye et al., 2016)
Fuel, maintenance, insurance, taxes, etc. for ambulances	$2.158,59	$2.158,59
Ambulance Rental	$62.059,64	$62.059,64
Ambulance Amortization (11 months)	$39.998,42	$22.856,24
Amortization of computers complete with printers, operating system, and various accessories (4-year usage)	$894,61	$894,61
Telephone credit for emergency reference system from health centres to central hospital	$156,11	$156,11
Amortization quota for cell phones for ambulance service management (4-year usage)	$5.214,06	$5.214,06
Medical supplies, disposable materials, drugs	$10.713,74	$10.713,74
Total Running Costs (11 Months) 2022	**$172.070,82**	**$154.928,64**

Note: All amounts are in US dollars. CUAMM's balance sheet is reported in Euro. To convert values into USD for this analysis, we used Banca D'Italia exchange rate on the 31st December 2022 - 1 Euro = 1,0666 USD

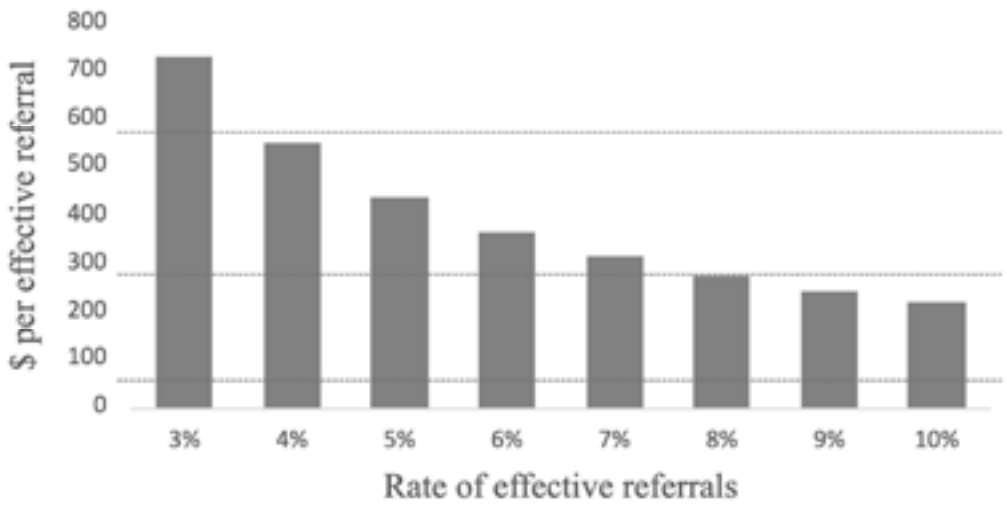
Considering only effective referrals (n = 6295), the cost per effective referral was $27,33, which is well below $58.20, and thus fulfils the *Very Attractive* criterion for our acceptability threshold (see Table 7).

Table 7. Cost Effectiveness Ratio per total referrals (including ineffective) and per effective referrals.

Cost Effectiveness Ratio	4-year amortization	7-year amortization	Acceptability Threshold
Cost per referral (Tot. Cost/Tot. referrals)	$21,92	$19,74	< $58.20 Very Attractive
Cost per effective referral (Tot. Cost/Tot. *effective* referrals)	$27,33	$24,61	< $58.20 Very Attractive

We then carried out a sensitivity analysis to assess the consistency of our results. We used different amortization rates for the proprietary ambulances and included in the analysis also ineffective referrals (blue and green codes). The intervention remains very attractive in both cases.
As mentioned in Section 4, the rate of effective referrals recorded, used for our analysis was equal to 80% (n = 6295). We conducted a simulation to determine the cost-effectiveness of the intervention if the rate of effective referral was lower at current costs. We compared this with the acceptability threshold, as shown in Figure 1. Our results indicate that the intervention remains attractive up to a rate of effective referrals of 8.5% and acceptable up to a rate of 4.25%. Similarly, effective referrals equal, the intervention remains Very Attractive up to an 11-month cost of the AbRSE of $366301, Attractive up to a cost of $1831861 and still Acceptable for $3675000.
This confirms the robustness of our analysis and suggests that even if the triage code criterion used to classify referrals is subject to selection error by CUAMM nurses, the intervention remains cost-effective with ample margins.

Figure 1. Sensitivity Analysis



Note: Sensitivity analyses according to the proportion of effective referrals. The dotted lines represent our acceptability thresholds to define the intervention as acceptable ($582, upper line), attractive ($291, middle line), and very attractive ($58,20, lower line). The costs refer to 11 months of AbRSE usage.

5. Discussion and Conclusion

Our results showed that the implementation of an AbRSE connecting peripheral minor HCs delivering primary care to a central hub hospital for further emergency care is highly cost-effective in LICs. Our findings are in line with previous research (Werner et al., 2020), confirming that relatively low investments can save lives and drive a high increase in the quality of life of beneficiaries (WHO, 2022). Our main analysis focused on the cost-per-effective referral, excluding transfers of green and blue codes that should have been assisted at the primary care level. The cost-per-effective referral was $27,33, falling below our Very Attractive threshold of 1/10 of national GDP per capita. This result is robust, corroborated by sensitivity analysis taking into consideration different amortization rates and rates of effective referrals. It remains consistent even when comparing it to more restrictive thresholds such as the WHO (1996), which sets Very Attractive interventions < $30. These results are ulteriorly confirmed if we adjust WHO's thresholds for inflation using the Consumer Price Index method - from 1996 to 2022, the compounded inflation rate in Mozambique was approximately 610%, pushing the cut-off values of Attractive and Very Attractive tiers much higher than our GDP-based ones.

Although the specificity of our context and analysis makes comparison with similar projects difficult, our results are in line with most studies and complement previous research. For example, Accorsi et al., (2017), found that implementing an AbRSE for Emergency Obstetric and Neonatal Care (EmONC) services in a rural setting in Ethiopia was highly cost-effective, with a cost per year saved of $ 24.7. Similarly, Tayler-Smith et al., (2013) demonstrated the effectiveness of emergency obstetric care through a referral network, emphasizing the importance of timely interventions in reducing neonatal mortality. Finally, Adene, T. (2016) highlighted the positive impact of dedicated ambulance service in facilitating referrals and improving resource utilization in Ethiopia.

Our research provides novel evidence on the economic profile of AbRSE as it isolates the referral process cost and benefits. However, the AbRSE studied is an intervention part of a more complex multistakeholder strategy committed to improving access to healthcare. Moreover, as Accorsi et al., (2017) point out, the effectiveness of a referral also depends on factors such as "the timeliness of the decision for referral, pre-referral care, en-route stabilizing care, time taken to arrange referral vehicle, time taken to reach higher facility and promptness with which the case was attended at the higher facility", which were not taken into account for this study.

Our study objective was solely to determine the cost-per-effective referral, on average, across types of emergencies. We did not therefore include any consideration regarding central hospital buffer or workload increase, although a relevant factor that decision-makers have to take into account. Our study extends throughout a larger period in comparison to previous studies which generally consider shorter time-frames and smaller samples. This allowed us to overcome some of our study's limitations which can however serve as prompts for future research. For example, road conditions and weather seasonality were ruled out by the 11-month time frame chosen for the study, whereas previous studies were impacted by rain seasons impacting road viability. Our criterion for the selection of effective cases was based on CUAMM-trained nurses assigned triage codes. Although the large number of

referrals might rule out a lack of accuracy and misspecification of codes, our classification criterion remains sub-optimal as it was not performed by health professionals with specific skills across types of emergencies. Moreover, the judgment on effectiveness remains theoretical and there is no way to assess the counterfactual, i.e., whether referral assessed by other means would have caused patient deaths or irremediable damages such as disability.

More broadly, especially in the case of emergency services, the benefits or losses in health cannot be measured (only) in economic terms, as dealing with human life pertains also to the ethical domain. Finally, this was a retrospective study and although weekly monitoring and supervision by experts were performed, erroneous recording and data entry may have been still possible.

Despite the very high cost-effective economic profile of the AbRSEs recorded, it can still be enhanced in several ways. For example, HCs could refer patients only when needed, delivering primary care through the best of their means. This requires implementing a change in the organizational culture of the HCs, which needs to recognize the actual utility of AbRSEs. It also requires specific personnel training, improved drug availability, and strengthened supervision at peripheral units, as noticed by Conti et al. (2022). Thus, the room for improvement is still very relevant.

Research on the cost-effectiveness of emergency services, particularly in LICs settings, is an area that has not been explored enough. This issue falls within the so-called 10/90 gap, where only 10% of medical research is dedicated to conditions affecting 90% of the world's population. The objective of this study was thus to contribute also to this issue by evaluating whether the model tested in Beira can be replicated at the provincial and national levels.

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ANNEX

One of the main objectives of the intervention is the reduction of maternal and neonatal mortality, we run a complementary analysis focusing on obstetric and neonatal emergencies. Using the same dataset, we focused on the subgroup of mothers referred from the HCs and hospitalized in the delivery room of the HCB to estimate the total number of years saved (YLS) of mothers and newborns, using local life expectancy data, similar to previous studies (e.g., Accorsi et al., 2017). As this is a retrospective study, we only had limited control over data collection. As such, we could not include prevention of disabilities in the model as we lacked information in this respect. We included a 6% (WHO, 1996) discount rate for the life years gained and used only the proportion of costs referring to obstetric referrals, multiplying their total number for the average cost per referral.
The total YLS for mothers admitted to the delivery room was calculated by summing the difference between the life expectancy of Mozambique and the age of each mother admitted to the delivery room. Maternal deaths were excluded from the count. To calculate the YLS for the newborns, the number of live births was multiplied by the life expectancy of Mozambique. Eighty-three neonatal deaths were reported and thus excluded from the count.
In our case, the discounted total YLS are 150504 whereas the proportion of the cost for an effective maternal and obstetric emergency which led to hospitalization in the delivery room and to delivery was $48.546,11.
The $/year of life saved for this specific type of emergency is $0,32, indicating an extremely convenient and cost-effective intervention.

Annex 1. Calculation of discounted YLS obstetric and maternal emergencies.

CEA YLS Effective obstetric and maternal emergencies	**Units**	**YLS Delivering Mothers** Σ Life Expectancy Mozambique – Age of delivering mothers
Obstetric emergencies transported from health centers to the HCB and admitted to the delivery room	1776	60388
Maternal Death	3	-105
Total YLS Obstetric emergencies	(1776-3)1773	60283

	Units	**YLS Alive Births** Life Expectancy Mozambique * n. Alive Births

Total births	1775	
Neonatal deaths	83	
Total YLS Alive Births	(1775-83) 1692	99828

TotaleYLS (Mothers + Alive Births)		(60283+99828) **160111**
6% Discount		9606,66
Discounted Total YLS		**150504,34**

Annex 2. Cost per year of life saved obstetric and maternal emergencies.

	Tot. cost-effective obstetric referral (cost per referral * effective obstetric emergencies)	**$/year per saved life**	**Acceptability Threshold**
C/E 4 years amortization	$48.546,11	$0,32	< $58.20 Very Attractive
C/E 7 years amortization	$43.709,81	$0,29	< $58.20 Very Attractive

Knowledge, attitudes and practices for blood safety in a worldwide perspective

PAPER

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COLLECTION, PRODUCTION AND STORAGE OF BLOOD COMPONENTS

Editorial

Knowledge, attitudes and practices for blood safety in a worldwide perspective

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"The KAP (Knowledge, Attitude, and Practice) survey on bacterial contamination of blood components"[1] addresses a crucial aspect of blood safety: raising awareness among healthcare staff regarding the risk of bacterial contamination in blood components and the importance of safe preventive practices. This becomes even more critical in the context of developing countries, such as the Democratic Republic of Congo, where some facilities (reliable cold chains, sterile connection devices, digital check systems, bacteriological controls, etc.) may not always be available, leading to a higher risk of infection transmission, whether viral or bacterial.

In recent years, blood transfusion practices have increasingly relied on the implementation of procedures and operational instructions that have significantly improved blood safety. However, a question arises: are frontline operators sufficiently aware of the root causes from which these procedures originated? More recent approaches to quality systems in healthcare necessitate that health professionals perform detailed and documented risk assessments when introducing significant changes or new activities[2]. This is essential to implement all effective and feasible preventive measures before it's too late. In complex systems, all actors, regardless of their roles, are key informants in identifying possible "points of failure" in the process itself.

Hence, a thorough understanding of the transfusion process is crucial for ensuring transfusion safety. This understanding is derived from both formal and informal training, along with individual experience. Effective training depends on evidence-based content, suitable teaching methodologies, and regular re-evaluation within a continuous education program. Numerous relevant online training tools are available globally, regularly updated, and issued by international institutions such as WHO[3] and ISBT[4]. A survey on transfusion medicine training facilities and programs in Africa[5] revealed a persistent gap between training needs and available resources, particularly in remote areas. Similar gaps might exist in other regions worldwide. Over the last decade, accelerated by the pandemic, accessible online training packages have become valuable supplementary educational opportunities[6]. However, face-to-face exchanges and practical sessions are irreplaceable by digital tools, as training content needs real-world contextualization, and education is inherently a bidirectional process requiring mutual understanding.

But if safe practice implies knowledge and understanding what about the importance of attitudes?

Inclusive teamwork, participatory approach, sharing knowledge and doubts, paying attention to critical steps, and accepting corrections in a continuous improvement cycle

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are all elements that require positive attitudes from all healthcare personnel, and this is for the sake of patient and operator safety[7].

Procedures and technologies may vary based on available resources in different healthcare systems. Nonetheless, assessing and strengthening knowledge and encouraging proactive attitudes and critical thinking towards transfusion safety are universal assets that can be promoted in all settings. It's crucial to remember that the most important resources are human resources. This underlies the strong message conveyed by the paper from Heroes and colleagues from the Democratic Republic of the Congo, which is applicable to all.

Nevertheless, this should not overshadow the shortages of structural, technological, and financial resources in the field of blood safety and availability in developing countries, particularly in Sub-Saharan Africa (SSA). In recent times, programs like PEPFAR funded by the US and other projects funded by EU countries have provided substantial support to National Blood Bank services in SSA[8,9]. These efforts have had a significant impact on blood safety, even though the centralized and top-down approach has been the subject of criticism due to high costs and limited availability of safe blood in peripheral areas[10]. In any case, reliable and sufficient funding, coupled with appropriate implementing strategies, should be maintained and strengthened in contrast to signs of "donor fatigue" that have emerged in recent years[11]. Blood transfusion from voluntary non-remunerated donors is considered an essential medicine by the WHO, but it remains challenging for healthcare services in the lowest-income countries, especially if we aim to continue asserting that blood safety is a global health objective.

Keywords: bacterial contamination, Africa South of the Sahara, allogenic blood transfusion.

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PAPER

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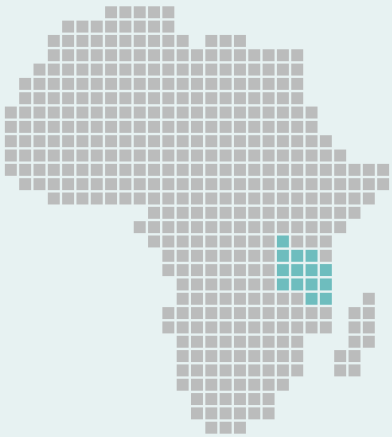

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Decentralization Matters: Association of Adherence to Treatment and Distance for the Management of Non-Communicable Diseases in Rural Tanzania

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Abstract: Since March 2019, a non-communicable diseases program has been established at hospital level, with enrollment and clinical reassessment every 6 months. Since July 2023, monthly enrollment and visits have also been conducted at health center level. This study aimed at assessing the adherence to scheduled follow-up visits following the decentralization of the integrated NCDs program from Hospital to Health Center level and investigate factors influencing follow-up adherence. The study was performed in a rural district in Iringa Region, Tanzania. Adherence was measured at both levels. Multivariate regression analysis was conducted to describe socio-demographic and clinical factors influencing attendance at the 6-month hospital-level visit. Among 2198 patients enrolled at the hospital level, weighted adherence over 42 months was 40.8% (95% CI 39.0–42.6%) at the 6-month visit. Multivariate analysis revealed that as the distance from the hospital increased, the probability of attendance decreased (OR 0.17; 95% CI: 0.08–0.39). Among 571 patients enrolled at the residence level, adherence over the first 10 months of program implementation was 91.6% (90.4–92.8%). The findings showed that distance was by far the most important barrier to follow-up adherence and suggested that decentralizing the program from the hospital to peripheral health centers may ensure high follow-up rates.

Keywords: non-communicable disease; NCD; Tanzania; diabetes; hypertension; decentralization; health service development

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1. Introduction

Cardiovascular diseases (CVD) represent one of the major public health challenges worldwide [1,2]. Globally, 17.9 million people were estimated to die from cardiovascular diseases in 2019, accounting for 32% of all deaths [3]. Of these, 85% were attributed to myocardial infarction or strokes [3,4]. Notably, more than three-quarters of CVD deaths occur in low- and middle-income countries (LMIC) [5]. In Sub-Saharan Africa (SSA), the total number of deaths due to CVD across all age groups exceeded one million in 2019, marking a 78.0% increase compared to 1990 [6]. While CVD mortality rates have declined in most regions over the past 40 years—largely due to advancements in early detection and the treatment of hypertension (HTN), diabetes mellitus (DM), and hypercholesterolemia—LMICs continue to bear the brunt of the burden. An estimated 1.28 billion people aged 30–79 worldwide are affected by HTN, with nearly two-thirds residing in LMICs. Alarmingly, 46% of adults with HTN are unaware of their condition [5].

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According to the international literature, CVDs-related death rates have been 2.1 times higher in SSA Countries than in High-Income Countries (HIC) [6]. This disparity has been largely driven by increasing urbanization and the adoption of Western lifestyles, which have led to higher body mass index (BMI), blood pressure (BP), and fasting blood glucose (FBG) levels [7]. Between 1990 and 2019, the number of DM cases in SSA increased by 131.7%, with a 2.1% rise in age-standardized prevalence rates [8]. While elevated BP prevalence has steadily declined in HICs since the 1970s, it has continued to rise in SSA, resulting in a doubling of deaths attributable to high BP [9]. The World Health Organization (WHO) reports a higher prevalence of HTN in Africa, with approximately 46% of adults aged 25 years and older, compared to 35% in the Americas and other developed countries, and 40% in other parts of the world [10,11]. Non-communicable diseases (NCDs) are becoming the leading cause of death in Africa, with the percentage of deaths rising from 24% in 2000 to 37% in 2019. By 2021, 24 million people in the region were living with DM, and this number is projected to increase by 129% to 55 million by 2045 [12].

NCDs are a significant public health issue in Tanzania. In 2021, the age-standardized death rate for the four main NCDs, CVD, chronic respiratory disease, cancer, and diabetes was 557 per 100,000 in men and 498 per 100,000 in women [13]. Tanzania has made progresses on NCD regulations such as tobacco taxes, national policies and guidelines. However, progress has been limited in other areas such as alcohol control, salt and trans fat consumption and physical activity guidelines [13–15]. HTN is the most common NCD and impacts approximately 25% of the adult population, representing the leading cause of death after HIV [13]. Diagnosed individuals often are neither in BP treatment nor seeking care [15–17]. Specifically, rural populations are less likely to be aware of their HTN and are, therefore, less likely to be on treatment [18–21]. DM also plays a significant role, with a prevalence of 10.3% among adults aged 20–79, accompanied by a high incidence of complications [22].

In SSA, healthcare systems struggle to provide continuous long-term care for patients affected by HTN and DM [15,16,18,23], including limited healthcare infrastructure, healthcare workforce shortages, limited access to medications, lack of awareness, and education, cultural, and social factors [24–28]. Additionally, the 2012 WHO STEPs survey revealed that three-quarters of participants with HTN or DM had never been previously diagnosed, and less than half of those with a known diagnosis were receiving care [18,19,21]. International studies suggested that individuals from lower socioeconomic backgrounds and those living in rural areas are less likely to have their blood glucose or BP measured regularly [16,17,29,30]. The factors associated with low adherence rates to treatment and follow-up care are mainly due to social, cultural and economic conditions, as demonstrated in several studies in LMICs [31–35].

In 2010, the WHO launched the Package of Essential NCD Interventions (WHO PEN) to facilitate the decentralization of healthcare services to primary care settings [36]. Particularly, this approach aimed to provide accessible treatment at community health centers (HC) for common NCDs through an integrated outpatient care model, which has been scaled up to different countries [36–38]. In March 2019, an integrated management system of HTN and DM was implemented in rural Tanzania. In the first phase of the program, each patient underwent initial medical assessment at the hospital level [39]. According to the WHO dedicated package, reassessment visits were conducted at the hospital, every six months [40]. In July 2023, based on the PEN PLUS approach, a significant change in the program occurred with the launch of the second phase, shifting enrollment and routine follow-up to peripheral HCs.

Despite numerous efforts and initiatives at macro level, a limited number of studies have evaluated the effects of decentralizing HTN and DM care from hospitals to peripheral health facilities in SSA [41–44].

To contribute to addressing the gap in evaluating the impact of decentralizing NCDs interventions to lower-level health facilities, this study aimed at assessing the adherence to the scheduled follow-up visits following the decentralization of the integrated NCDs

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program from the hospital to the HC level. Additionally, this study illustrated the factors influencing adherence to follow-up care for patients enrolled during the first five year of the integrated NCDs Program at Hospital level, which in turn contributed to the decision to decentralize the clinical activities to the lower-level facilities.

2. Materials and Methods

2.1. Study Design

This is a retrospective observational study on adherence to follow-up among hypertensive and diabetic patients in rural Tanzania.

2.2. Study Setting

Iringa District Council (Iringa DC) is located in a rural area 500 km southwest of Dar es Salaam, with a population of around 330,000 inhabitants spread over a surface area of about 20,000 km^2 [45]. Iringa DC is one of the five districts of the Iringa region, which has a total population of 1,192,728 people [45]. The majority of inhabitants are peasants, others own businesses, and only a handful have formal jobs. The local healthcare system of Iringa DC includes Iringa DC Public Hospital, Tosamaganga Regional Referral Hospital (TRRH), 10 HCs, and 103 dispensaries serving 134 sparsely populated villages. Particularly, TRRH is a not-for-profit faith-based hospital, which counts 192 beds, recently recognized as Referral Hospital at Regional Level. The 10 HCs are spread and serve as peripheral referral centers within the reference territory.

2.3. The NCDs Program

Starting in October 2016, Doctors with Africa CUAMM and the Iringa DC established an outpatient service for individuals with NCDs at the TRRH outpatient department. In March 2019, an integrated management system for HTN and DM was commenced following the completion of the Protocol of Cooperation Agreement among the Iringa DC, TRRH, and the international NGO Doctors with Africa CUAMM [39]. The overarching goal was to ensure access to quality and equitable healthcare for the district's population. The agreement was designed to enhance and strengthen the healthcare system in Iringa DC, specifically focusing on the prevention and treatment of HTN and DM at both the Hospital and HC levels.

The initial protocol included an assessment at TRRH, where patients underwent medical visits, BP and finger-stick FBG measurements, along with laboratory exams (creatinine, in DM patients and total cholesterol in selected cases). After receiving their diagnosis from a medical doctor and health education from a nutritionist, patients were provided with a personalized treatment card (TC). Patients were required to return to the hospital for a reassessment visit every six months ($\pm$1 month), following guidelines provided by the WHO for a dedicated NCDs package of care [40]. Further visits could also have been performed at the closest HC for drug refilling, additional BP, and finger-stick FBG controls, if needed. Clinical and treatment information were documented in the TCs at each reassessment visit at TRRH. This organizational setting is referred to hereafter as the TRRH Program.

In July 2023, a major change was implemented: enrollment (medical visit, BP, and finger-stick FBG measurements) and supervision visits were routinely conducted in nine HCs. After enrollment, a thorough clinical assessment at TRRH was recommended for patients with HTN or DM (medical visit, BMI and BP measurements, serum FBG, and HbA1c for those with diabetes), but excluding those above 80 years old and those who declared financial or transportation constraints for traveling to TRRH. Supervision visits at the HCs were scheduled every month, while reassessment visits at the TRRH are considered for selected patients (e.g., resistant HTN, diabetic decompensation, established organ damage in adult and elderly young patients). This setting is referred to hereafter as the HC Program.

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Screening, diagnosis, and treatment of HTN and DM as well as criteria for referral to a higher level of care during follow-up were provided according to national NCDs guidelines [46].

2.4. Inclusion and Exclusion Criteria

Patients aged 18 years and above, diagnosed with both new and known HTN and/or DM, who were enrolled in the TRRH program between March 2019 and March 2024, and in the HC program between July 2023 and March 2024, were included in the study. Pregnant women were excluded.

The outcome measures included in the study were the following:

- for patients enrolled in the TRRH program: adherence to scheduled reassessment visits at TRRH at 6, 12, 18, 24, 30, 36, and 42 months;
- for patients enrolled in the HC program: adherence to scheduled supervision visits at the HCs at 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 months.

Adherence was considered as the completion of the visit within the deadline scheduled in the previous visit. In each program, a delay of up to one month was considered acceptable.

2.5. Data Collection and Covariates

Data were collected retrospectively from the hospital's electronic medical records and HCs registers. The healthcare staff on duty were responsible for collecting data on patients' Enrollment and TCs. The information was verified by a Medical Doctor before being entered anonymously into a specifically designed database using the software EpiInfo v. 7.2.3 [47].

The data collection forms for patients visited within the TRRH program included socio-demographic factors (such as age, gender, occupation, health insurance status, and distance from the TRRH) and clinical factors (previous/new diagnosis of HTN or DM, previous diagnosis of cardiovascular diseases such as myocardial infarction, stroke, heart failure, renal failure according to eGFR results, diabetic foot or amputation, lifestyle factors such as alcohol consumption, smoking, and physical inactivity, previous registrations of BP or FBG if any, BP, height, weight, body mass index (BMI), finger-stick FBG, and HbA1c for patients with Diabetes Mellitus). We considered CVD complications at baseline if there were not (i) previous medical diagnosis of myocardial infarction, stroke or heart failure; (ii) previous medical diagnosis of diabetic foot or amputation in DM patients; (iii) chronic kidney disease (CDK) stage $\geq$ 3a according to the baseline creatinine and estimation of eGFR (through CKD-EPI equation). The lifestyle was considered according to the clinical history: Alcohol abuse (Y/N), Sedentary (Y/N), Smoking (Y/M).

The data collection forms for patients enrolled in the HC program comprised the following variables: age, gender, health insurance status, distance from the hospital, and essential clinical data recorded at each visit (BP; height, weight, BMI in obese patients; finger-stick FBG in obese or symptomatic patients; pharmacological treatment at each visit). BP was measured using a manual sphygmomanometer, after five minutes of rest, in a seated position, with the arm at heart level. Elevated values were confirmed twice. Patients were classified as hypertensive if a BP of $\geq$140/90 mmHg was recorded on two separate occasions. FBG levels, either fasting (after at least 8 h since the last meal) or random, were measured using a GlucoPlus™ glucometer, GLUCOPLUS INC. 2323 Halpern, St-Laurent (Montreal) Québec, Canada H4S 1S3.

2.6. Statistical Analysis

Socio-demographic and clinical variables were dichotomized or grouped into classes, namely sex, age, distance from the TRRH (0–19/20–39/40–59/60–79/80+ km), health insurance status, diagnosis, disease awareness, (<140/90, $\geq$140/90, $\geq$160/100, $\geq$180/110 mmHg), FBG (<7, $\geq$7, $\geq$9, $\geq$11 mmol/L). Among patients enrolled at the TRRH, occupation

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(other/peasant/skilled workers), lifestyle (correct/uncorrect), complications (yes/no), and BMI (<18, 18–24, 25–29, ≥30 kg/m^2) were also recorded.

The proportion of adherence along the subsequent visits was considered separately for those enrolled at the TRRH (6-month reassessment visits) and those enrolled at the HC level (1-month supervision visits). Adherence was analyzed as panel data of autocorrelated observations clustered at the patient level, using a random-effects logit model.

A multivariate random-effects logit model was also implemented to assess the influence of socio-demographic and clinical variables on adherence to re-assessment visits among patients participating in the TRRH program. Statistical analysis was performed using Stata 17 [48].

3. Results

3.1. Socio-Demographic and Clinical Characteristics in the Two Programs

The study included 2198 patients enrolled in the TRRH program between March 2019 and March 2024. The majority of participants were females (75%), aged 60 and above (51%), and without health insurance (75%). HTN was the most prevalent condition, affecting 1542 patients (70%). Additionally, 313 patients (14%) had DM, while 343 (16%) were diagnosed with both conditions. Approximately one-third of patients with HTN and DM were newly diagnosed, with about one-third of HTN patients showing very high BP (≥180/110 mmHg) and nearly half of DM patients presenting very high FBG levels (≥11 mmol/L). A detailed summary of the enrollees' characteristics is provided in Table 1.

Table 1. Socio-demographic and clinical characteristics of the enrollees in the TRRH program (n = 2198).

		No.	%
Population	Total Population	2198	100%
	Male	548	25%
	Female	1650	75%
Age classes	15–39 years	173	8%
	40–59 years	884	40%
	60–79 years	1065	48%
	80+ years	76	3%
Occupation	Retired/Housewives/Unemployed	305	14%
	Peasant	1438	68%
	Skilled workers	368	17%
Distance from the TRRH	0–19 km	611	29%
	20–39 km	540	26%
	40–59 km	353	17%
	60–79 km	393	19%
	80+ km	175	8%
Health Insurance	no NHIF	1650	75%
	NHIF	548	25%
Diagnosis	Hypertension	1542	70%
	Diabetes Mellitus	313	14%
	Both	343	16%
Disease Awareness	Yes	1505	68%
	No	693	32%
	Already known HTN	1258	67%
	HTN new diagnosis	627	33%
	Already known Diabetes	446	68%
	Diabetes new diagnosis	210	32%
Baseline CVD complications	No complications	1605	73%
	Complications	593	27%

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Table 1. *Cont.*

		No.	%
Blood Pressure	BP < 140/90 mmHg	242	13%
	BP ≥ 140/90 mmHg	409	22%
	BP ≥ 160/100 mmHg	603	32%
	BP ≥ 180/110 mmHg	625	33%
Fasting Blood Glucose	FBG < 7 mmol/L	125	20%
	FBG 7–8.9 mmol/L	107	17%
	FBG ≥ 9 mmol/L	93	15%
	FBG ≥ 11 mmol/L	313	49%
Body Mass Index	<18 kg/m^2	76	4%
	18–24 kg/m^2	693	34%
	25–29 kg/m^2	650	32%
	≥30 kg/m^2	592	29%
Lifestyle	Correct lifestyle	1114	51%
	Uncorrect lifestyle	1084	49%

As shown in Table 2, 571 patients were enrolled between July 2023 and March 2024 in the HC program. Almost all the enrollees were females without insurance. Most of the patients (87%) had a diagnosis of HTN (n = 499), 33 (6%) had a diagnosis of DM, and 41 (7%) were diagnosed with both diseases. Approximately half of the patients (49%) lived more than 20 km away from the TRRH clinic. Almost one-third of HTN patients had a very high BP level (≥180/110 mmHg), and 36% of DM patients presented the highest level of FBG (≥11 mmol/L).

Table 2. Socio-demographic and clinical characteristics of the enrollees in the HC program (n = 571).

		No.	%
Gender	Total Population	571	100%
	Male	89	16%
	Female	482	84%
Age	15–39 years	18	3%
	40–59 years	146	25%
	60–79 years	289	51%
	80+ years	118	21%
Distance from the TRRH	0–19 km	0	0%
	20–39 km	294	51%
	40–59 km	134	23%
	60–79 km	96	17%
	80+ km	47	8%
Health Insurance	no NHIF	535	94%
	NHIF	36	6%
Diagnosis	Hypertension	498	87%
	Diabetes Mellitus	33	6%
	Both	40	7%
Disease Awareness	Already known HTN	218	41%
	HTN new diagnosis	163	30%
	Already known Diabetes	157	29%
	Diabetes new diagnosis	41	55%
Blood Pressure	BP < 140/90 mmHg	17	3%
	BP ≥ 140/90 mmHg	157	29%
	BP ≥ 160/100 mmHg	173	32%
	BP ≥ 180/110 mmHg	191	36%

Table 2. *Cont.*

		No.	%
Fasting Blood Glucose	FBG < 7 mmol/L	29	40%
	FBG ≥ 7 mmol/L	10	14%
	FBG ≥ 9 mmol/L	8	11%
	FBG ≥ 11 mmol/L	26	36%

3.2. Follow-Up Adherence and Influencing Factors in the TRRH Program

After 6 months, 18 patients were either dead or discharged or transferred, 767 did not attend the 6-month visit, and 201 of them were traced back later, as they skipped the scheduled visit but attended a subsequent one. Considering the overall period of enrollment from the first visit (42 months), the percentage of patients on follow-up visits (patients attending their scheduled visit over the patients eligible for reassessment) decreased from 50.6% to 38.5% in 6 and 42 months, respectively, accounting for an overall weighted average 42-month adherence rate equal to 40.8% (CI 95%: 39.0–42.6%). The details of the follow-up attendances are explained in Table 3.

Table 3. Patients attending 6-month reassessment visits of the TRRH program (n = 2198).

	6 Months	12 Months	18 Months	24 Months	30 Months	36 Months	42 Months
Patients attending their scheduled visit	1008	682	535	426	363	318	265
Patients who were traced back	767	734	701	617	594	497	403
Patients eligible for reassessment §	1976	1644	1424	1182	1051	870	704
% of patients attending their scheduled visit (CI 95%) *	50.6% (48.5–52.7%)	40.7% (38.4–43.0%)	37.3% (34.9–39.8%)	36.7% (34.1–39.3%)	35.9% (33.2–38.6%)	38.1% (35.2–41.0%)	38.5% (35.4–41.6%)
Overall weighted average 42-month adherence (CI 95%) *	40.8% (39.0–42.6%)						
Last visit ≤ 210 days before	204	526	737	969	1093	1271	1436
Dead/Transferred/Discharged Patients	18	28	37	47	54	57	58

* Estimates from the random effects logit model (8851 visits among 1976 patients). § Include traced-back patients skipping the scheduled visit but attending a subsequent one.

Table 4 presents the results of multivariate analyses of factors influencing attendance in the TRRH program. Factors positively associated with higher attendance included having NHIF insurance coverage, being peasant and aged 40–59 years old. In contrast, males and those residing farther from the TRRH clinic were found to have lower attendance rates for scheduled follow-up appointments.

Table 4. Factors influencing attendance reassessment visits. Multivariate random effects logit model (n = 8342 visits among 1811 patients) *.

		OR	CI 95%		p
Gender	Male	**0.48**	**0.3189**	**0.7345**	**0.001**
	Female	1.00			
Age	15–39 years	1.00			
	40–59 years	**2.38**	**1.14**	**4.99**	**0.021**
	60–79 years	1.80	0.83	3.88	0.135
	80+ years	1.46	0.44	4.85	0.540
Occupation	Retired/Unemployed/Housewife	1.00			
	Peasant	**2.48**	**1.45**	**4.22**	**0.001**
	Skilled worker	0.76	0.39	1.50	0.432
Health Insurance	no NHIF	1.00			
	NHIF	**1.82**	**1.20**	**2.77**	**0.005**

Table 4. *Cont.*

		OR	CI 95%		*p*
Distance from TRRH	**0–19 km**	1.00			
	20–39 km	**0.58**	**0.36**	**0.95**	**0.031**
	40–59 km	**0.49**	**0.28**	**0.84**	**0.011**
	60–79 km	**0.45**	**0.26**	**0.77**	**0.004**
	80+ km	**0.17**	**0.08**	**0.36**	**0.000**
Diagnosis	Diabetes Mellitus	1.00			
	Hypertension	0.73	0.43	1.25	0.249
	Both	1.04	0.53	2.03	0.906

* Adjusted for reassessment visit number. In bold character: results with a statistical significance $p < 0.05$.

Greater distances were associated with an increasing lower probability of attendance, particularly for patients living more than 80 km from the TRRH clinic.

3.3. Follow-Up Adherence in the HC Program

Table 5 summarizes the patient adherence to supervision visits over 10 months in the HC program. Particularly, the overall weighted average 10-month adherence rate increased to 91.6% (CI 95%: 90.4–92.8%), with all patients attending their scheduled visits by months 9 and 10.

Table 5. Patients attending 1-month supervision visits in the HC program (n = 571).

	1 Month	2 Months	3 Months	4 Months	5 Months	6 Months	7 Months	8 Months	9 Months	10 Months
Patients attending their scheduled visit	406	344	293	228	195	172	142	112	77	50
Eligible for follow-up	501	374	309	243	201	179	143	115	77	50
% of patients attending their scheduled visit (CI 95%) *	80.6% (77.0–84.1%)	92.0% (88.9–84.6%)	94.8% (91.8–97.0%)	93.8% (90.1–96.5%)	97.0% (93.7–98.9%)	96.1% (93.7–98.9%)	99.3% (96.2–100%)	97.4% (92.7–99.5%)	100.0% (95.4–100%)	100.0% (92.9–100%)
Overall weighted average 10-month adherence (CI 95%)	91.6% (90.4–92.8%)									
Last visit ≤ 60 days	70	197	262	328	370	392	428	456	495	523

* Estimates from the random effects logit model (2605 visits among 501 patients).

4. Discussion

This study demonstrated high adherence rates to scheduled follow-up visits after decentralizing the NCD program from hospital-based care to residence-level services. Additionally, data from the first four years of the integrated NCD program, conducted at the hospital level, indicated that the distance from the point of care was the most significant factor influencing adherence to follow-up visits. Our findings reinforced this, showing a clear inverse relationship between distance and adherence, with an OR of 0.17 (95% CI: 0.08–0.36) for distances of 80 km or more.

These results aligned with findings from three similar studies, which considered the feasibility and impact of decentralization from district-level hospitals to primary healthcare centers in SSA countries, namely Malawi, Rwanda, and South Africa. Malawi, Pfaff et al. reported a 70% short-term retention rate of diabetic patients attending follow-up visits after a pilot project decentralized care across eight HCs in four health districts, with no significant differences in adherence and adequate DM and HTN control between hospitals and HCs [41]. Similarly, a South African pilot study, implemented across 10 community NCD clinics, evaluated the short-term impact of decentralization in nurse-led clinics. The short-term adherence rate was approximately 85%, and this improvement was accompanied by enhanced physiological outcomes for patients with NCDs [42]. A study in Rwanda showed that the odds of being retained in the program were lower (OR 0.11, CI 95% 0.02–0.62) among HTN patients accessing three district hospitals in comparison with

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patients accessing seven peripheral HCs. In addition, for those retained, there was no significant difference in achieving blood pressure targets between those accessing district hospitals and HCs [43].

DM and HTN represent a major public health concern in Tanzania [15,23]. However, healthcare services for such diseases are largely concentrated in urban areas and hospital settings, despite the fact that 4 out of 10 Tanzanians live in rural areas [18].

Adherence to NCD programs must be viewed within the context of the limited awareness of cardiovascular risk among rural populations in SSA countries [17]. Unlike acute conditions such as malaria, managing DM and HTN requires patients to have a basic understanding of the chronic and often asymptomatic nature of these conditions, along with a shift in health-related attitudes and a long-term commitment to therapy adherence and trustworthy relationships with health providers [49].

Notably, health-seeking behaviors through screening, diagnosis, and treatment programs for TB and HIV have been largely assessed in many rural communities in SSA [50–52]. However, the approach to NCDs in these populations remains largely underexplored [16,53–55], and there is still a need for more efficient and cost-effective interventions, including decentralization to community levels [56]. Lessons learned from TB and HIV programs have demonstrated that distance is a major barrier to the implementation of widespread and effective screening and long-term treatment interventions at the primary care level [57–61]. In Tanzania, high-quality HIV care has been successfully established, with nearly 80% of people living with HIV receiving regular care and 90% achieving viral suppression [62].

In contrast, the long-term, multifaceted, and integrated interventions of DM and HTN remain, nowadays, a significant challenge for the health systems in SSA [16,17,63]. The Pragmatic cluster randomized controlled trial (INTE-AFRICA) and the concurrent process evaluation (INTE-COMM), currently underway in Tanzania and Uganda [56], demonstrated that the integrated management of HIV, HTN, and DM is feasible and impactful. Indeed, some experts proposed that existing HIV and TB platforms could serve as a foundation for implementing and improving primary care services for HTN and DM [64–66]. However, the integration of these services is not without challenges. Factors like limited trained healthcare staff, infrastructural gaps, and drugs availability across facilities have affected the success of such integration in some settings, as seen in Ethiopia [64].

From the outset, it is essential to account for economic constraints and ensure the long-term sustainability of such programs [63]. This involves capacity building through task-sharing and task-shifting initiatives aimed at empowering local health personnel and community health workers. Furthermore, strengthening referral systems, establishing diagnostic and treatment protocols that utilize simple, cost-effective technologies, and ensuring efficient transport and logistics for drug supply and distribution are key elements. There is no ideal model, and it is necessary to start with pilot projects, like the WHO PEN-PLUS initiative [36], rigorously assess their outcomes, and refine these interventions to achieve the overarching goal: bridging the final gap between primary healthcare services and the underserved communities that need them most [38,67–69]. To enhance the accessibility of prevention, screening, and treatment interventions for HTN and DM in rural settings, a participatory approach to community health promotion and prevention is also crucial [68].

Two recent scoping reviews assessed studies on community-based care models for managing HTN and DM [70,71]. The health system saw benefits such as task sharing among various professionals and expanded access to services, as well as the prevention of other cardiovascular diseases. From the patients' perspective, the main advantages included greater flexibility in accessing services, along with reduced costs and waiting times. However, significant drawbacks included high dropout rates and the fact that these care models often operated in parallel, rather than being fully integrated.

This achievement is highly demanding, as it needs to develop, support, and enhance the construction of professional training networks, the delivery of innovative healthcare technologies, mainly drugs and diagnostic tools, the strengthening of logistical organization,

data management and information sharing, the integration with existing primary health services and platforms. It also requires long-term collaborative programs among a variety of stakeholders who play different roles in local healthcare systems.

The main limitation of the study, which paves the way for future research possibilities, came from its descriptive design, depicting two distinct cohorts of patients and not allowing specific causal inferences. However, this limit was partially offset by the extent of the patients enrolled (2198), data collection period (5 years) and the fact that the patients enrolled in the two programs were largely overlapping.

5. Conclusions

This study suggested that bringing primary care and diagnostic services for HTN and DM closer to people living in rural areas may increase program adherence.

Breaking down the barrier of distance and providing primary care and diagnostic services for HTN and DM in rural areas may foster substantial benefits. For patients, it reduces the need to spend time and resources traveling to distant reference points of care where such services are typically concentrated. For the broader community, it fosters regular interactions with healthcare personnel and community health workers, thus strengthening local networks and promoting health awareness and prevention initiatives.

Further research could determine the impact of NCDs integrated models at the lowest levels of the healthcare system by assessing the accessibility to screening, diagnosis and clinical treatment.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Particularly, patients' related information was retrieved for the purpose of the management of health-care services provision through the consent given by the patient when accessing the health facility.

Data Availability Statement: All data used in the manuscript are available upon request by contacting the lead author.

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A necessary interplay: the health system as a privileged entry point for the delivery of ECD interventions

POSTER AND ORAL PRESENTATION

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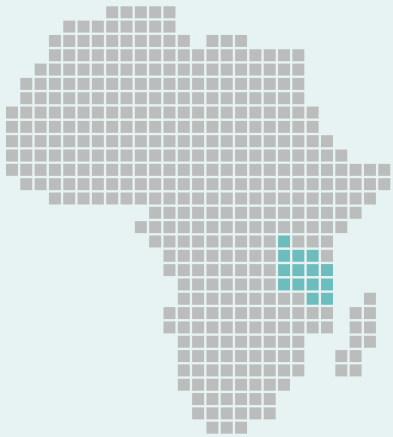
Location
Dar es Salaam, Tanzania

Presentation date
March 2024

Authors
R. Itambu and R. Lazzaro

Focus country
Tanzania



The ECD corner at Tosamaganga Hospital: an infrastructural and functional descriptive analysis

POSTER AND ORAL PRESENTATION

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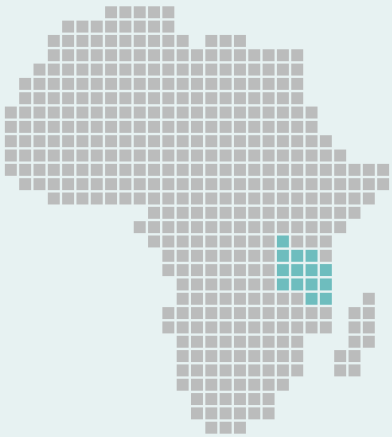

Repairing Communities. Tumesharudi Nyumbani Cabo Delgado - Mozambique armed conflict affected IDPs communities coming back home

POSTER AND ORAL PRESENTATION

Conference
Anthropology of Southern Africa Annual Conference 2024

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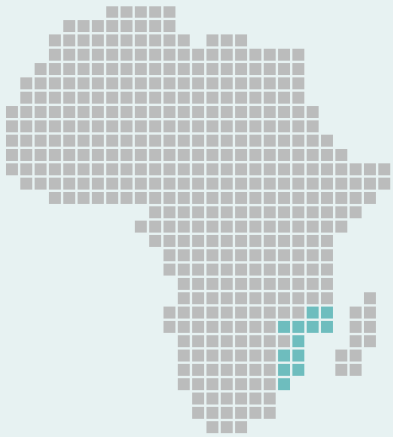
Authors
E. Occa

Focus country
Mozambique



Prevenzione e Multiculturalità

POSTER AND ORAL PRESENTATION

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Florence, Italy

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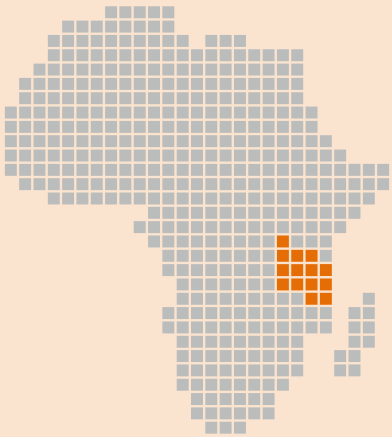

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RESEARCH ARTICLE

Stability in care and risk of loss to follow-up among clients receiving community health worker-led differentiated HIV care: Results from a prospective cohort study in northern Tanzania

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Abstract

Background: HIV services in Tanzania are facility-based but facilities are often overcrowded. Differentiated care models (DCM) have been introduced into the National Guidelines. We piloted a Community Health Worker (CHW)-led HIV treatment club model (CHW-DCM) in an urban region, and assessed its effectiveness in comparison to the standard of care (SoC, facility-based model), in terms of stability in care, loss to follow-up (LTFU) and treatment adherence.

Methods: In two clinics in the Shinyanga region, clients established on ART (defined as stable clients by national guidelines as on first-line ART >6 months, undetectable viral load, no opportunistic infections or pregnancy, and good adherence) were offered CHW-DCM. This prospective cohort study included all stable clients who enrolled in CHW-DCM between July 2018 and March 2020 (CHW-DCM) and compared them to stable clients who remained in SoC during that period. Multivariable Cox regression models were used to analyse factors associated with continued stability in care and the risk of LTFU during 18 months of follow-up; treatment adherence was assessed by pill count and compared using Chi-square tests.

Results: Of 2472 stable clients, 24.5% received CHW-DCM and 75.5% SoC. CHW-DCM clients were slightly older (mean 42.8 vs. 37.9 years) and more likely to be female (36.2% vs. 32.2%). Treatment adherence was better among CHW-DCM than SoC: 96.6% versus 91.9% and 98.5% versus 92.2%, respectively (both $p = 0.001$). SoC clients were more likely to not remain stable over time than CHW-DCM (adjusted Hazard ratio [AHR] = 2.68; 95% CI: 1.86–3.90). There was no difference in LTFU (adjusted hazard ratio [AHR] = 1.54; 95%CI: 0.82–2.93).

Conclusion: Clients attending CHW-DCM demonstrated better stability in care and treatment adherence than SoC, and the risk of LTFU was not increased. These findings demonstrate the potential of CHW in delivering community-based HIV services in the local Tanzanian context. These results could be used to extend this CHW-DCM model to similar settings.

KEYWORDS
ART, community health worker, differentiated care delivery model, HIV, lost to follow-up, Tanzania, task shifting

INTRODUCTION

Globally, approximately 39 million people were living with HIV (PLWH) in 2022 [1], of which about two-thirds (25.7 million) were in the African region. The region had the highest number of HIV deaths reported in 2022: 385,300, equivalent to 61.2% of total AIDS-related deaths globally [1]. In Tanzania, the prevalence of HIV is decreasing but still high, with the most recent representative estimate at 4.7% among adults aged 15–49 years in 2017 [2]. In 2023, the country was among five in the African Region reported to have achieved the 95–95–95 targets [1]. However, multiple innovative approaches are needed to ensure all PLWH remain on treatment and virally suppressed.

In Tanzania, delivering HIV services is centred at the facility level. With an increased number of PLWH on ART resulting from the "Universal Test and Treat policy" (UTT) [3] and longer survival due to ART, there is a risk that facilities become overwhelmed and are unable to provide quality services [4]. Evidence on the effectiveness of innovative HIV service provision approaches such as differentiated HIV care models (DCM) is needed, especially in sub-Saharan African where evidence is still building [5–8]. DCM includes different care packages for clients based on their needs and expectations; these packages are tailor-made based on local needs and options, consisting of several building blocks (what, where, who, when; see Table A1) [6, 7, 9, 10]. Two reviews found evidence to suggest decentralised ART distribution leads to similar treatment outcomes, although the quality and quantity of evidence were limited [7, 11]. The client benefits of decentralised models include improved retention in care, improved adherence, reduced travel time, and increase in social support [12]. Apart from the health-related benefits, DCM was also found to be cost-efficient [13] and significantly reduce the workforce needed compared to the facility-based approach [14]. According to a Tanzanian study, this strategy is cost-effective, but the authors advised against concluding it because there was inadequate data on retention [13].

The Tanzanian National Guideline for the Management of HIV/AIDS [15] advocates the establishment of DCM for clients established on ART (referred to as stable on ART) in both facilities and communities; however, the guideline requires that the management of a community-based treatment model be carried out by a trained and certified healthcare worker. However, implementing this seems challenging because of the health staff shortage. It was estimated that the shortage of human resources for health was 52% in 2014 [16]. Any attempt to implement this part of the guideline would mean taking from the already limited available staff of the facilities to run community care. To facilitate the implementation of DCM we piloted a DCM of community-based ART provision in which community health workers (CHW) delivered decentralised HIV services at the community level including drug dispensing in Shinyanga, Tanzania.

We assessed whether our CHW-based DCM model (hereon referred to as CHW-DCM) yielded the same treatment outcomes as stable clients who received care in the health facility (standard of care-SoC). Our primary objective was to compare continued stability in care, and secondary objectives were to compare the risk of loss to follow-up (LTFU) and treatment adherence, all over 18 month follow-up period. The evidence from this study will add to the limited existing knowledge on CHW-led HIV care and will help the Tanzanian Ministry of Health determine how best to implement CHW-DCM in the country.

MATERIALS AND METHODS

Study setting

The Feasibility of Universal Access to HIV Test and Treat project was conducted in two regions of Shinyanga and Simiyu in the northern part of Tanzania, which has been described in detail by de Nardo et al. [17]. The main activities of the project were the implementation of UTT and a CHW-led HIV differentiated care model. Outcomes of the community-based testing component of the project were published by Martelli et al. [18], this paper focuses on the outcomes of the latter intervention. Data for this analysis comes from two project sites, Bugisi and Ngokolo health centres, both from the Shinyanga region, where the piloting of the DCM of community-based ART took place. These sites were chosen for piloting as they represented a rural (Bugisi) and urban (Ngokolo) setting. All HIV care in Tanzania is free of charge to the clients.

Study design and population

This was a prospective cohort study comparing two groups: a cohort of stable clients who received care and treatment from the clubs (referred to as CHW-DCM) and a cohort of stable clients who attended normal clinic visits at the health centres (referred to as SoC). The criteria used to determine the stability of the participants were based on the national guidelines at the time and are found in Table 1. All stable clients in care during the study period were included in the analysis (see Table A1); there was no predetermined sample size.

Implementation of the CHW-DCM began in Bugisi in July 2018, followed by Ngokolo in September 2018. Clients were included in the analysis if they met the criteria during the first 12 months after implementation of the CHW-DCM, to allow for a minimum of 6 months of follow-up time. The maximum follow-up time for this study was 18 months from the baseline date (i.e., July 2018 to January 2020 and September 2018 to March 2020 for Bugisi and Ngokolo respectively).

TABLE 1 Inclusion and exclusion criteria for participants in both CHW-DCM and SoC cohorts. These criteria for clients stable on ART were according to the national guidelines [15].

Inclusion criteria (Stable client)
- Age above 5 years
- Received ART for at least 6 months
- Not on TB treatment
- Have a good understanding of lifelong adherence of 95% and kept clinic visit appointments for the past 6 months
- Average adherence to ART >95% during the last 6 months (as calculated by pill count, using the formula % adherence = 100 − % of pills missed)
- On first-line ART
- Viral load less than 200 copies/mL (last available HVL)

Exclusion criteria (Unstable client)
- Age below 5 years
- Pregnancy
- HVL > 200 copies/mL
- Current ART for less than 6 months
- Presence of active opportunistic infections (including TB) in the past 6 months
- The presence of poorly controlled comorbidities
- Poor adherence to scheduled visits (defined as >1 missed scheduled visit or >1 drug refill through a treatment supporter in the past 6 months)
- Suboptimal adherence to ART (defined as missed ART doses on > = 2 days in a month during the preceding 6 months)

Study intervention: CHW-led differentiated HIV care model (CHW-DCM)

A detailed overview of the study intervention was published by De Nardo et al. [17]. CHW-led community-based HIV care services were provided to a group of stable clients (referred to as clubs, in this paper CHW-DCM), formed in locations close to clients' residences. Clubs were led by a CHW who managed club activities and were overseen by club nurses. During a meeting conducted every 3 months, the CHW screened all clients for TB, briefly checked for any symptoms (fever, weight loss, cough, skin rash), asked after pregnancy, measured weight and BP, provided adherence counselling, health education, and distributed ART drugs. If any of the exclusion criteria as outlined in Table 1 were met, the client was defined as 'unstable' and was referred back to the health facility. CHW also completed the registers which captured the same information as the facility register with additional information specific to the CHW-DCM (see data sources, below), and transferred them back to the facility for data entry. As per the national guidelines, the clients in the CHW-DCM returned to the facility for CD4 measurement and a clinician consultation every 6 months. There were no additional costs to the client for participating in the CHW-DCM.

During the first 6 months of club implementation, club nurses provided mandatory training and close supervision, after which clubs were independently run by the CHW. Club nurses were the main link between the club and health facility and were responsible for following up with the clients referred back from the club. Clients attending clubs were allowed to access the facility anytime they wished to do so. Each club had an elected club leader, chosen from among the clients who, together with CHW, assisted in communicating meeting dates to other members and following up on clients who failed to attend the club meeting. The CHW completed the reason for not being present and communicated this back to the facility through the responsible club nurses. The building blocks detailing differentiated service delivery for this project are shown in the Appendix (Table A1).

Participants enrolment into CHW-DCM

Clients were enrolled into CHW-DCM by clinicians based on the criteria for stable clients as presented in Table 1. All clients attending clinics during their routine clinic visits who met the stability criteria were invited to join CHW-DCM; those who accepted gave informed consent, were referred to the nearest CHW-DCM within their communities, and became part of the intervention group. CHW-DCM participants did not contribute follow-up time to the SoC group before they were enrolled in their CHW-DCM, despite potentially meeting stability criteria at an earlier time point. During the informed consent procedure, staff paid extra attention to confidentiality procedures that were in place to reduce the risk of stigma and disclosure by participating in CHW-DCM.

Control group: Standard of care (SoC)

The SoC group, comprised of all stable clients as defined by the criteria in Table 1 who opted to remain in facility care. This group received no specific intervention except routine care as per national guidelines. Clients attended their routine clinic visits at the health facilities, including two-monthly drug refill visits and a clinician review including CD4 measurements every 6 months.

Data sources

Two data sources were used; (1) routine data on HIV care and treatment (CTC) from the Tanzania National AIDS Control Program (NACP). At health facilities, CTC data were collected in hard copies filled by the clinician at the respective facility and later entered into an electronic database by trained facility data staff. (2) Additional data (not routinely collected for the NACP) on CHW-DCM participants collected by CHW during CHW-DCM visits; which included the date of CHW-DCM enrolment. All clients had identifiers (CTC numbers) captured in both data sources, which made it possible to link the two data sources. During the study period, facilities reported delays in the return of HIV viral load (HVL) results from a zonal laboratory

located in another region; the latest available HVL results were used for this analysis (January 2022).

Details of measurements

Information from CTC database relevant to this study included demographic information such as facility location, date of birth, sex, marital status (married, single, divorced, widowed, or cohabiting), and address (ward, village, street). Clinical information collected at each visit and included in the analysis were CD4 count, ART status (never, start, continue, stop, or restart), WHO clinical staging (stage 1–4), adherence (measured by pill count), HVL in copies/ml and the status of TB screening, and/or medication if on TB treatment. Other information included were dates: date of diagnosis, date enrolled into care at HIV clinic at the health facility (), date of start of ART, visit dates, and the client's status at the clinic (active, lost to follow-up, died, or transferred out).

The clients' baseline information for the CHW-DCM cohort was determined by their clinical and demographic characteristics at the time of joining the CHW-DCM. For the SoC cohort, this was set for July and September 2018 for Bugisi and Ngokolo respectively, if in care and stable (i.e., met inclusion criteria as indicated in Table 1) at that time, or whenever they became stable during the period of 1 year for Bugisi and Ngokolo (up to July and September 2019, respectively).

Study outcomes and definitions

Stability in care was defined as continuing to be stable as per the criteria defined in Table 1. Unstable clients were defined as those who required additional clinical care, adherence support, and switching to second line in case of treatment failure. LTFU was defined as per the national guidelines [19]: not having attended any project facility or CHW-DCM for 90 consecutive days from the last scheduled appointment and not known to be dead or transferred out; this included ART collection visits. For this analysis, the date of LTFU was calculated as the last seen visit date plus 180 days for those with a missing appointment date, or the last appointment date plus 90 days for clients whose appointment date was recorded but was missed. Poor adherence was defined as adherence to less than 95% of ART drugs since the last visit, calculated by pill count method (% adherence = 100 − % of pills missed) ([number of pills remaining divided by the total number of pills prescribed] × 100).

Data analysis

All data were analysed using Stata 15 software. Characteristics of the study clients by service delivery models were described and presented as mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables. Chi-square tests were used to compare the proportion of stability in care, treatment adherence, and HVL suppression. To compare the proportion of two samples (CHW-DCM vs. SoC), two-sample proportion test was used. Student's *t*-test and Mood's median tests compared the mean age of participants and median time since enrolled into care or start of ART. Uni- and multivariable Cox regression models analysed factors associated with clients becoming unstable, and with the risk of LTFU during the follow-up period. Factors significant at $p = 0.05$ in the univariable model were selected for the multivariable model. Kaplan–Meier curves were plotted to show the probability of being LTFU by CHW-DCM versus SoC.

Ethics approval

The conduct of this study was approved by the National Institute for Medical Research-NIMR(NIMR/HQ/R.8a/Vol. IX/2711), participation in the CHW-DCM was voluntary and informed consent was sought before participation. Permission to access the routine de-identified data on HIV care and treatment was granted by NACP through signed data transfer agreements.

RESULTS

Characteristics of participants

A total of 2472 stable clients were included in the two cohorts: 605 (24.5%) in CHW-DCM and 1867 (75.5%) in SoC, (see Figure A1 for a flow chart). In total, there were forty-six (46) clubs in the study, (33 in Bugisi and 13 in Ngokolo). The cumulative enrolment into the two groups is outlined in Figure 1. Characteristics of study participants by service delivery model are presented in Table 2. Clients receiving CHW-DCM were more often female and older than those in SoC (67.8% Female and mean age 42.8 years versus 63.8% Female and mean age 39.1 years). They had also been in care and on ART for a longer time (median time since starting ART of 3.8 versus 2.6 years for CHW-DCM and SoC respectively).

See Figure A1 for a flow diagram.

Study outcomes

The main outcomes are presented in Table 3. The proportion of clients who became unstable over time was higher among SoC than CHW-DCM (13% vs. 6%), also shown in Figure 2, mainly due to the difference in the

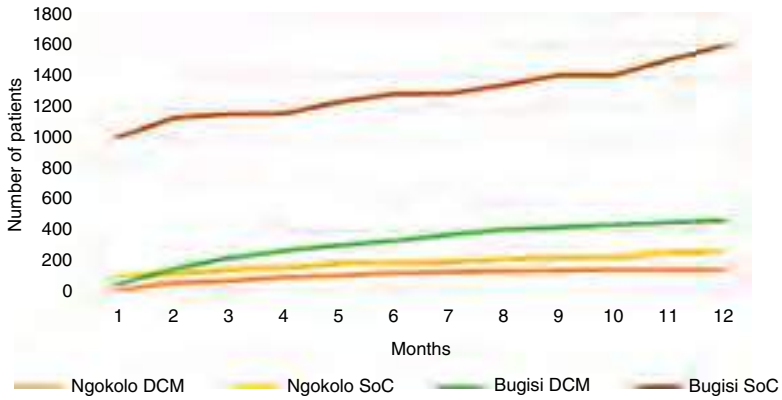

FIGURE 1 Cumulative number of clients enrolled in the CHW-led differentiated care model (CHW-DCM) or standard of care (SoC) in both facilities over time.

TABLE 2 Characteristics of study participants.

Characteristics	CHW-DCM $n = 605$ (24.5%)	SoC $n = 1867$ (75.5%)	Overall $n = 2472$ (100%)	*p*-value
Gender				
Male	195 (32.2)	676 (36.2)	973 (35.0)	0.04
Female	410 (67.8)	1191 (63.8)	1805 (65.0)	
Age at baseline in years (mean [SD])	42.8 (14.0)	37.9 (13.3)	39.1 (13.6)	<0.001
Age (years)				
5–15	30 (5.0)	89 (4.8)	119 (4.8)	<0.001
15–25	21 (3.5)	179 (9.6)	200 (8.1)	
25–50	392 (64.8)	1312 (70.3)	1704 (68.9)	
50 years and above	162 (26.8)	287 (15.4)	4490 (18.2)	
Age at ART initiation in years (mean [SD])	38.6 (14.1)	34.5 (13.3)	35.5 (13.6)	<0.001
Marital status				
Single	129 (21.3)	394 (21.1)	523 (21.2)	0.03
Married/cohabiting	322 (53.2)	1038 (55.6)	1360 (55.0)	
Separated/divorced	34 (5.6)	147 (7.9)	181 (7.3)	
Widow	56 (9.2)	115 (6.2)	171 (6.9)	
Children	32 (5.3)	(5.4)	132 (5.3)	
Missing	32 (5.2)	73 (3.9)	105 (4.2)	
Facility name/residence#				
Ngokolo(urban)	141 (23.3)	275 (14.7)	416 (16.8)	<0.001
Bugisi(rural)	464 (76.7)	1592 (85.3)	2056 (83.2)	
Median time (years) since enrolled in care (IQR)	3.8 (1.9–6.3)	2.7 (1.2–5.2)	2.9 (1.3–5.5)	<0.001
Median time (years) since the start of ART (IQR)	3.7 (1.9–5.9)	2.6 (1.2–4.7)	2.7 (1.2–5.1)	<0.001
Median CD4 at study baseline (IQR)	494 (341–688)	463 (294–685)	471 (305–687)	0.01
Median CD4 at ART start	375 (240–578)	368 (211–572)	370 (218–574)	0.53

Abbreviations: CHW-DCM-community health worker-led differentiated care model; IQR-interquartile range; SD, standard deviation; SoC, standard of care.

proportion with poor adherence (8% vs. 2%); there were no differences in the other causes of becoming unstable (detectable HVL, death, and presumptive or confirmed TB). The proportion of clients with LTFU by the end of the study period (18 months) was 77(3.1%), this was not different between the groups.

TABLE 3 Client stability and LTFU in both groups.

Characteristics	CHW-DCM $n = 605$ (24.5%)	SoC $n = 1867$ (75.5%)	Overall $n = 2472$	*p*-value
Client stability during follow-up				
Number becoming unstable (overall)	34 (5.6)	249 (13.3)	283 (11.4)	<0.001
Specific reasons for instability				
Poor adherence	9 (1.5)	145 (7.8)	154 (6.2)	<0.001
Presumptive TB	9 (1.5)	50 (2.7)	59 (2.4)	0.09
Confirmed TB	2 (0.3)	20 (1.1)	22 (0.9)	0.09
Detectable HVL (HVL > 200/μL)[a]	24 (4.9)	105 (7.4)	129 (6.8)	0.06
Death	11 (1.8)	31 (1.7)	42 (1.7)	0.75
Loss to follow-up (LTFU)				
Number (percentage) LTFU	12 (2.0)	65 (3.5)	77 (3.1)	0.07

Abbreviations: CHW-DCM, community-health worker-led differentiated care model; SoC, standard of care.
[a]Percentages were calculated using a denominator as the number of people with a follow-up viral load result ($n = 487$, 1416, and 1903, respectively).

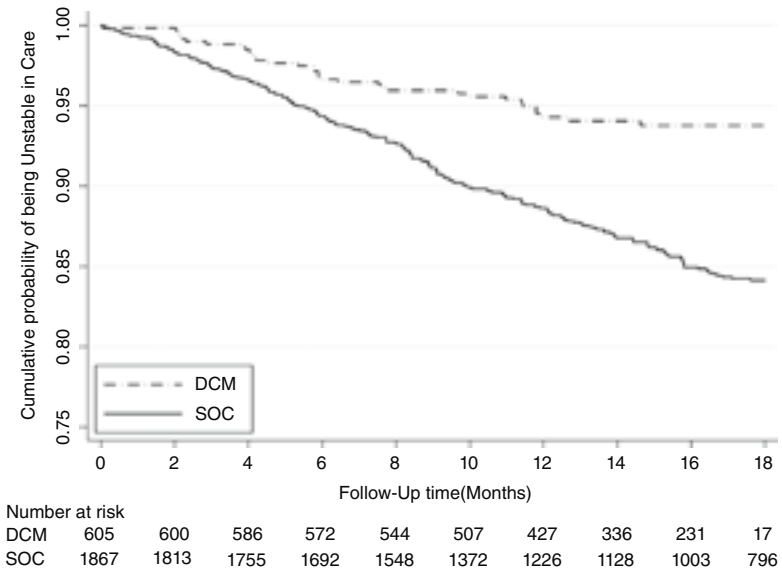

FIGURE 2 The Kaplan–Meier curve for the risk of becoming unstable in care during the study period by service type (DCM and SoC). CHW-DCM, community health worker-led differentiated HIV care model; SoC, standard of care; *p*-value = 0.001.

Factors associated with stability in care and the risk of LTFU

Table 4 presents univariable and multivariable associations with stability in care and risk of LTFU by service model. Clients receiving services via SoC were almost 3 times more likely to be unstable over time than CHW-DCM (adjusted HR 2.68; 95%CI (1.86–3.90)). Females, married clients, and clients receiving services from the rural facility were more likely to remain stable compared to their counterparts. Clients' age was not associated with stability over time.

There was no difference in LTFU between clients receiving CHW-DCM and SoC (HR = 1.54; 95% CI (0.82–2.93)). Clients who were married and/or were on ART for longer were less likely to become LFTU. Clients who had been on ART for more than 3 years were less likely to become LTFU than those less than 1 year on ART (HR = 0.38; 95%CI (0.20–0.71)). The CD4 count at cohort entry was not associated with the risk of LTFU.

TABLE 4 Crude and adjusted hazard ratios for becoming unstable in care and for becoming lost to follow-up by clients' demographics and clinical characteristics.

	Becoming unstable $n = 2472$		LTFU $n = 2472$	
Characteristics	**HR (95% CI)**	**Adjusted HR (95% CI)**	**HR (95% CI)**	**Adjusted HR (95% CI)**
Type of service				
CHW-DCM	**1**	**1**	1	1
SoC	**2.42 (1.69–3.46)**	**2.68 (1.86–3.90)**	1.62 (0.87–3.01)	1.54 (0.82–2.93)
Gender				
Male	1	**1**	1	1
Female	0.81 (0.64–1.02)	**0.72 (0.56–0.93)**	**1.95 (1.14–3.35)**	1.44 (0.82–2.56)
Age				
5–15 years	1.42 (0.85–2.41)	2.18 (0.71–6.72)	0.34 (0.10–1.21)	0.42 (0.05–3.29)
15–25 years	1	1	1	1
25–50 years	**0.68 (0.45–0.99)**	0.72 (0.48–1.09)	**0.44 (0.24–0.80)**	0.61 (0.31–1.18)
50 years and above	0.63 (0.39–1.00)	0.79 (0.47–1.31)	**0.26 (0.11–0.63)**	**0.37 (0.14–0.98)**
Facility location				
Bugisi (rural)	**1**	**1**	**1**	**1**
Ngokolo (urban)	**2.11 (1.62–2.75)**	**2.60 (1.95–3.48)**	**2.50 (1.54–4.04)**	**1.77 (1.02–3.05)**
Marital status				
Married	1	1	1	1
Single	**1.49 (1.11–1.97)**	**1.51 (1.13–2.01)**	2.22 (1.28–3.82)	**2.02 (1.65–3.49)**
Divorced/separated	**2.05 (1.37–3.05)**	**1.92 (1.28–2.88)**	**2.84 (1.34–6.04)**	**2.21 (1.02–4.77)**
Widowed	0.56 (0.28–1.10)	0.63 (0.32–1.27)	**2.40 (1.09–5.26)**	**2.83 (1.23–6.51)**
Child	2.19 (1.44–3.34)	0.87 (0.28–2.68)	1.49 (0.52–4.23)	1.88 (0.28–12.44)
CD4 count at study baseline				
CD4 < 500 cells/mm	1		**1**	1
CD4 > =500 cells/mm	1.05 (0.82–1.33)		**1.64(1.04–2.58)**	1.51(0.93–2.42)
Time since the start of ART				
Less than a year	1	1	1	1
1–3 years	0.72(0.52–1.00)	1.07(0.76–1.52)	**0.48(0.27–0.82)**	0.60(0.33–1.09)
More than 3 years	**0.64(0.46–0.87)**	1.04(0.74–1.48)	**0.29(0.16–0.51)**	**0.38(0.20–0.71)**

Note: Bold values: $p < 0.05$.
Abbreviations: CI, confidence interval, HR, Hazard ratio, LTFU, lost to follow-up.

DISCUSSION

We found that clients attending CHW-led DCM demonstrated better treatment stability and treatment adherence than SoC over 18 months. Additionally, we found there was no difference in the risk of LTFU between the two approaches. CHW-DCM clients were more likely to remain stable than those in SoC over a maximum of 18 months follow-up. The difference in stability in care seemed to be due to poorer adherence among clients in SoC; despite this, the proportion virally suppressed did not differ significantly, however, this may lag behind poor adherence. An important contributing factor to better treatment stability could be more individualised caregiving as reported in a study assessing quality of care in the same study population [20]. The authors of this study reported clients attending CHW-DCM spend almost half the time as those attending SoC, having better access to health providers (CHW), and receiving adequate reminders for appointments and explanations on the benefits of regular use of ART [20].

The absence of risk difference in LTFU between CHW-DCM and SoC in this study suggests the potential of CHW in delivering ART to PLWHA in the CHW-led DCM approach. Other studies found a lower risk of LTFU among clients attending community-based compared to facility-based care [9, 21–23], although this may be explained by differences in the comparator group. For example, facility clients of a Cape Town study [9] included the general ART population including unstable clients as the comparator group, who are more likely to default than our stable clients in SoC. Of note, the proportion of LTFU in our study was low (3.1%), although in the same range as a recent study of outcomes among clients stable on ART in Zambia [24]. These low proportions are likely reflective of a population well established on ART which is evidenced by the high median time on ART in both groups (2.7 years).

Our finding that CHW-DCM clients had better adherence than the SoC clients confirms what was found in previous studies done in sub-Saharan Africa [21, 23, 25], suggesting better adherence among clients receiving community-based compared to facility-based HIV care services. The CHW-DCM was formed within proximity to the clients' residences, lowering the distance to treatment services. We did not have data on the exact difference in distance, but the location of the CHW-DCM ranged between 3 and 35 km from the health facility [20]. Longer distances to health facilities were associated with poor adherence to ART [26]. Community-based care is also generally less crowded than facilities; overcrowding in the facilities with longer waiting hours is associated with poor retention in care [27, 28]. Our findings provide important evidence to suggest the potential of running community-based HIV care led by CHW alongside facility-based services.

To the authors' knowledge, this is the first community-based CHW-DCM study done in a rural district setting in Tanzania where CHW independently ran the DCM and led distribution of ART with support from the facility. Previous studies done in Tanzania used trained nurses or clinicians [29]. There have been a number of CHW-led HIV care initiatives: CHW-led distribution of ART to stable clients done individually in clients' homes [29–31]. While it was feasible to deliver ART to individual homes in the urban city [30, 31], this approach may not be practically feasible in a rural setting where the road infrastructure is poor, houses are scattered, and the mobile network is limited. In contrast to our study, a study in Dar es Salaam [31] restricted their DCM intervention to clients living in the neighbourhood of the facilities; however, with perceived fear and stigma [32] some people accessing services would come far from the facilities within the catchment area. Our evidence on successfully piloting the implementation of a CHW-DCM model in a rural district has the potential to reach a large number of PLWHIV in care if scaled up, as 70% of people in Tanzania live in rural areas [33]. Piloting CHW-led DCM in a country where CHWs are not allowed to dispense drugs provides a unique insight and will hopefully stimulate the discussion around and facilitate change of current guidelines.

This study has several limitations. There was a lack of ability to differentiate within the SoC group between the participants who had not yet been offered CHW-DCM and those who had opted out. It is imaginable that these participants might differ in their risk of LTFU; however, there are various reasons for opting out (distance, stigma, convenience) that make the effect of this selection bias difficult to predict. Another limitation includes concern about disclosure in community-based care also: despite staff training regarding confidentiality in CHW-DCM, clients who would not want to reveal their HIV status to the community may hesitate to participate leading to selection bias towards those with HIV status already known to the community or who have no fear to disclose. Fear of being recognised when participating in CHW-DCM has been reported previously [22]. Recent qualitative data in the same region showed the opposite for some people: they preferred the anonymity of CHW-DCM versus crowded facility [20].

The project reported missing HVL results from government testing sites. However, this was not different between the two groups, which makes it unlikely that our conclusions regarding viral suppression were affected. Other important limitations include the relatively short follow-up time, 18 months may not be enough to detect the development of viral failure, especially if HVL is not performed frequently.

CONCLUSION

The results from this study among a population well established on ART show the care provided by the CHW-DCM model was equal to, if not better than, care provided in the SoC. These findings provide evidence of the potential of CHW in delivering HIV services while maintaining the same or higher level of desired treatment outcome as that of facility-based clients. This could lead to recognition and integration of CHW in the healthcare system and national guidelines, and continued opportunities for training on subject-specific to enhance their skills beyond formal training. These findings could be used to extend this CHW-DCM model to similar settings.

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CONFLICT OF INTEREST STATEMENT

The authors have declared no conflicts of interest.

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APPENDIX A

TABLE A1 Differentiated service delivery building blocks of the CHW-DCM model implemented.

Who	*What*
Clinician, nurse (club nurse), community health worker-CHW (club responsible) and expert client (club leader)	PLWHIV attending routine care and treatment at project facilities are assessed by a clinician for inclusion (stable clients and consented) into community-based care (clubs) formed by clients residing from the same community
	Routine club activities include ART drug refill; adherence assessment and counselling; counselling on index testing; health education; TB screening and provisional referrals
When	*Where*
Quarterly—Every 3 months	Community-based, in locations close to clients' residences

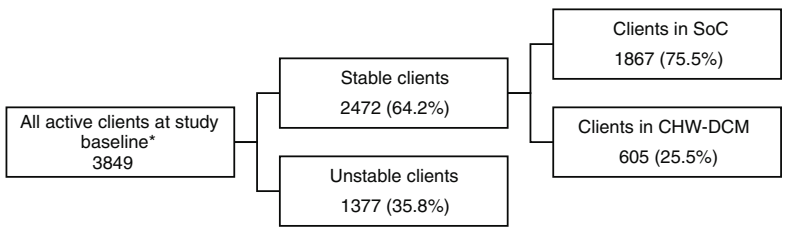

FIGURE A1 Flow chart of enrolment of participants. *Study baseline was the start of the CHW-DCM, July 2018 for Bugisi and September 2018 for Ngokolo Health Centres, respectively. CHW-DCM, community-health worker-led differentiated care model; SoC, standard of care.

Cardiac Tuberculosis: A Case Series from Ethiopia, Italy, and Uganda and a Literature Review

PAPER

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Prevalence of Sexually Transmitted Infections and Predictors for Loss to Follow Up among Marginalized Homeless and Migrant Communities: a Cross-Sectional Study

PAPER

Authors
Segala F.V., Novara R., Panico G., Laforgia R., Raho L., Schiavone M., Civile G., Laforgia N., Di Gregorio S., Guido G., Cormio M., Dargenio A., Papagni R., L'Erario A., L'Erario L., Totaro V., Spada V., Valentini L., Frallonardo L., Lattanzio R., Falanga C., Putoto G., Saracino A., Di Gennaro F.

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ABSTRACT

Background: In Europe and Italy, marginalized communities have a higher risk for both contracting sexually transmitted infections (STI) and progressing towards adverse outcomes.

Objectives: This study focuses on the screening of HIV, HBV, HCV, and syphilis among homeless individuals and agricultural migrant workers living in Apulia, Italy. It aims to assess STI prevalence and investigate factors that might hinder return to collect test results. In addition, it explores STI knowledge, attitudes, and practices among these vulnerable populations.

Methods: A cross-sectional study was conducted from September 1, 2022, to September 30, 2023. Participants were recruited from community health centers and migrant camps. Blood tests for HBV, HCV, HIV, and syphilis were performed, and Knowledge, Attitude, and Practices (KAP) survey were conducted via face-to-face interviews. Descriptive and logistic regression analyses were used to assess factors influencing the return for test results.

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Results: A total of 149 persons were recruited, including 64 agricultural migrant workers and 85 homeless people. Overall, 24.8% (n = 37) tested positive for at least one infection, and only 50.3% (n = 75) of the screened participants returned to collect their test results. Significant disparities in STI knowledge and healthcare access were observed between the two populations, with only 14.1% (n = 9) of migrants having access to primary healthcare. At multivariable analysis, the strongest predictor for not returning for test results was being positive for HCV.

Conclusions: Among homeless people and agricultural migrant workers, STI prevalence was high, and only half of the population returned to collect test results. The study underscores the urgent need for targeted interventions and policy reevaluation to address healthcare disparities in marginalized communities.

BACKGROUND

Despite the concerted efforts in Europe and Italy to eradicate discrepancies in healthcare, substantial gaps in disease burden persist in disadvantaged populations, disparities that worsened during the COVID-19 pandemic [1]. Individuals living in poverty are significantly more prone to experiencing healthcare inequities due to a limited access to public health system and longer diagnostic delays, resulting in more severe clinical outcomes and overall worse prognosis [2, 3]. In this scenario, both undocumented migrants and homeless people constitute a highly vulnerable population, with their health being significantly influenced by social determinants such as housing, poverty, and education [4]. Specifically, these populations are deemed to be particularly at high risk for sexually transmitted infections (STI), including human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) [3].

Given that these infections are characterized by a prolonged asymptomatic phase, many individuals with HIV, HBV, and HCV are unaware of their condition. In the year 2020, within the WHO European Region, a total of 2.6 million people were living with HIV. Among them, 77% were aware of their HIV status, 83% of those diagnosed were on antiretroviral therapy (ART), and 95% of individuals receiving ART achieved viral suppression [5]. Also, it is estimated that only one fifth of people currently living with HBV and a quarter of people living with HCV are diagnosed, with higher rates of undiagnosed infections among vulnerable populations [6, 7].

As a consequence, continuous STI surveillance in marginalized communities is a key step in the pursuit of United Nations Sustainable Development Goals [8] and in the optimization community-based preventive and therapeutic strategies. Specifically, even within the context of a well-designed screening program, it is well described that, in under-resourced communities, a significant challenge is represented by linkage and retention in care [9].

In line with these objectives, we aimed to assess the rate of return for test results (RTR) after screening for HIV, HBV, HCV, and syphilis in homeless people and agricultural migrant workers living in the Apulia region of Italy. Furthermore, we aimed to assess the prevalence of these infections and to explore STI knowledge, attitude, and practices (KAPs) about STIs among these two vulnerable populations.

METHODS

STUDY DESIGN, POPULATION AND SETTING

We performed a cross-sectional study from September 1, 2022, to September 30, 2023. Recruitment and data collections were performed by a multidisciplinary group comprising an infectious diseases specialist, an infectious diseases medical resident, two nurses, one cultural mediator, and one volunteer healthcare worker affiliated with the Italian non-governmental

organization Doctors with Africa CUAMM (University College for Aspiring Medical Missionaries). This organization has been actively engaged in assisting the agricultural migrant worker communities since 2015. STI and KAP screening surveys were delivered concurrently by face-to-face interviews.

Study sites included four community health centers for homeless people situated in the City of Bari and five resettlement camps located in the municipality of Foggia, so-called 'ghettos,' where agricultural migrant workers (AMW) reside. A more detailed description of sites included in the study is provided in the supplementary file.

The eligible population included all adult individuals who were beneficiaries or residents in the mentioned facilities throughout the study period. No exclusion criteria were applied for this study. Participants had the option to withdraw from the study at any time, and their decision did not impact their medical care.

Blood test result delivery was scheduled approximately 10 days after screening, and the failure to return for results rate (FTR) was assessed. Participants who tested positive for any of the infections included in the study were referred for further diagnostic evaluation and treatment to the Clinic of Infectious Diseases of the Polyclinic of Bari. Positive-screened participants received the same standard of care, in accordance with national and international guidelines [10–13].

QUESTIONNAIRE DEVELOPMENT AND DATA COLLECTION

Questionnaire development was informed by literature review and administered through face-to-face interviews conducted by nurses and trained doctors. Every interaction with the subjects involved in the study was facilitated by linguistic and cultural mediators, when needed. To minimize the social desirability bias, interviewers provided clear instructions at the beginning of the questionnaire, explaining the purpose of the survey, the importance of honest responses, and reassuring participants about data confidentiality.

The questionnaire was organized into the following sub-sections:

- Socio-demographic information (age, education, occupation, marital status, how long they were homeless, possible employment contract, residence document in Italy): 6 questions.
- Risk factors for STI: multiple sexual partners, use of condoms, smoking and alcohol habits, chem-sex (defined as "voluntary intake of psychoactive drugs with the intention of facilitating and/or enhancing sexual activity [14]") and medical history (including symptoms of TB and other communicable-non-communicable diseases): 6 questions.
- Knowledge, attitude, and practices on HIV, HBV, HCV, and Syphilis: 25 questions.

All study participants underwent the following blood tests:

- Serologies for HBV (HBsAg, anti-HBs, and anti-HBc), HCV (anti-HCV), human immunodeficiency virus (HIV), and syphilis (VDRL and TPHA).
- The study participants, resulting positive for the screening, performed confirmation tests according to the standard of care: HBV-DNA for HBV, HCV-RNA and genotype for HCV, HIV-RNA, immune cell count, and resistance profile for HIV.

All data were entered into a secured online platform (Kobo Ttoolbox [15]), and a quality control check of the data entry was performed before data analysis.

STATISTICAL ANALYSIS

A descriptive analysis was performed to define the distribution of the characteristics of the sample. Continuous data were summarized as median and interquartile range (IQR). Return For Test Results (RTR) was identified as the dependent variable. World regions were classified according to the United Nation Geoscheme [16]. The distribution of continuous variables was assessed with the Shapiro-Wilk normality test, and the Mann-Whitney U test was used to compare groups for continuous variables. A chi-squared test (with the Fisher's correction if less than five cases were

present in a cell) was applied for categorical variables. A logistic regression model was implemented as follows. RTR was considered as a dependent variable and each of the available factors at the baseline evaluation as independent variables (univariate analysis). The effect sizes were reported as odds ratio (OR) with 95% confidence interval (CI). All tests were 2-sided, and a p-value <0.05 was considered statistically significant. The model included a set of clinically relevant candidate predictors and variables resulted to be significant at the bivariate analysis. Statistical analyses were performed using R Statistical Software (v4.1.3; R Core Team 2021) in R Studio Version [17].

ETHICAL CONSIDERATIONS

Prior to recruitment, written informed consent (prepared in 4 languages: Italian, French, English, and Arabic) was obtained from all participants. The objectives of the study, along with methods used and data confidentiality, were explained with the aid of cultural mediators, when needed. The study has been approved by Ethics Committee 'Azienda Ospedaliero-Universitaria Consorziale Policlinico,' protocol number DG1563. During the screening process, we actively worked to establish and enhance personalized pathways for connecting individuals to healthcare through various social and healthcare services. We raised awareness about the potential progression of HIV and liver diseases, as well as the risk of transmission to others, by directing these individuals to the Infectious Disease Clinic at the Policlinic of Bari for counseling, diagnosis, and appropriate treatment.

RESULTS

CHARACTERISTICS OF THE POPULATION

From September 1, 2022, to September 30, 2023, a total of 149 participants were recruited in the study, of which 64 (42.9%) were agricultural migrant workers and 85 (57.1%) were homeless, with a median age of 35 (IQR: 27–45) years. Characteristics of the sample stratified for study subpopulation and RTR are displayed in Table 1. Males accounted for 87.5% (n = 56) of agricultural migrant workers and 75.3% (n = 64) of homeless people. The most frequently reported comorbidities were diabetes (8.1%, n = 12), hypertension (6%, n = 9), and respiratory pathologies (4%, n = 6). Among agricultural migrant workers, countries of origin were located mainly in sub-Saharan Africa (64.1%, n = 41) and North Africa (20.3%, n = 13), while 32.9% (n = 28) and 31.8% (n = 27) of homeless people were originally from Sub-Saharan Africa and Italy. Educational level was low, with 64.4% (n = 96) of the included subjects reporting only primary school or no formal education. Overall, 69.1% (n = 103) of the participants did not have access to primary healthcare, and this rate was alarmingly high among people residing in the Apulian ghettos (85.9% n = 55 vs 56.5% n = 48, p < 0.001). Apart from country of origin (p < 0.001) and access to care, the migrant and homeless subpopulation differed significantly on the following variables: reporting chem-sex (p = 0.049) and HCV and HIV knowledge (p < 0.001 and p = 0.02)—with homeless people scoring better.

Table 1 Characteristics of the population stratified for subpopulation and return rate.

	OVERALL (N = 149)	SUB-POPULATION			RETURN FOR TEST RESULTS		
		AGRICULTURAL MIGRANT WORKERS (N = 64)	HOMELESS PEOPLE (N = 85)	P-VALUE FOR SETTING	NOT RETURNED (N = 74)	RETURNED (N = 75)	P-VALUE FOR RETURNING
Age, median [Q1, Q3]	35 [27, 45]	34 [26, 42]	35 [29, 48]	0.328	33.0 [26.3, 41.8]	36.0 [28.5, 50.0]	0.171
Gender							
F	29 (19.5%)	8 (12.5%)	21 (24.7%)	0.0982	11 (14.9%)	18 (24.0%)	0.23
M	120 (80.5%)	56 (87.5%)	64 (75.3%)		63 (85.1%)	57 (76.0%)	
Sub-populations							
Agricultural migrant workers	64 (43.0%)	–	–	–	38 (51.4%)	26 (34.7%)	0.0585
Homeless people	85 (57.0%)	–	–		36 (48.6%)	49 (65.3%)	

(Contd.)

	OVERALL (N = 149)	SUB-POPULATION			RETURN FOR TEST RESULTS		
		AGRICULTURAL MIGRANT WORKERS (N = 64)	HOMELESS PEOPLE (N = 85)	P-VALUE FOR SETTING	NOT RETURNED (N = 74)	RETURNED (N = 75)	P-VALUE FOR RETURNING
Marital Status							
Divorced	11 (7.4%)	3 (4.7%)	8 (9.4%)	0.442	3 (4.1%)	8 (10.7%)	0.478
In an open relationship	4 (2.7%)	2 (3.1%)	2 (2.4%)		2 (2.7%)	2 (2.7%)	
Single	84 (56.4%)	34 (53.1%)	50 (58.8%)		44 (59.5%)	40 (53.3%)	
Married	49 (32.9%)	25 (39.1%)	24 (28.2%)		25 (33.8%)	24 (32.0%)	
Missing	1 (0.7%)	0 (0%)	1 (1.2%)		0 (0%)	1 (1.3%)	
Region of origin							
Eastern Europe	10 (6.7%)	6 (9.4%)	4 (4.7%)	**<0.001**	4 (5.4%)	6 (8.0%)	0.25
Middle East	10 (6.7%)	1 (1.6%)	9 (10.6%)		8 (10.8%)	19 (25.3%)	
North Africa	24 (16.1%)	13 (20.3%)	11 (12.9%)		4 (5.4%)	6 (8.0%)	
Other	2 (1.3%)	1 (1.6%)	1 (1.2%)		14 (18.9%)	10 (13.3%)	
Southeast Asia	7 (4.7%)	2 (3.1%)	5 (5.9%)		1 (1.4%)	1 (1.3%)	
Sub-Saharan Africa	69 (46.3%)	41 (64.1%)	28 (32.9%)		3 (4.1%)	4 (5.3%)	
Italy	27 (18.1%)	0 (0%)	27 (31.8%)		40 (54.1%)	29 (38.7%)	
Education							
Primary school	56 (37.6%)	29 (45.3%)	27 (31.8%)	0.0872	33 (44.6%)	23 (30.7%)	0.373
Lower secondary school	36 (24.2%)	13 (20.3%)	23 (27.1%)		15 (20.3%)	21 (28.0%)	
Higher secondary school	14 (9.4%)	4 (6.3%)	10 (11.8%)		5 (6.8%)	9 (12.0%)	
University	3 (2.0%)	3 (4.7%)	0 (0%)		1 (1.4%)	2 (2.7%)	
No formal education	40 (26.8%)	15 (23.4%)	25 (29.4%)		20 (27.0%)	20 (26.7%)	
Comorbidities							
Diabetes	12 (8.1%)	2 (3.1%)	10 (11.8%)	0.106	4 (5.4%)	8 (10.7%)	0.379
Hypertension	9 (6.0%)	2 (3.1%)	7 (8.2%)	0.343	4 (5.4%)	5 (6.7%)	1
Cardiopathy	4 (2.7%)	0 (0%)	4 (4.7%)	0.212	1 (1.4%)	3 (4.0%)	0.622
Pneumopathy	6 (4.0%)	0 (0%)	6 (7.1%)	0.0803	3 (4.1%)	3 (4.0%)	1
Neuropsychiatric disorder	4 (2.7%)	0 (0%)	4 (4.7%)	0.212	2 (2.7%)	2 (2.7%)	1
Cancer	2 (1.3%)	1 (1.6%)	1 (1.2%)	1	0 (0%)	2 (2.7%)	0.482
TB History	3 (2.0%)	1 (1.6%)	2 (2.4%)	1	1 (1.4%)	2 (2.7%)	1
Chem sex	14 (9.4%)	2 (3.1%)	12 (14.1%)	**0.0494**	4 (5.4%)	10 (13.3%)	0.177
Missing	1 (0.7%)	1 (1.6%)	0 (0%)		1 (1.4%)	0 (0%)	
Consistent condom use	21 (14.1%)	10 (15.6%)	11 (12.9%)	0.819	9 (12.2%)	12 (16.0%)	0.662
Access to primary healthcare	46 (30.9%)	9 (14.1%)	37 (43.5%)	**<0.001**	15 (20.3%)	31 (41.3%)	**0.009**
Fear of community exclusion in case of HIV positivity	88 (59.1%)	37 (57.8%)	51 (60.0%)	0.92	43 (58.1%)	45 (60.0%)	0.946

(Contd.)

	OVERALL (N = 149)	SUB-POPULATION			RETURN FOR TEST RESULTS		
		AGRICULTURAL MIGRANT WORKERS (N = 64)	HOMELESS PEOPLE (N = 85)	P-VALUE FOR SETTING	NOT RETURNED (N = 74)	RETURNED (N = 75)	P-VALUE FOR RETURNING
Fear of community exclusion in case of HCV positivity	38 (25.5%)	16 (25.0%)	22 (25.9%)	1	16 (21.6%)	22 (29.3%)	0.372
Being tested for HIV or HCV in the past	38 (25.5%)	14 (21.9%)	24 (28.2%)	0.489	18 (24.3%)	20 (26.7%)	0.889
HCV Knowledge Score, median [Q1, Q3]	0 [0, 2]	0 [0, 1]	1 [0, 3]	**0.001**	0 [0, 1]	0 [0, 3]	**0.04**
HIV Knowledge Score, median [Q1, Q3]	2 [0, 4]	2 [0, 3]	3 [1, 4]	**0.019**	2 [0, 3]	2 [0, 4]	0.512
Infections							
HIV	3 (2.0%)	2 (3.1%)	1 (1.2%)	0.803	1 (1.4%)	2 (2.7%)	1
Syphilis	5 (3.4%)	2 (3.1%)	3 (3.5%)	1	5 (6.8%)	0 (0%)	0.0665
HCV	14 (9.4%)	6 (9.4%)	8 (9.4%)	1	12 (16.2%)	2 (2.7%)	**0.01**
HBV Infection	21 (14.1%)	10 (15.6%)	11 (12.9%)	0.819	11 (14.9%)	10 (13.3%)	0.974
Any infection	37 (24.8%)	17 (26.6%)	20 (23.5%)	0.816	24 (32.4%)	13 (17.3%)	**0.052**
More than one infection	6 (4.0%)	3 (4.7%)	3 (3.5%)	1	5 (6.8%)	1 (1.3%)	0.205
Vaccinated against HBV	21 (14.1%)	5 (7.8%)	16 (18.8%)	0.078	7 (9.5%)	58 (77.3%)	0.138
Missing	3 (2.0%)	0 (0%)	3 (3.5%)		0 (0%)	14 (18.7%)	
Returned for test results	75 (50.3%)	26 (40.6%)	49 (57.6%)	0.058		–	–

KNOWLEDGE, ATTITUDES, AND PRACTICES TOWARDS SEXUALLY TRANSMITTED INFECTIONS

Concerning HIV/AIDS, only 60% (n = 90) of the recruited individuals were aware that the disease can be transmitted through sexual contact. Additionally, 45.7% (n = 65) were not aware of the protection offered by condoms. A notable 34.9% (n = 52) agreed or strongly agreed that HIV/AIDS might be transmitted by sharing utensils or having a meal together. Moreover, over 75% (n = 111) of the sample did not agree with the statement 'thanks to HIV treatment, people can lead a high-quality life and not be contagious anymore.' Awareness of Hepatitis C was notably low, with limited knowledge about its modes of transmission, potential complications, and available treatment options in both subpopulations. Details about the distribution of responses to the KAP questionnaire are provided in **Supplementary Table 1**. Both HIV ($p < 0.001$) and HCV ($p = 0.02$) knowledge were significantly lower among agricultural migrant workers (Table 1).

Regarding the perception of stigma, the majority (59.1%, n = 88) of participants expressed fear that a positive HIV test would lead to social exclusion, while only 25.5% (n = 38) held similar concerns about a positive HCV test. In terms of practices, the majority of participants (85.9%, n = 128) reported inconsistent condom use, while 14.1% (n = 12) of homeless individuals stated that they had engaged in chem-sex.

SEXUALLY TRANSMITTED INFECTIONS SCREENING

The total number of infections detected is illustrated in Figure 1. Overall, out of 149 participants screened, 3 tested positive for HIV (2%), 14 for HCV (9.4%), 21 (14.1%) for HBV, and 5 (3.4%) for syphilis. Only 14% were vaccinated for HBV. HBV serology results (Figure 2) indicate that most of the study participants have neither been vaccinated against HBV nor have they ever been exposed

to the virus. Approximately one out of four people (24.8%, n = 37) were positive for at least one infection, while three people out of four (74.5%, n = 111) reported that they had never undergone prior testing for these infections.

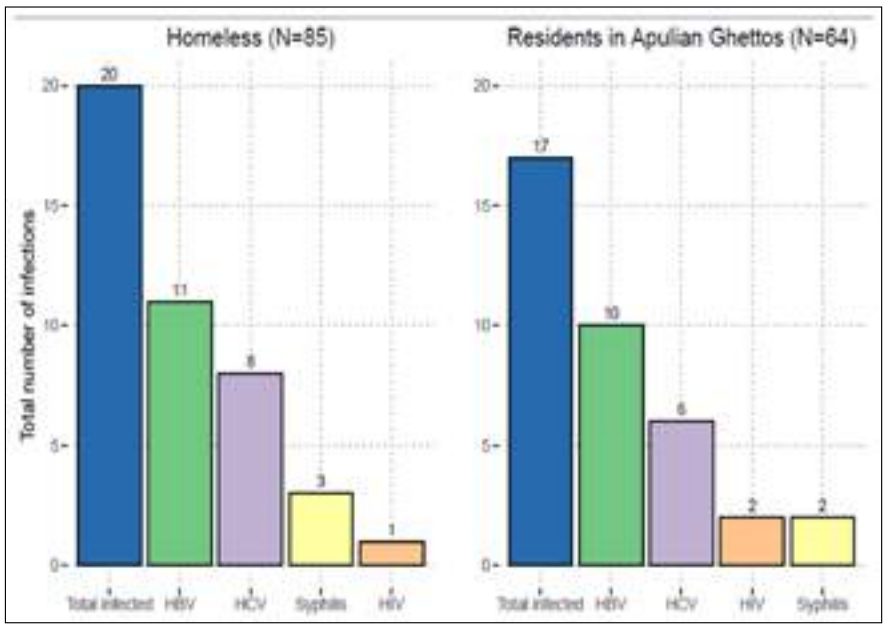

Figure 1 Distribution of infections among migrants and homeless people.

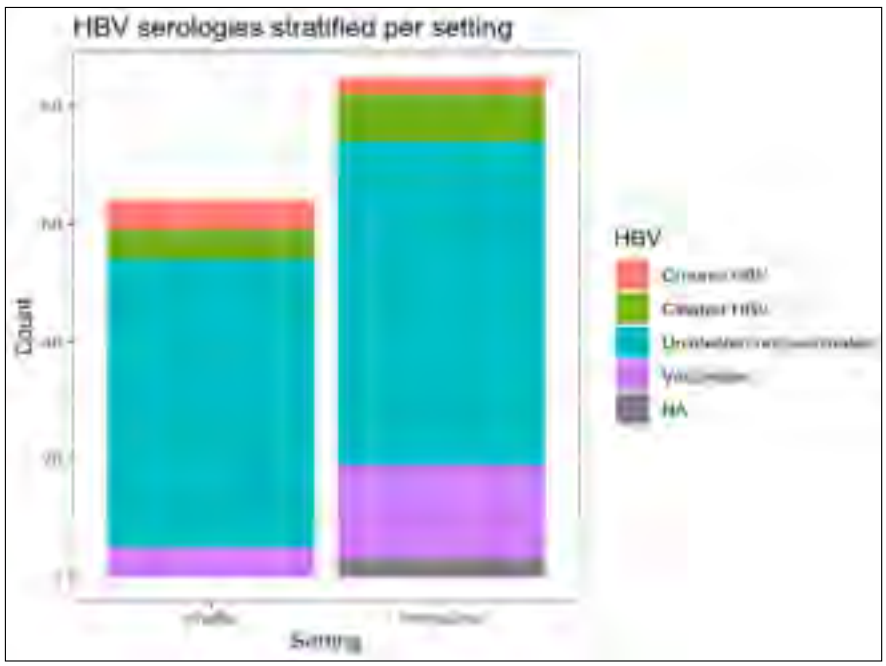

Figure 2 HBV serologies stratified per subpopulation.

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MONO AND MULTIVARIABLE ANALYSIS FOR RETURN RATE FOR TEST RESULTS

Overall, only half of the screened participants (50.3%, n = 75) returned to collect test results. As shown in Table 1, at univariate analysis, people who had access to primary healthcare were significantly associated with returning (41.3% n = 31 vs 20.3% n = 15, $p < 0.009$), as well as people who performed better at HCV knowledge questionnaire ($p = 0.04$). Alarmingly, people whose results indicated infection with HCV or with at least one STI were more likely to be lost to follow-up.

At multivariable analysis, the only factor independently associated with reduced odds of returning to collect test results was being positive to HCV (Table 2).

Table 2 Multivariable logistic regression model for return for test results.

FACTOR	aOR	lowCI	highCI	pVALUE
(Intercept)	0.845	0.398	1.775	0.657
Living in Apulian Ghettos	0.697	0.332	1.462	0.337
Having access to primary healthcare	2.101	0.928	4.881	0.077
Good HCV knowledge	2.208	0.911	5.583	0.083
Having contracted HCV	0.136	0.017	0.703	**0.028**
Having contracted at least one STD	0.870	0.334	2.249	0.773
Fear that positive HIV test would result in social exclusion	1.214	0.596	2.483	0.592

DISCUSSION

In our study, which included 85 homeless people and 64 agricultural migrant workers living in Southern Italy, the cumulative prevalence of STI was high, and only half of the overall population returned to collect test results. Overall knowledge of STI modes of transmission was low and, in line with other studies [18, 19], only 14% of the population reported consistent condom use.

In the present study, almost one homeless person out of ten reported having been engaged in chem-sex. This is concerning, because it is likely a proxy of the high rate of substance use disorder—and possibly also other mental health disorders—described in this and other marginalized populations [20]. Indeed, marginalization is correlated with increased high-risk behaviors [21] as well as higher disease burden and mortality [22]. In our population, the cumulative prevalence of STI was 24% and, interestingly, rates were similar among agricultural migrant workers (26.6%) and homeless people (23.5%), substantially exceeding the prevalence rates observed in the general population [23]. This data might be explained by the fact that the root causes of the disease burden lay in marginalization and social vulnerability themselves, rather than individual misconceptions or diverse cultural background [24], thus underscoring the intricate relationship between socio-economic vulnerability, substance abuse, barriers to healthcare, mental health, and the transmission of these viral infections.

Regarding the perceived stigma of HIV, the majority (59.1%) of the participants were afraid that a positive HIV test would result in social exclusion, and this conviction was likely supported by common misconception about disease route of transmission, as it is highlighted by the high rate of people who believed that HIV/AIDS might be contracted by sharing objects or by having meals together. This data, if combined with high STI prevalence might lead infected people to experience further social isolation, imprisoning them in a vicious circle of disease and marginalization.

Indeed, the main finding of our study was that, alarmingly, half of our population did not come back to collect test results, and the strongest predictor for not returning was having contracted HCV. This phenomenon highlights a critical gap in the healthcare system's ability to engage and retain marginalized populations in the continuum of care. The situation is significantly exacerbated by the lack of consistent healthcare access, as evidenced by 69.1% of participants not having access to primary healthcare. The implications of this limited access are profound, contributing to delayed diagnosis and treatment, and consequently, to worse health outcomes and continued infection transmission [25].

For policymakers, this situation demands a reevaluation of current health policies and systems. It is crucial to implement strategies that not only increase healthcare accessibility but also build trust and engagement with marginalized communities. Furthermore, there is a demand for integrated care models that address not only the medical needs but also the social determinants of health, such as housing, employment, and mental health services [26]. These models can provide a more holistic approach to healthcare, addressing the root causes of healthcare disparities. Moreover, community-based interventions that involve peers or community leaders could significantly improve engagement and trust in healthcare services. This approach demonstrated to be effective in both migrant [27] and homeless [28] populations.

The present study has several limitations. Primarily, the generalizability of our findings is constrained by the study's specific demographic and geographic focus on homeless individuals and agricultural migrant workers in Southern Italy. Secondly, our study's reliance on self-reported data poses a risk of introducing bias, as participants' responses may be influenced by recall and social desirability biases—including the potential underreporting of high-risk behaviors. Additionally, the cross-sectional design of the study inherently limits our ability to establish causality between the observed factors and the prevalence of STIs. Lastly, the absence of longitudinal follow-up in our study design precludes the assessment of long-term outcomes, which are crucial for understanding the progression of STIs and the effectiveness of interventions over time. These limitations highlight the need for further research with diverse populations and marginalized communities, preferably with longitudinal designs to explore the impact of interventions on health outcomes and retention in care.

CONCLUSIONS

Among marginalized homeless and migrant communities, the prevalence of STIs and the failure to return to collect test results were high, and people who contracted HCV were more likely to be lost to follow-up. There is an urgent need to design interventions and policies that address vulnerable communities and explicitly target marginalization and socio-economic inequalities as key determinants of population health.

ADDITIONAL FILE

The additional file for this article can be found as follows:

- **Supplementary file.** Description of study sites and Supplementary Table 1. DOI: https://doi.org/10.5334/aogh.4388.s1

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- Doctors with Africa CUAMM, an Italian non-governmental organization that has been present in the ghettos of Foggia since 2015, guaranteeing primary healthcare and awareness-raising activities. For the purposes of the project, it guaranteed logistical support and volunteer medical staff;
- Municipality of Bari, department of Welfare, personal services, social inclusion and fight against poverty, reception, and integration. It is the key department in social services dedicated to the homeless such as dormitories, day services, and canteens. He gave patronage to the Project;
- The School of Specialization in Infectious and Tropical Diseases of the University of Bari, which was the infectious disease and epidemiological partner of our screening activity. For the purposes of the project, the school guaranteed the human resources with the infectious disease skills used in the administration of the tests and the questionnaire;

- The Clinic of Infectious Diseases of Bari University provides second and third level assistance in the field of infectious diseases. For the purposes of the project, it guaranteed the care of the screened positive participants;
- C.A.P.S. (Psycho-Social Help Centre) this cooperative manages numerous facilities and services for migrants and/or people without residence.

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

Conceptualization, F.D.G. and F.V.S.; methodology, F.V.S., R.P., and V.T.; validation, L.R. and R.L. (Renato Laforgia); data collection, G.G.P., A.D., S.D.G., M.C., V.S, R.L. (Rossana Lattanzio), M.S., R.P., G.C., L.V., and R.N.; data extraction and statistical analysis, F.D.G. and F.V.S.; writing—original draft preparation, R.N. and G.G.P.; writing—review and editing, R.N., and F.V.S.; supervision, A.S. and G.P.; project administration, F.D.G.; funding acquisition, F.D.G., C.F., and A.S. All the authors approved the final version of the full text. All authors have read and agreed to the published version of the manuscript.

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PAPER

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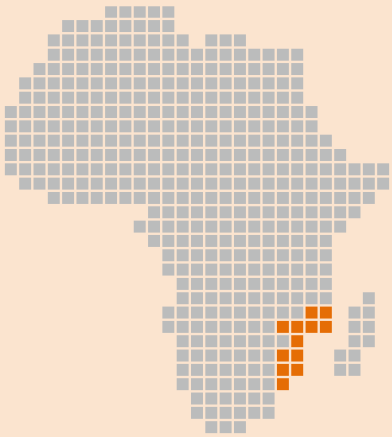

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Assessing the resilience of HIV healthcare services provided to adolescents and young adults after the COVID-19 pandemic in the city of Beira (Mozambique): an interrupted time series analysis

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Abstract

Background The COVID-19 pandemic has put the provision of health services globally at risk. In Sub-Saharan Africa, it had a major impact on HIV services. However, there is a lack of data on the post-pandemic period. This study aims to evaluate the resumption of HIV services and retention in care for adolescents and young people in the period following the COVID-19 pandemic.

Methods A retrospective cohort study was conducted using interrupted time series analysis. Three periods were considered: pre-pandemic (form June 2019 to March 2020), pandemic (form April 2020 to March 2022) post-pandemic (from April 2022 to March 2023). Six outcome measures were considered: number of outpatient visits, HIV tests, HIV positivity ratio, the antiretroviral treatment (ART) non-adherence ratio, recall ratio, and the return ratio for adolescent and young adults on ART.

Results During the study period, 447,515 outpatient visits and 126,096 HIV tests were recorded. After a reduction at the beginning of the pandemic period, both visits and tests increased during the pandemic ($p < 0.05$) and decreased in the post-pandemic ($p < 0.05$), recovering the pre-pandemic trends. The HIV positivity ratio slightly decreased from 3.3% to 1.7% during the study period ($p < 0.05$). The ART non-adherence ratio decreased from 23.4% to 2.4% throughout the study period ($p < 0.05$), with a drop at the beginning of the post-pandemic period ($p < 0.05$). The recall ratio increased during the study period ($p < 0.05$) with a drop at the beginning of the pandemic and post-pandemic periods ($p < 0.05$). The return ratio decreased at the beginning of the pandemic ($p < 0.05$) but returned to the pre-pandemic ratio in the post-pandemic period.

Conclusions The post-pandemic values of the investigated outcomes were comparable to pre-pandemic period, or even improved. Differently from other services, such as the community activities, that have been severely affected by COVID-19 pandemic, the HIV service system has shown resilience following emergency situation.

Keywords HIV, COVID-19, Healthcare access, Adolescents and young people, Mozambique

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Introduction

The onset of the COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was expected to be an extremely worrying event for the African continent. However, the direct health impact of COVID-19 was milder than anticipated [1]. The limited spread and mortality from SARS-CoV-2 may have been driven by several factors, including poor testing levels, policy makers and socio-epidemiological characteristics of the population. When evaluating these data, another issue to consider is the large degree of uncertainty associated with COVID-19-directed mortality which depends on different mortality modelling approaches [2]. When the World Health Organization (WHO) declared the end of COVID-19 as a public health emergency on 5 May 2023, 233,417 cases were confirmed in Mozambique, with 2243 deaths [3]. On the contrary, the indirect effects of the pandemic have heavily afflicted Sub-Saharan Africa (SSA) in terms of food insecurity, lack of medical supplies, loss of income and livelihoods [3]. Particularly affected was access to health services at different levels: Human Immunodeficiency Virus (HIV) care, treatment for malaria and tuberculosis, and maternal and child health services [4]. In SSA, the lockdown was associated with an estimated 47.6% decrease in HIV testing in April 2020 and a 46.2% decrease in Antiretroviral Therapy (ART) initiation in the first week after the COVID-19 pandemic lockdown [5]. Availability of ART and consistent adherence are the key pillars to sustain viral suppression and thus prevent disease outbreaks and reduce HIV morbidity, mortality, and transmission in all age groups [6]. Hence, it was estimated that HIV-related deaths will increase by up to 10% over the next five years due to ART interruptions caused by COVID-19 in low- and middle-income countries (LMICs) [7].

In a region such as SSA accounting for 77.5% of the new HIV infection in the population aged 15–24 years in 2022, it is particularly important to monitor the impact of COVID-19 pandemic on HIV health services [8]. Eastern and Southern Africa (ESAR) account for 53.3% (20.8 million/39.0 million) of global people living with HIV (PLHIV) [8]. In 2021, Mozambique registered 94,000 new cases of HIV and became the second country in SSA with the highest number of infections [9]. In the same year, nearly 2 million PLHIV (5.1% of global PLHIV) were estimated to live in the country [9].

Most ESAR countries suffered major reductions in access to HIV services and adherence to ART following the COVID-19 pandemic, especially for the adolescents and youth [10]. Available ESAR data showed a drop ranging from 37.4% (Ethiopia) and 36.1% (Malawi) to 47.6% (South Africa) in monthly HIV testing after the beginning of the COVID-19 pandemic [11–13].

Despite the extensive literature on the disruption of HIV health services caused by the lockdown during the pandemic, little is known about their status after the end of the restrictive measures. Hence, this study aimed to evaluate the resumption of HIV services and retention in care for adolescents and young people in the period following the end of the COVID-19 pandemic in a low-resource setting. In addition, potential differences in service provision according to the location of the health center (central or peripheral) were explored.

Methods

Study design and ethical approval

A retrospective, observational, multicenter study was conducted to evaluate the resumption of services after the declaration of the end of State of Public Calamity for the COVID-19 pandemic in Mozambique. The research was performed following the ethical standards of the 1964 Declaration of Helsinki and was approved by the Comité Interinstitucional de Bioética para Saúde (CIBS) (protocol number 057/CIBS/2022).

Setting and pandemic phases

The city of Beira is located in the province of Sofala, in the central area of Mozambique. It has an estimated population of 2,528,442, of which 897,467 (35.5%) are aged between 10 and 24 years [14]. For this age group, the government of Mozambique has a special service within the health centers (HC) that provides education, prevention, and treatment for adolescents and young adults (AYA) called "Adolescent and youth friendly services" (*Serviços amigos dos adolescentes e jovens*—SAAJ). Seven SAAJ of Beira district, where the Non-Governmental Organization (NGO) Doctors with Africa CUAMM works, were selected. Of these, four SAAJ (Ponta Gea, Munhava, Hospital Central de Beira—HCB, Macurungo) are in a central and three (Inhiamizua, Mascarenha, Nhaconjo) in a peripheral area.

SAAJ provides assistance to people aged between 10 and 24 years ranging from sexual and reproductive health counselling to prevention and treatment of HIV and sexually transmitted infections (STIs). In addition to these services, a recall intervention is provided for PLHIV who discontinue ART. They are defined according to the Mozambican HIV guidelines as all persons who discontinued ART within a period of 5 to 59 days; after 60 days, they are considered lost to follow-up [15]. The recall intervention involves a maximum of three phone calls, held by community health workers, and then, if unsuccessful or the person is unreachable (and if they have given their consent), they receive a home visit. During this contact (telephone or face-to-face), the community

health worker provides brief counselling to motivate the person to come back to treatment.

The first case of COVID-19 in Mozambique was reported on 22 March 2020. The declaration of the State of Emergency occurred on 30 March 2020 with the adoption of several prevention and control strategies. These included school closures, prohibition of public and sporting events, mandatory wearing of face masks in public places, curfews, social distancing, and mandatory quarantine for travelers from international travel [16]. It was converted into State of Calamity in September 2020, with an easing of the restriction measures, and it lasted until April 2022, when its end was declared [16].

Data source

Data were collected routinely monthly by the clinical staff of the HCs aiming at providing reports for local and national health authorities. These data were available at aggregate-level. Data collection at the HC level continued during the study period with the support of the NGOs working in Mozambique and the coordination of the Ministry of Health. Data quality was assured through monthly review by a monitoring and evaluation officer and quarterly data discussions with the staff involved in data collection.

Study periods

The overall study period (from 1 September 2019 to 31 March 2023) was divided in three periods of interest: the before-pandemic period (from 1 September 2019 to 31 March 2020; the pandemic period (from 1 April 2020 to 31 March 2022) and the post-pandemic period (from 1 April 2022 to 31 March 2023). Data between March and September 2019 were not available due to the cyclone Idai that hit the city of Beira on 14 March 2019 [17]. All data were extracted from monthly HC records by a researcher who was not involved in any clinical activities.

Outcome measures

Two sets of outcomes were considered. The first set referred to the general population aged 10–24 years old and included the number of outpatient visits, HIV tests and the HIV positivity ratio among individuals attending health facilities. The second set referred specifically to PLHIV in the same age group and included non-adherence, recall, and return ratio.

The non-adherence ratio was estimated by a proxy indicator that included the percentage of PLHIV who did not pick up ART out of the total PLHIV on treatment; the recall ratio was the number of non-adherent PLHIV, as defined above receiving a re-engagement invitation out of the total non-adherent PLHIV; the return ratio was calculated as the number of recalled persons who returned to treatment.

Statistical analysis

Interrupted time series modelling was applied to monthly data of outcome measures, and the resumption of HIV health services was evaluated by assessing the changes in level and slope of each time series [18]. Since before-pandemic period and pandemic periods included different subset of months, we anticipated some contribution of the seasonality on the observed variations between the periods, without associations with the pandemic itself. The restricted comparison of similar subset of months in the periods was ruled out because it would have reduced the volume of data and limited the estimation capability of the time trends. As the indirect impact of the pandemic could be assessed by the variation in the trend component of the time series, trend and seasonal components of each time series were estimated separately, and the analysis of each outcome measure was performed on the trend component [18]. The analysis employed linear mixed effect models (for outpatient visit and HIV tests) and generalized linear mixed effect models using the beta distribution family (for HIV positivity ratio, non-adherent ratio, recall ratio and return ratio). The models included the time (from September 2019 to March 2023), the period (pre-pandemic, pandemic, and post-pandemic) and the interaction term time*period, with the HC incorporated as random effect. A sensitivity analysis explored the possible indirect effect of the location of the HC (central or peripheral) by adding a three-terms interaction time*period*location in the models. All tests were 2-sided and a $p<0.05$ was considered statistically significant. Statistical analysis was performed using R 4.3 (R Foundation for Statistical Computing, Vienna, Austria) [19].

Results

Outcome measures for the general population

During the study period, the HCs recorded a total of 447,515 outpatient visits and 126,096 HIV tests, with an average HIV positivity ratio of 2.4%. Figure 1 shows the overall trends in outpatient visits, HIV tests, and HIV positivity ratio. Average monthly outpatient visits decreased by 597 visits at the beginning of the pandemic ($p<0.0001$) then increased by 49 visits/month during the pandemic ($p=0.0003$); after the pandemic, the trend inverted ($p=0.0001$) and was not statistically different when compared to the pre-pandemic ($p=0.09$) (Fig. 1). Similarly, average monthly HIV tests decreased by 108 tests at the beginning of the pandemic ($p<0.0001$) then increased by 17 tests/month during the pandemic ($p=0.005$); after the pandemic,

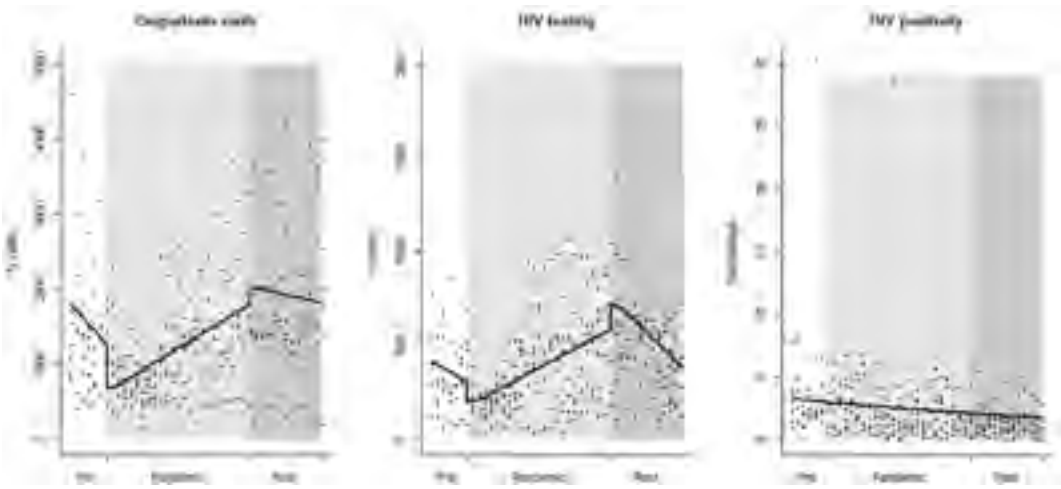

Fig. 1 Interrupted time series of outpatient visits, HIV testing and HIV positivity ratio at seven SAAJs in Beira (Mozambique) between September 2019 and March 2023. White background: before-pandemic period (September 2019 to March 2020); silver background: pandemic period (April 2020 to March 2022); grey background: post-pandemic period (April 2022 to March 2023). Line: predicted trend based on the regression model

the trend inverted ($p < 0.0001$) and was not statistically different when compared to the pre-pandemic ($p = 0.35$) (Fig. 1). On the other hand, the average HIV positivity ratio slightly decreased from 3.3% to 1.7% during the study period ($p < 0.0001$), without any indirect effects of the pandemic (Fig. 1). Full details of the analysis were reported in Table 1.

Outcome measures for PLHIV

During the study period, the HCs recorded an average non-adherent ratio of 8.2%, an average recall ratio of 95.3% and an average return ratio of 79.2%. Figure 2 shows the overall trends in non-adherent ratio, recall ratio, and return ratio. Average non-adherent ratio decreased from 23.4 to 2.4% during the study period ($p < 0.0001$), with a significant drop at the beginning of the post-pandemic period ($p = 0.0003$) (Fig. 2). Average recall ratio increased from 90.2 to 95.5%, with a significant drop at the beginning of the pandemic period ($p < 0.0001$) which affected also the post-pandemic period ($p < 0.0001$) (Fig. 2). Average return ratio did not show any significant trend over time ($p = 0.42$) but decreased from 83.2 to 74.7% at the beginning of the pandemic period ($p = 0.0001$), before returning to pre-pandemic figures (Fig. 2). Full details of the analysis are reported in Table 1.

Sensitivity analysis on the effect of the location of the HC

When exploring the possible indirect effect of the location (central HCs vs. peripheral HCs), the sensitivity analysis did not show any statistically significant association between the location and the outpatient visits (pandemic period: $p = 0.17$; post-pandemic period: $p = 0.40$), HIV testing (pandemic period: $p = 0.43$; post-pandemic period: $p = 0.26$), HIV positivity ratio (pandemic period: $p = 0.70$; post-pandemic period: $p = 0.98$), non-adherence (pandemic period: $p = 0.68$; post-pandemic period: $p = 0.66$), recall ratio (pandemic period: $p = 0.88$; post-pandemic period: $p = 0.69$), or return ratio (pandemic period: $p = 0.62$; post-pandemic period: $p = 0.31$).

Discussion

This study explored the resumption of HIV services for AYAs in the period after the end of the state of emergency following the COVID-19 pandemic in Mozambique. Both the number of outpatient visits and HIV testing showed a downward trend compared with the steady increase during the COVID-19 pandemic returning to values comparable with the pre-pandemic period. Throughout the study period, the HIV positivity ratio decreased, reaching 1.7% in the post-pandemic period. Similarly, the non-adherence ratio decreased across the three periods, reaching the lowest value in the post-pandemic period. The recall ratio increased

Table 1 Results from the interrupted time series analysis

Variable	Outpatient visits		HIV tests		HIV positivity ratio		Non-adherent ratio		Recall ratio		Return ratio	
	Coef (SE)	p-value	Coef (SE)	p-value	Coef (SE)	p-value	Coef (SE)	p-value	Coef (SE)	p-value	Coef (SE)	p-value
Time	− 86 (36)	p = 0.020	− 19 (12)	p = 0.130	− 0.02 (0.003)	p < 0.001	− 0.03 (0.006)	p < 0.001	0.06 (0.01)	p < 0.001	− 0.004 (0.005)	p = 0.420
Period (pre-pandemic)												
Pandemic	− 1591 (203)	p < 0.001	− 377 (70)	p < 0.001	Not in the model		− 0.16 (0.13)	p = 0.210	− 1.22 (0.23)	p < 0.001	− 0.51 (0.13)	p < 0.001
Post-pandemic	714 (637)	p = 0.260	1282 (219)	p < 0.001	Not in the model		− 0.90 (0.25)	p < 0.001	− 1.88 (0.38)	p < 0.001	Not in the model	
Time * period (pre-pandemic)												
Time * pandemic	135 (37)	P < 0.001	36 (12)	p = 0.005	Not in the model		Not in the model		Not in the model		Not in the model	
Time * post-pandemic	68 (40)	p = 0.090	− 12 (13)	p = 0.350	Not in the model		Not in the model		Not in the model		Not in the model	

Pre-pandemic period (September 2019 to March 2020); pandemic period (April 2020 to March 2022); post-pandemic period (April 2022 to March 2023)

Coef regression coefficient, *SE* standard error, Model selection was performed using the Akaike Information Criterion (AIC)

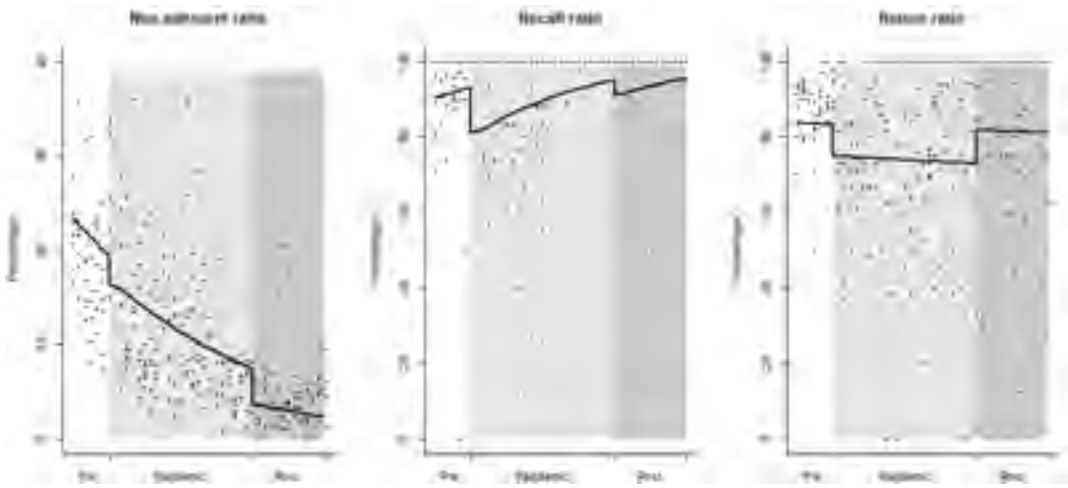

Fig. 2 Interrupted time series of non-adherent ratio, recall ratio, and return ratio at seven SAAJs in Beira (Mozambique) between September 2019 and March 2023. White background: before-pandemic period (September 2019 to March 2020); silver background: pandemic period (April 2020 to March 2022); grey background: post-pandemic period (April 2022 to March 2023). Line: predicted trend based on the regression model

across the three periods, while the return ratio did not show any significant trend despite a decrease during the pandemic period. There was no evidence that the location influenced the indirect impact of the pandemic on the outcome measures.

As already highlighted in the literature, the COVID-19 pandemic had a negative indirect impact on the provision of HIV services for PLHIV in many different countries [20]. In SSA, the major impact occurred between the second and third quarter of 2020 with a reduction of 33.5% and 30.8% in number of HIV test and new ART initiations, respectively, in adolescents aged 10–19 years [21]. On the other hand, an increase from 78.5% to 80.5% in viral load suppression was observed between second and third 2020 quarters [21].

According to our results, both the number of HIV tests and the ART pick up, a proxy measure of adherence, showed an ameliorating trend during the two years of the pandemic, although the HIV tests experienced an initial decline at the beginning of the pandemic. This is in line with findings in other studies where ART services were prioritised and generally maintained even during the early stages of the pandemic while HIV testing was more heavily affected [5, 22]. The constant ameliorating trend found in the present study during the pandemic period for the number of outpatient visits and tests, and for non-adherence and recall ratio could be also due to the fact that the most strict measures were taken during the first wave of the COVID-19 pandemic in Mozambique, similarly to other countries in SSA, while during the second wave, despite its greater severity, there was not the same public health response [23].

In the Fourth round of the global pulse survey on continuity of essential health services during the COVID-19 pandemic conducted by the WHO between November 2022 and January 2023, a general recovery of services was reported in this quarter [24]. In particular, the percentage of disruption of services compared to the pre-pandemic period decreased from 48% in the first quarter of 2021 to 24% in the quarter analyzed for HIV testing and from 32 to 8% for the continuation of established ART [24]. Based on these data, not only there was evidence of a reduction in service disruption, but some countries also experienced an improvement in some HIV services. In particular, an increase over pre-pandemic levels in adherence to ART and in the number of HIV tests was reported by 15% and 9% of the countries surveyed, respectively [24]. Similarly, our findings showed a reduction in the non-adherence rate at the beginning of the post-pandemic period. Both the number of outpatients visits and the number of tests, however, showed a downward trend in the post-pandemic period compared to the pandemic one, although not different from the pre-pandemic period. This could be attributed to a rebound effect after the initial drop at the beginning of the pandemic. Nevertheless, this trend should be closely monitored to avoid losing the positive results obtained during the pandemic. The 2023 executive summary by the Joint United Nations Program on HIV/AIDS (UNAIDS) shows that a total of

US$ 20.8 billion was allocated for HIV programs in low- and middle-income countries in 2022. This is 2.6% lower than the funds allocated in 2021 and much lower than the estimated US$ 29.3 billion needed [25]. The provision of adequate economic resources and funding for HIV programs is crucial to maintaining positive trends in the health services delivery. Indeed, although the COVID-19 pandemic has brought a partial increase in investments in the health sector, this must be maintained and adapted to be sustainable and to support health services where it is needed such as HIV services in SSA countries [26]. Maintaining the necessary funds after the COVID-19 pandemic in these services would have a triple beneficial effect by improving the health, social and economic gains of the countries in a virtuous circle [27]. Especially allocating more economic resources to community-based programs is believed to be essential to achieve the 95-95-95 goals for HIV [27].

Among the HIV services most affected by the COVID-19 pandemic along with the number of HIV tests were community programs, such as community support groups, patient tracing activities and outreach activities [28]. The data from our study showed how re-engagement activities were heavily affected by the pandemic, with a decrease compared to the pre-pandemic period, and even at the beginning of the post-pandemic period, the recall ratio made by community health care workers was still at a lower level than in the pre-pandemic period.

The disruption of community activities and testing at the very beginning of the pandemic period may also explained the decreasing positivity rate observed during the study period. Community-based testing is a key pillar for reaching population groups at high risk of HIV. The systematic review on 16 PEPFAR-supported countries found a similar slight decrease from 1.9% before COVID-19 to 1.7% during COVID-19 [21]. The discontinuation of outreach and testing services in communities due to the pandemic suppressed many of the case-finding strategies for key populations. Among these there may be the AYAs who were most affected by the reduction in HIV testing and diagnoses in SSA [29].

In LMICs, the adaptation of HIV services mainly relayed on differentiated service delivery (DSD), in particular for ART services [30]. In Mozambique, managers and providers from the Ministry of Health acknowledged a positive effect of the COVID-19 pandemic, as it loosened eligibility criteria for enrolment in fast-track and 3-months ART dispensing [31]. DSD has the advantage of being a person-centred approach that simplifies and adapts HIV services throughout the cascade, reducing unnecessary burdens on the health system [31]. This model not only was effective in maintaining HIV services but also had the advantage of limiting the impact of COVID-19 infection in a fragile and at-risk population such as PLHIV [32]. Indeed, seroprevalence studies showed no significant differences in SARS-CoV-2 infection probability between the general population and PLHIV [33]. Throughout the pandemic period, HIV services were never interrupted and, as in other countries, Mozambique prioritised healthcare workers, as well as other at-risk groups, for vaccination for SARS-CoV-2 [34].

In the present study, no differences in HIV service delivery were found based on the HC being located in a central or peripheral area within an urban setting. This may be due to the fact that HCs located in rural areas were not included in the study, as these areas showed the greatest fragility and difficulties in HIV service delivery as they are also highly reliant on community-based activities [28, 35]

This study has some limitations. First, the pre-COVID period encompassed a time frame of less than one year and following cyclone Idai, so it may not represent a standard of normality reference for HIV services. Second, data on testing and outpatient visits were collected on an aggregate level, so we could not assess how many new people were reached by HIV services during the reporting period nor explore possible differences in access to care based on sex. Finally, data on HIV disease stage and viral load were not collected and analysed, which would also have enabled an assessment of the clinical status of PLHIVs over the three periods included in this study.

Conclusions

This study showed that the trend of the six outcome measures got back comparable to the pre COVID-19 period in the post pandemic one. The non-adherence ratio had a stable downward trend, probably thank to the improvement of the differentiated delivery of the service, through the extension of the ART delivery and the application of less restrictive criteria. Despite some drops in the early stage, almost all outcome measures showed improvement during the two-year pandemic period, except for the return ratio that nevertheless returned to pre-pandemic levels in the post-pandemic one. The HIV service system proved adaptability and resilience and can serve as a model for other emergency situations, related to new infectious outbreaks, climate change and extreme natural events.

Abbreviations

ART	Anti-retroviral therapy
AYA	Adolescents and young adults
DSD	Differentiated service delivery
ITS	Interrupted time series
HC	Health Centres
LMIC	Low Middle-Income Countries

PLHIV People living with HIV
WHO World Health Organization

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Author contributions
In this work RB, conceptualized and designed the study and made substantial contributions to original writing. FCa was responsible for the data analysis and contributed to original writing. VCa contributed to study conceptualization and data interpretation. DG contributed to study design. AZ and GB contributed to data interpretation and original writing. IC, VCi and FCh contributed to data collection. GP and DD supervised the study phases. CG reviewed the study critically and contributed to data interpretation. All authors reviewed the study critically.

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Availability of data and materials
The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Inter-institutional Bioethics Committee for Health of Sofala (Comité Interinstitucional de Bioética para Saúde, CIBS—Sofala) on the 07 of June 2023 (protocol number 057/CIBS/2022).

Consent for publication
Not applicable.

Competing interests
Nothing to declare.

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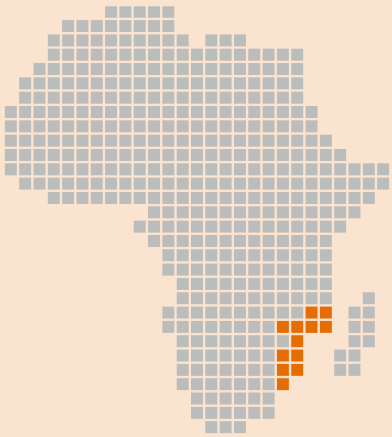

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Measuring preparedness to infectious diseases among people exposed to climate disasters in Cabo Delgado, Mozambique: a cross-sectional study

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Abstract

Introduction Climate change is contributing to increase the frequency and severity of climate disasters in Mozambique, leading, since 2019, to extensive damage to infrastructure and displacement 1.3 million people. Aim of this study is to evaluate baseline preparedness to vector-borne and water-borne infections among households and internally displaced people exposed to climate disasters in Mozambique.

Methods This was a cross-sectional, community-based survey assessing the preparedness to infectious diseases outbreaks among people exposed to climate disasters in six districts in Mozambique. Structured form was delivered via face-to-face between October 15th and November 7th, 2022. Study outcome was defined as a seven-point score of preparedness to infectious disease outbreaks. Multivariable analysis of the score was conducted using Conway-Maxwell-Poisson regression.

Results This study included 2,140 households and 11,239 people, with IDPs accounting for 30% of them. Overall, 1,186 (55.4%) households were overcrowded. Median score of preparedness was 3 points (IQR 2–4). At multivariable analyses, districts with low preparedness were Montepuez and Mueda. Higher preparedness was associated with family planning ($p < 0.0001$), access to primary education for all children living in the household ($p < 0.001$) and possession of a birth certificate for all children aged < 5y ($p < 0.0001$), while preparedness was heterogeneous among the districts ($p < 0.05$). Households composed by IDPs were not associated with a lower preparedness score.

Conclusions In climate-vulnerable communities in Mozambique, households practicing family planning, providing access to primary education and birth certificate for all children were less vulnerable to water-borne and vector-borne infectious disease outbreaks. Being family planning and childcare primarily performed by women, our findings can

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inform policymakers and practitioners on the importance of addressing women to mitigate the impact of climate disasters and reduce the risk of infectious disease outbreaks.

Keywords Climate change, WASH, Cholera, Malaria, Internally displaced people, Climate-sensitive infectious diseases, Low- and middle-income countries, Sub-saharan africa, Mozambique

Background

Human-induced climate change is exacerbating the frequency and severity of climate disasters in Mozambique [1]. Since 2019, extremely vulnerable communities in Mozambique were hit by Ciclone Idai, Cyclone Kenneth, Tropical Storm Ana, Cyclone Guambe and Cyclone Freddy [2]. These disasters have impacted over 3.1 million people, resulting in the destruction of approximately 318,000 houses and displacing up to 1.3 million people [3–6]. Internally displaced people (IDPs) are especially vulnerable to infectious diseases due to their profoundly under-resourced living conditions [7].

Frequent floods, droughts, and cyclones have caused extensive damage to infrastructure, including water and sanitation systems. These disruptions in hygiene and prevention practices have escalated the risk of waterborne [8] and vector-borne diseases [9]. Malaria and cholera – two highly climate-sensitive diseases tracked by the Lancet Countdown [10] – frequently lead to epidemics following cyclones and floods.

Only Cyclone Freddy, which made landfall in Mozambique twice in less than a month (24 February and 11 March 2023) [11], lead to nearly 30,000 cholera cases [6], while cyclone Idai led to nearly 26,000 cumulative cases of malaria [3]. Risk factors for cholera include poverty, overcrowding, inadequate access to clean water and poor hygiene conditions such as the impossibility to wash hands, dispose waste and access to proper sanitation facilities. At present, Cabo Delgado province is facing the deadliest cholera outbreak in the country in the past 25 years. Since September 2022, the outbreak has resulted in over 6,000 reported cases, with 801 (3.1%) of these cases originating from Cabo Delgado itself [12]. On the other hand, prevention against vector-borne diseases if heavily affected by humanitarian emergencies, which disrupt access to health facilities and public health programs such as mass insecticide-treated nets (ITN) distribution, or indoor residual spraying [13]. Cabo Delgado, this exacerbates the disease burden in the province with the highest malaria prevalence, which reaches 57.3% in children aged 0–5 years. The situation is further exacerbated by severe malnutrition and ongoing armed conflicts, resulting in the displacement of up to one million individuals. These conflicts are fueled by the socioeconomic exclusion experienced by northern Mozambique, alongside political and religious beliefs, and are intensified by the inequalities stemming from mineral and natural gas discoveries in the area [14].

In response to the recurrent outbreaks exacerbated by climate disasters, Doctors with Africa CUAMM (University College for Aspiring Missionary Doctors) and UNICEF (United Nations Children's Fund) Mozambique, conducted a multi-stakeholder, Social Behavioural Change program titled "Support adoption of key behaviors to prevent Covid-19, cholera, malaria, malnutrition and improve access to services in Cabo Delgado". Implemented in six districts of the Cabo Delgado province, the program focuses on piloting the national strategy for preventing communicable diseases, primarily cholera. Its objective is to encourage family units to adopt fourteen observable, low-cost behaviors that immediately reduce vulnerability to climate-sensitive outbreaks.

Aim of this study is to evaluate baseline preparedness to vector-borne and water-borne infections among family units and internally displaced people exposed to climate disasters in Mozambique.

Methods

Study design

This was a cross-sectional, community-based survey assessing the preparedness to vector-borne and water-borne infectious diseases outbreaks among people exposed to climate disasters in Mozambique. The survey was conducted between October 15th and November 7th, 2022, with face-to-face interviews. This reports follows the STROBE statement for cross-sectional studies [15].

Study setting

In Cabo Delgado province, resettlement started as early as March 2019, when both Cyclone Idai and non-state armed group (NSAG) violence hit local communities and continued through COVID-19 pandemic until mid-2022. As of today, roughly one million IDPs are living in the Cabo Delgado province. The present study was conducted in six of the seventeen districts in Cabo Delgado, which were supported by both CUAMM and UNICEF: Ancuabe, Balama, Chiure, Ibo, Montepuez, Mueda. The study involved both IDP sites and villages hosting sedentary population. At the time the study was conducted, all districts were affected by conflicts involving the Islamist armed group Ahlu Sunna Wal Jama [16].

Data collection and sampling

Data collection was conducted by trained community health workers who administered structured

questionnaires through face-to-face interviews. Responses were standardized as either "available" or "not available". All variables included in the questionnaire were initially derived from the 2028 Mozambique Malaria indicator survey [17] and from the annual Global World Health Organization report on water, sanitation, and hygiene [18]. Subsequently, they were adjusted to suit the local context with the assistance of community leaders. A convenience, non-probability sampling method was employed, relying on the availability of family units and approval from local authorities. Prior to study implementation, residents in target resettlement sites and villages were extensively informed through dedicated meetings led by community leaders, who also supervised and assisted in the fieldwork.

Study outcome

To assess the household preparedness for waterborne and vector-borne infectious disease, seven variables were identified as indicators of adaptation to climate-sensitive outbreaks. These included (i) presence of insecticide treated mosquito nets (ITNs) [13]; (ii) presence of a functional latrine; (iii) presence of a sanitary landfill to dispose waste; (iv) capacity to dry food; (v) possibility to protect aliments from domestic animal contamination (i.e.: availability of a pylon stick); (vi) possibility of handwashing and (vii) disposal of safe water treatment and water storage system [19, 20]. Each of these practices was assigned a score of 1 point if present, resulting in a final score ranging from 0 (indicating complete unpreparedness) to 7 (indicating high preparedness).

Statistical analysis

Continuous data were summarized as median and interquartile range (IQR), and categorical data as number and percentage. Multivariable analysis of the score of preparedness to infection disease outbreaks was conducted using Conway-Maxwell-Poisson regression, which was preferred to Poisson regression due to the underdispersion of the dependent variable in the model [21]. Multivariable analysis was performed in different sets of family units, as follows. In the whole sample, the model included the following independent variables: district, family planning, overcrowding (at least 5 people in the family unit), and the presence of IDP, children aged 0–5 months, children aged 6–60 months, children aged 6–14 years, pregnant women, lactating women, adults with disability and children with disability. In the subset of family units with children of any age, a variable about nutrition (all children eating at least three times a day) was added to the original list of independent variables. In the subset of family units with children aged ≥6 years, a variable about nutrition (all children eating at least three times a day) and a variable about school (all children aged ≥6 years go to school) were added to the original list of independent variables, while the variables about child age (presence of children aged 0–5 months, children aged 6–60 months, and children aged 6–14 years) were removed. In the subset of family units with children aged 0–60 months, a variable about nutrition (all children eating at least three times a day) and having the birth certificate were added to the original list of independent variables, while one variable about child age (presence of children aged 6–14 years) was removed. All tests were 2-sided and a p-value < 0.05 was considered statistically significant. Statistical analysis was performed using R 4.3 (R Foundation for Statistical Computing, Vienna, Austria) [22].

Ethical approval

Data collection that informs this study served as a pilot activity for the program implementation mentioned earlier. The project operates under a framework agreement between CUAMM and the government of Mozambique, and an agreement with Cabo Delgado province, which authorizes all study activities. Participation was voluntary, anonymous, and without compensation. Data were collected anonymously at the family-unit level and aggregated for analysis.

Results

This study included a total of 2,140 households and 11,239 people. Characteristics of the study participants are summarized in Table1. Most households lived in the Mueda district (n=803, 37.5%), followed by Ancuabe (n=416, 19.5%) and Montepuez (n=371, 17.3%). Overall, IDPs accounted for 30% (n=3,375/11,239) of the participants and 37.5% (n=803/2,140) of all households. Displacements were non-uniformly geographically distributed, ranging from 74.1% (n=1100) of all people living in Chiure to 10.8% (n=1,215) of the people living in Balama district. Also, 979/1,857 (52.7%) households with children were able to provide at least 3 meals a day and 484/1,496 (32.4%) households with school-aged children were able to provide primary education.

Information regarding adaptation to climate-sensitive outbreaks is reported in Fig. 1. The median score of preparedness to infection disease outbreaks was 3 out of maximum 7 points (IQR 2–4). Overll, the most available adaptation strategy to climate-sensitive outbreaks was insecticide-treated mosquito net (n=1,697, 79.3%), while the least available ones were the pylon stick (n=203, 9.5%) – a tool used to protect food from domestic animal contamination – and the availability of handwashing facilities (n=282, 13.2%).

Table2 presents the results from multivariable analyses of the preparedness score for infectious disease outbreaks. In synthesis, family planning was associated with higher score of preparedness (p<0.0001) across

Table 1 Characteristics of the study participants, overall and stratified per study district

N of family units	**Overall 2140**	**Ancuabe 416 (19.5)**	**Balama 251 (11.7)**	**Chiure 319 (14.9)**	**Ibo 306 (14.3)**	**Montepuez 371 (17.3)**	**Mueda 477 (22.3)**
Households with IDP [b]	803 (37.5)	129 (31.0)	16 (6.4)	246 (77.1)	183 (59.8)	94 (25.3)	135 (28.3)
Households with at least one child aged 0–5 months	395 (18.5)	62 (14.9)	82 (32.7)	57 (18.2)	60 (19.6)	61 (16.4)	72 (15.1)
Households with at least one child aged 6–60 months	1201 (56.1)	255 (61.3)	151 (60.2)	180 (56.4)	201 (65.7)	211 (56.9)	203 (42.6)
Households with at least one child aged 6–14 years	1496 (69.9)	286 (68.8)	167 (66.5)	219 (68.7)	222 (72.5)	267 (72.0)	335 (70.2)
Households with at least one pregnant woman	275 (12.9)	53 (12.7)	52 (20.7)	46 (14.4)	42 (13.7)	33 (8.9)	49 (10.3)
Households with at least one lactating woman	684 (32.0)	144 (34.6)	106 (42.2)	104 (32.6)	96 (31.4)	116 (31.3)	118 (24.7)
Households with at least one adult with disability	110 (5.1)	21 (5.0)	0 (0)	15 (4.7)	24 (7.8)	9 (2.4)	41 (8.6)
Households with at least one child with disability	65 (3.0)	14 (3.4)	1 (0.4)	12 (3.8)	18 (5.9)	3 (0.8)	17 (3.6)
Households with overcrowding (at least 5 people)	1186 (55.4)	251 (60.3)	129 (51.4)	153 (48.0)	183 (59.8)	225 (60.6)	245 (51.4)
Households doing family planning (contraception)	712/2139 (33.3)	127 (30.5)	88 (35.1)	108 (33.9)	139/307 (45.6)	111 (29.9)	139 (29.1)
Households with all children eating at least 3 times a day	979/1859 (52.7)	175/362 (43.3)	181/232 (78.0)	93/283 (32.9)	137/272 (50.4)	207/316 (65.5)	186/394 (47.2)
Households in which all children aged ≥ 6 years go to school	1115/1496 (74.5)	221/286 (77.3)	131/167 (78.4)	180/219 (82.2)	197/222 (88.7)	163/267 (61.0)	223/335 (66.6)
Households in which all children aged ≥ 6 years concluded primary school	484/1496 (32.4)	74/286 (25.9)	78/167 (46.7)	34/219 (15.5)	63/222 (28.4)	101/267 (37.8)	134/335 (40.0)
Households where all children aged 0–5 years have a birth certificate	867/1367 (63.4)	195/282 (69.1)	135/190 (71.1)	92/208 (44.2)	190/215 (88.4)	132/230 (57.4)	123/242 (50.8)
Total n of people	**Overall 11,239**	**Ancuabe 2285 (20.3)**	**Balama 1215 (10.8)**	**Chiure 1485 (13.2)**	**Ibo 1775 (15.8)**	**Montepuez 2071 (18.4)**	**Mueda 2408 (21.4)**
N of IDP	3375 (30.0)	553 (24.2)	56 (4.6)	1103 (74.3)	718 (40.5)	508 (24.5)	437 (18.1)
N of children aged 0–5 months	430 (3.8)	66 (2.9)	85 (7)	63 (4.2)	63 (3.5)	74 (3.6)	79 (3.3)
N of children aged 6–60 months	1660 (5.9)	379 (16.6)	210 (17.3)	231 (15.6)	296 (16.7)	271 (13.1)	273 (11.3)
N of children aged 6–14 years	2863 (24.4)	594 (26)	298 (24.5)	401 (27)	421 (23.7)	520 (25.1)	629 (26.1)
N of people aged > 14 years	6286 (55.9)	1246 (54.5)	622 (51.2)	790 (53.2)	995 (56.1)	1206 (58.2)	1427 (59.3)
N of pregnant women	291 (2.6)	59 (2.6)	54 (4.4)	50 (3.4)	44 (2.5)	34 (1.6)	50 (2.1)
N of lactating mothers	739 (6.6)	160 (7)	108 (8.9)	109 (7.3)	103 (5.8)	130 (6.3)	129 (5.4)
N of children aged 0–14 years with disabilities	73 (0.6)	21 (0.9)	1 (0.1)	13 (0.9)	18 (1)	3 (0.1)	17 (0.7)
N of people aged > 14 years with disabilities	128 (1.1)	29 (1.3)	0 (0)	17 (1.1)	24 (1.4)	10 (0.5)	48 (2)

Data summarized as n (%) or [a] median (IQR). [b] The median proportion of IDP within the household was 100% (IQR 57–100%). IDP: internally displaced people

the entire sample and in each subset. Additionally, the analyses indicated varying levels of adaptation to water-borne and vector-borne outbreaks among the six study districts ($p<0.001$), with Mueda and Montepuez showing the lowest preparedness. Among households with at least one child aged≥6 years, the variable related to school attendance ("all children aged≥6 years go to school") ($p<0.001$) and the presence of adults with disabilities were associated with a higher preparedness ($p<0.05$). Moreover, in family units with children aged 0–60 months, possessing birth certificates for all children was associated with higher preparedness for infectious disease outbreaks ($p<0.0001$). Notably, the variable regarding child nutrition ("all children eating at least three times a day") was not associated with the preparedness score in households with children.

Discussion

In this study, we observed varying levels of vulnerability against infectious diseases among people exposed to climate disasters in Mozambique, with factors such as district of residence, access to family planning, and key child development indicators influencing preparedness for these outbreaks. Following cyclones, tropical storms and floods, the risk for water-borne [20] and vector-borne [23] outbreaks increases substantially, with both cholera and malaria monitored by The Lancet Countdown for climate change's impact on human health [10]. Since, under current trends of fossil fuel extraction, global temperatures and extreme weather events are expected to rise [24], assessing adaptation strategies for climate-sensitive diseases imperative for public health in low- and middle-income countries (LMICs). Mozambique, despite producing roughly 0.02% of the annual share of global CO2

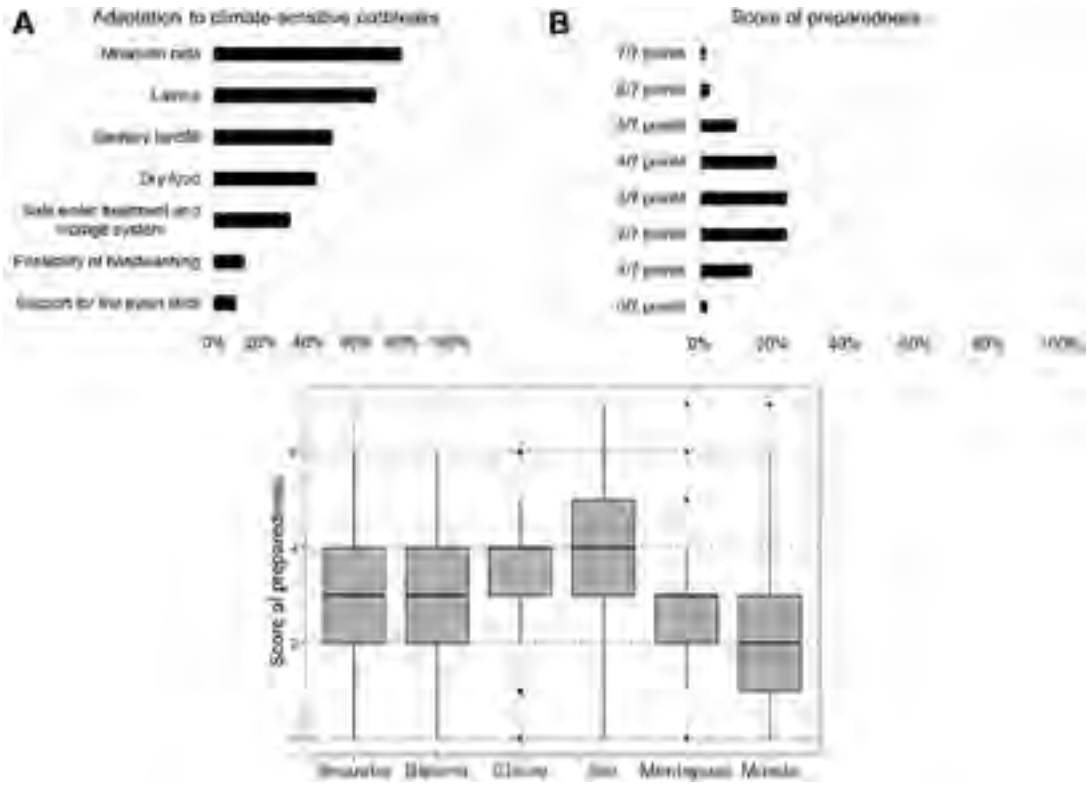

Fig. 1 Adaptation to climate-sensitive outbreaks (**A**), score of preparedness to climate-sensitive outbreaks in the overall population (**B**) and score result distribution stratified per study district (**C**)

emissions [25], is profoundly affected by human-induced climate change [26].

In this study, we assessed vulnerability to climate-sensitive outbreaks using a validated score comprising seven low-cost prevention strategies applicable during humanitarian emergencies, including insecticide-treated nets [13], and practices related to water, sanitation, and hygiene (WASH) [27]. A peculiar finding of our study was that, even afted adjusting for other variables, household with internally displaced people did not did not exhibit significantly different preparedness levels for water- and vector-borne infectious diseases. This could be attributed to the equitable access to sanitation resources among both internally displaced people and residents, along with comparable participation in public health initiatives such as insecticide-treated net distributions. Additionally, our survey targeted areas where people were displaced since early 2019, when Cyclone Idai made landfall, potentially equalizing access to sanitation services over time. Furthermore, despite the lack of association between outbreak preparedness and the provision of three meals per day for all children, this finding may be explained by the region's status as the most food insecure province in Mozambique during the study period, as reported by The United Nations World Food Programme. [28].

Interestingly, our multivariable analysis showed that indicators positively associated with high preparedness against climate-sensitive infectious diseases were were predominantly tasks associated with women: family planning and childcare [29]. Qualitative studies conducted in Mozambique [30, 31] and other sub-Saharan countries have consistently indicated low male participation in family planning, and in some cases, obstruction' [32]. This assumption is supported by by the lack of association between other indicators, such as overcrowding and presence of IDP in the household, and preparedness score. While acknowledging that the correlation found in our analysis does not imply causation – we highlight that family planning serves as an indicator of socio-economic wellbeing and positive female personal agency. It is associated with low child mortality [33], fewer unsafe abortions [34] and overall lower maternal mortality rates [35]. Thus, family planning may serve as a proxy for household resilience against climate-sensitive infectious diseases.

Table 2 Multivariable analysis of the score of preparedness to infection disease outbreaks (as proxy of household adaptation to climate-sensitive outbreaks)

	All family units		Family units with children of any age		Family units with children aged ≥ 6 years		Family units with children aged 0–60 months	
	Regression coefficient (95% confidence interval)	*p*-value	Regression coefficient (95% confidence interval)	*p*-value	Regression coefficient (95% confidence interval)	*p*-value	Regression coefficient (95% confidence interval)	*p*-value
Districts:								
Ancuabe	Reference	-	Reference	-	Reference	-	Reference	-
Balama	-0.10 (-0.22 to 0.01)	0.08	-0.07 (-0.20 to 0.05)	0.23	-0.22 (-0.45 to 0.01)	0.06	-0.07 (-0.21 to 0.07)	0.34
Chiure	0.25 (0.14 to 0.36)	**< 0.0001**	0.31 (0.19 to 0.43)	**< 0.0001**	0.18 (-0.01 to 0.36)	0.06	0.33 (0.18 to 0.47)	**< 0.0001**
Ibo	0.41 (0.30 to 0.52)	**< 0.0001**	0.44 (0.32 to 0.56)	**< 0.0001**	0.35 (0.16 to 0.53)	**0.0002**	0.40 (0.26 to 0.53)	**< 0.0001**
Montepuez	-0.21 (-0.32 to -0.10)	**0.0001**	-0.18 (-0.30 to -0.07)	**0.001**	-0.31 (-0.49 to -0.13)	**0.0005**	-0.13 (-0.26 to 0.01)	0.06
Mueda	-0.33 (-0.44 to -0.23)	**< 0.0001**	-0.32 (-0.44 to -0.21)	**< 0.0001**	-0.35 (-0.52 to -0.19)	**< 0.0001**	-0.31 (-0.45 to -0.16)	**< 0.0001**
Household with IDP	0.01 (-0.05 to 0.09)	0.61	0.00 (-0.07 to 0.07)	0.97	-0.02 (-0.14 to 0.09)	0.72	0.06 (-0.02 to 0.15)	0.16
Households with at least one child aged 0–5 months	0.06 (-0.04 to 0.17)	0.22	0.06 (-0.04 to 0.17)	0.25	-	-	0.08 (-0.04 to 0.20)	0.18
Households with at least one child aged 6–60 months	-0.06 (-0.14 to 0.01)	0.06	-0.06 (-0.14 to 0.01)	0.10	-	-	-0.04 (-0.19 to 0.10)	0.57
Households with at least one child aged 6–14 years	0.04 (-0.03 to 0.12)	0.26	0.05 (-0.04 to 0.15)	0.27	-	-	-	-
Household with at least one pregnant woman	0.02 (-0.06 to 0.12)	0.53	0.02 (-0.07 to 0.12)	0.66	-0.02 (-0.19 to 0.14)	0.79	0.03 (-0.07 to 0.15)	0.52
Households with at least one lactating woman	-0.01 (-0.10 to 0.08)	0.84	0.00 (-0.09 to 0.08)	0.91	0.02 (-0.33 to 0.38)	0.88	0.00 (-0.09 to 0.09)	0.95
Households with at least one adult with disability	0.04 (-0.10 to 0.18)	0.56	0.00 (-0.15 to 0.16)	0.94	0.22 (0.01 to 0.45)	**0.04**	-0.09 (-0.28 to 0.10)	0.34
Households with at least one child with disability	-0.05 (-0.23 to 0.12)	0.55	-0.02 (-0.20 to 0.16)	0.83	0.00 (-0.39 to 0.37)	0.97	-0.05 (-0.26 to 0.15)	0.62
Households with overcrowding (at least 5 people)	-0.02 (-0.10 to 0.06)	0.61	-0.01 (-0.09 to 0.06)	0.72	-0.10 (-0.22 to 0.01)	0.09	0.00 (-0.09 to 0.09)	0.95
Households doing family planning (contraception)	0.22 (0.16 to 0.29)	**< 0.0001**	0.20 (0.13 to 0.28)	**< 0.0001**	0.22 (0.10 to 0.35)	**0.0003**	0.21 (0.12 to 0.29)	**< 0.0001**
Households with all children eating at least 3 times a day	-	-	0.02 (-0.04 to 0.09)	0.51	-0.04 (-0.16 to 0.07)	0.47	0.03 (-0.04 to 0.12)	0.40
Households where all children aged ≥ 6 years go to school	-	-	-	-	0.19 (0.08 to 0.62)	**0.0007**	-	-
Households where all children aged 0–5 years have a birth certificate	-	-	-	-	-	-	0.22 (0.12 to 0.31)	**< 0.0001**

Each model did not include variables that could pose restrictions to the family units or could be incompatible with the subset of family units

p values < 0.05 are reported in bold

Recognizing the pivotal role of women during humanitarian crises in LMICs is essential in the fight against climate change and climate-sensitive infectious diseases. In sub-Saharan Africa, prioritizing women empowerment and agency through comprehensive strategies is essential for building resilient communities [36]. Beyond improving WASH behaviors, empowering women can lead to a better access to healthcare, increased education and awareness, enhanced economic growth, and contribute to long-term community resilience [37]. Despite facing disproportionate burden from the impacts of climate change – in terms of reduction of agency, increased unpaid workload and exacerbated gender-based violence [38] – women are pivotal in both adaptation and mitigation to the climate crisis [39]. The results of our study suggest that, by empowering women to lead community-based interventions, vulnerable people in Mozambique can enhance their capacity to combat cholera, malaria, and other infectious diseases that will be fostered by the ongoing climate crisis.

This study has some limitations that need to be considered. Firstly, our study was limited to six district in the Cabo Delgado province followed by CUAMM and UNICEF, thus limiting the generalizability of our findings to the broader Mozambican population. While our sample included data from more than two-thousands households, variations may exist between other provinces heavily impacted by cyclones and floods, such as Zambezia, Sofala, Nampula and Tete), which were not included in our study. Secondly, the unpredictable dynamics of extreme weather events, as well as the unique characteristics of a population both affected by climate disasters and conflicts, may further restrict the generalizability of our results. Thirdly, due to the challenging-to-reach nature of the population under study, we used convenience sampling, potentially affecting the representativeness of our findings. Fourthly, the outcome selected for this study served as a proxy of the overall prevention measures against post-disaster epidemics available to households at the time of the survey was conducted. Finally, we did not collect any clinical or microbiological data, precluding inferences regarding the true impact of water-borne and vector-borne outbreaks among the included population.

Among climate vulnerable people and IPD living in Mozambique, microbiological and syndromic surveillance of vector-borne and water-borne diseases is urgently needed. Further evidence is required to assess effective preventive strategies in reducing the burden of water-borne and vector-borne outbreaks in post-disaster humanitarian emergencies.

Conclusions

In climate-vulnerable communities in Mozambique, households practicing family planning and providing access to primary education and birth certificate to all children were foud to be less vulnerable to water-borne and vector-borne outbreaks. Our findings can inform policymakers and practitioners on the importance of addressing women to mitigate the impact of climate disasters and reduce the risk of infectious disease outbreaks. Also, our study clearly identifies two districts in which people are more vulnerable to climate-sensitive epidemics, which should be prioritized by local policymakers: Montepuez and Mueda.

Abbreviations

IDP	Internally displaces people
ITN	Insecticide-treated nets
LMIC	Low- and middle-income countries
NSAG	Non-state armed group

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Author contributions

FVS, EO, FDG and CM contributed to study concept and design. EC, AN, RC, GG, VL, SC, AC, IC, AG, AM, MAM contributed to patient inclusion and data collection. FC and FVS cleaned the data and FC contributed to the statistical analysis. FVS, EO, FDG, CM and FC interpreted the data. FVS, FC, GP and EO drafted the manuscript. FDG, AS and KC critically revised the manuscript. All authors approved the final manuscript.
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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Data collection that informs this study was performed within a framework agreement between CUAMM and the government of Mozambique. The study was reviewed and approved by ethics committee of MINEC Ministerio dos Negocios Estrangeiros e Cooperaçao, Nota 1883/MINEC.DAJC.DONG/2022. Participation was voluntary, anonymous, and without compensation, and informed consent to participate in the study was obtained from all included households. This study has been conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Impact of the COVID-19 pandemic on malaria in pregnancy indicators in Northern Uganda: a joinpoint regression analysis

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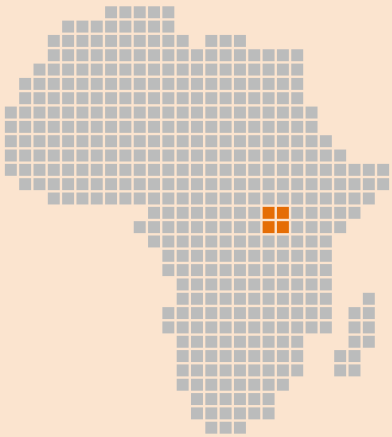

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Predictors of Cholera and Acute Watery Diarrhea among Climate-Vulnerable People Living in Cabo Delgado, Mozambique: A Cross-Sectional Study

PAPER

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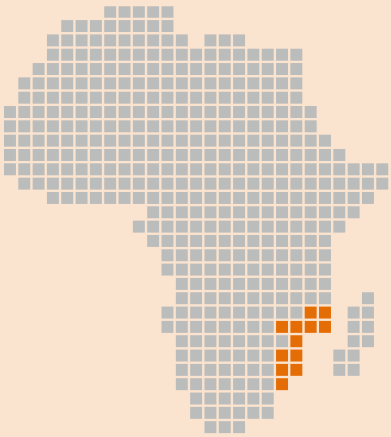

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Comparative effectiveness of chest ultrasound, chest X-ray and computer-aided diagnostic (CAD) for tuberculosis diagnosis in low-resource setting: study protocol for a cross-sectional study from Ethiopia

PAPER

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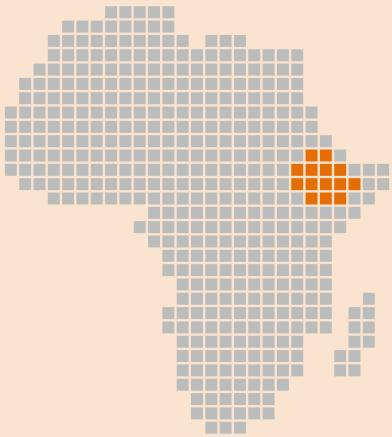

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Comparative effectiveness of chest ultrasound, chest X-ray and computer-aided diagnostic (CAD) for tuberculosis diagnosis in low-resource setting: study protocol for a cross-sectional study from Ethiopia

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Introduction: Early and accurate diagnosis of pulmonary tuberculosis (TB) is crucial for timely treatment and prevention of transmission, but diagnostic challenges persist due to complex symptoms and limitations in diagnostic tools. Chest X-ray (CXR) is the standard imaging modality, but its sensitivity and specificity may vary. Recently, some promising alternatives emerged such as chest ultrasonography (CUS) – particularly valuable in resource-limited settings – and computer-aided diagnosis (CAD) systems – helping clinicians in the reading and interpretation of the CXR. However, direct comparisons of CUS, CXR, and CAD score in TB diagnosis are limited.

Methods and analysis: This cross-sectional study will assess the diagnostic effectiveness of CUS in diagnosing TB compared to CXR and CAD score among index cases and household contacts. The study will be conducted at Wolisso St. Luke Hospital (Wolisso, Ethiopia). Index cases will be subjects with diagnosis of pulmonary tuberculosis within 7 days. Household contacts will be identified by administering a screening questionnaire to index cases. They will undergo CXR as for standard of care and consequent CAD analysis and CUS. The anticipated sample size is 136 subjects. The common accuracy metrics (sensitivity, specificity, positive and negative predictive values) will be calculated.

Ethics and dissemination: The protocol was approved by the Oromia Health Bureau Research Ethics Committee (BFO/MBTFH/1-16/1908). All information obtained will be confidential. Selected investigators will have access to data,

while international partners will sign a dedicated Data Protection Agreement. Eligible subjects will receive a brief information about the study before being asked to participate and they will provide a written informed consent. Results will be conveyed to stakeholders and disseminated through conferences and peer-reviewed journals.

Clinical trial registration: NCT06409780, https://clinicaltrials.gov.

KEYWORDS

CAD, tuberculosis, chest ultrasound, Ethiopia, Africa, diagnosis, CAD4TB, pulmonary tuberculosis

Highlights

- This study will assess the effectiveness of CUS in diagnosing TB in a broad population, as opposed to targeted populations such as people living with HIV.
- This study will also involve household contacts in a deeper screening program.
- CUS is easy to perform without risks for the patient.
- Index cases will be diagnosed using molecular tests instead of cultural tests.
- CUS performance may vary according to operator's skills.
- Cavitations are less frequently observed with CUS.

Introduction

Pulmonary Tuberculosis (TB) is caused by the *M. tuberculosis complex*, a slow-growing bacteria with a particular cell wall composition that confers resistance to the main antibiotics. Despite being one of the oldest known diseases, TB remains one of the biggest concerns in global health, especially in at-risk populations such as HIV/AIDS subjects. In 2022, over 1.2 million deaths were attributed to TB globally, with 167,000 of these cases involving coinfection with HIV (1). The clinical presentation of TB can vary according to the site of infection and the individual's immune status. TB typically affects the lungs and is associated with persistent cough, low-grade fever, night sweats, weight loss and hemoptysis, while extrapulmonary TB may affect any other site of the body, with different manifestations and treatment strategies (2). The main determinant for TB is poverty, and most people developing TB live in low-middle income countries (LMIC) where healthcare resources are often limited (3, 4). Further risk factors include diabetes, malnourishment, and alcohol use disorders (5, 6). Recently, the COVID-19 pandemic has constrained the TB eradication programs planned by the World Health Organization due to diagnostic delay (7), along with climate change and internal and international conflicts.

Early and accurate TB diagnosis is crucial for timely initiation of treatment and prevention of transmission, yet it presents challenges due to several factors including complexity of symptoms and limitations in diagnostic tools (8). The widespread adoption of molecular tests such as GeneXpert has significantly simplified and enhanced the sensitivity of microbiological diagnosis for TB, to the extent that it has replaced smear microscopy as the diagnostic gold standard in many national guidelines, especially in LMICs (9). Furthermore, GeneXpert provides clinicians with a rapid assessment of TB strain susceptibility, enabling timely initiation of appropriate treatment. For instrumental diagnosis of TB, chest X-ray (CXR) is the standard imaging modality for TB diagnosis, but its sensitivity and specificity can vary according to some factors such as disease stage and image quality (10). Computed tomography scans may offer higher resolution and details, but availability and accessibility can be limited particularly in resource-constrained settings (11, 12). In Ethiopia, a recent study on the facilitators of pulmonary TB diagnosis emphasized the importance of integrating radiographic screening with symptom-based screening in health facilities, while acknowledging the high cost of such implementation (13). The constraints in implementing CXR-based screening included the requirement for radiological equipment (which may not always be accessible), the exposure to ionizing radiation (with potential risks for vulnerable populations such as children and pregnant women), and the shortage of personnel trained in acquiring and interpreting quality images in the health facilities.

In an era marked by the proliferation of artificial intelligence, efforts have been made to overcome the shortage of trained personnel (14). Recently, a software for radiographic image analysis (CAD) has been introduced to provide clinicians with a probability score for TB detection (15). Furthermore, chest ultrasonography (CUS) has emerged as a promising adjunctive tool in TB diagnosis, especially in at-risk populations (16). Its advantages include portability, lack of radiation exposure, and potential for bedside use, making it particularly valuable in LMICs where access to advanced imaging techniques may be limited (15, 17). The initial evidence has suggested that CUS may offer high sensitivity in detecting microbiologically confirmed TB among adults, but available data are still limited (18, 19). Furthermore, limited research has directly compared the diagnostic performance of CUS, CXR, and CAD score in the diagnosis of TB, and no evidence has been produced for household contacts of index cases (20).

Understanding the comparative effectiveness of these diagnostic modalities is essential for optimizing TB diagnosis strategies and improving patient outcome, especially in high-risk populations such as household contacts who are at increased risk of TB transmission (21, 22). Therefore, this study aims to fill this gap by evaluating the diagnostic accuracy of CUS, CXR, and CAD score in identifying TB in index cases and household contacts. The findings may provide valuable insights into the effectiveness of these modalities and inform the development of contextually appropriate TB diagnostic strategies to improve patient outcome.

Methods and analysis

Study design

This study will employ a cross-sectional design to compare the diagnostic effectiveness of CUS with CXR and CAD score in identifying TB among index cases and household contacts.

Study setting

The study will be conducted at St. Luke Hospital in Wolisso (Ethiopia), which is a second level, not-for-profit hospital covering a catchment area of about 1.2 million inhabitants. The Medical Ward has 23 beds and accounts for around 1,800 admissions every year. Wolisso is the largest city in the South-western Shewa area of the Oromya Region. According to WHO TB Report 2023, in Ethiopia the incidence of TB is 126 cases every 100,000/people, of which 4.9 cases of co-infection HIV/TB every 100,000 people, 1.6 case of rifampicin-resistant/multidrug resistant TB every 100 k people (1,1% of all new cases), with TB case fatality ratio of 15%.

Participant and eligibility criteria

Eligible subjects will be all consecutive index cases during the study period and their household contacts. Index cases will be identified following a microbiological diagnosis of pulmonary tuberculosis using GeneXpert (Xpert MTB/RIF assay) within 7 days from the beginning of anti-tubercular treatment, in accordance with the standard of care in the Outpatient Department or the Medical Ward at St. Luke hospital. Household contacts will be identified by administering a screening questionnaire to index cases. Household contacts are defined as individuals who live in the same household as the index case or who had close and prolonged interactions with the index case during the infectious period. To minimize recruitment attrition, research assistants will reach out to household contacts and offer transportation to St. Luke hospital to facilitate their participation in the screening program. Eligible subjects of both sexes and aged over 5 years will be included, and all participants will be asked to provide informed consent. Exposure to any antitubercular treatment prior 7 days than the enrollment and refusing consent to participate will be the only exclusion criteria.

Procedures

After enrollment, all participants will undergo imaging examination including CUS and CXR according to standard protocols. Considering the high interoperator variability of the ultrasounds, two expert and trained sonographers will perform CUS. In case of discordance, the final decision will rest with the senior sonographer.

During CUS, the participant will stay in a supine or seated position, exposing the chest area for ultrasound examination. A thin layer of ultrasound gel will be applied to the skin to facilitate acoustic coupling and improve image quality. During CXR, the participant will stay in an upright or standing position, facing the X-ray machine. Images will be captured in the posteroanterior view, ensuring adequate visualization of the chest area. The acquired chest X-ray images will be transferred to the CAD4TB software platform (15), which may highlight regions of interest and assess a score according to the findings.

Reference standard for TB diagnosis in household contacts will be based on microbiological confirmation according to local protocol (molecular diagnosis with GeneXpert MTB/RIF assay) or clinical-radiological criteria.

Biological specimens will be collected and managed according to TB local standard of care. A volume of 5 to 10 mL of sputum is considered adequate for the purpose and there is no advantage in collecting a larger volume. The sample should contain recently discharged material from the bronchial tree with minimal saliva content. Samples will be handled as per local routine laboratory procedures and will not be stored for research purposes.

All household contacts will also be screened for the presence of any symptom suggestive of TB, including cough of any duration, hemoptysis, fever, poor weight gain or weight loss, night sweats, chest pain, and shortness of breath.

Standard of care for index cases and household contacts will be provided according to the Ethiopian National Guidelines for Tuberculosis. The study procedures are not expected to interfere with the routinary activities related with the admission and the care of the patients.

Outcome measures

The primary outcome measures will include the sensitivity and the specificity of CUS, CXR, and CAD in TB diagnosing. The secondary outcome measures will include (i) the positive predictive value and the negative predictive value of CUS, CXR, and CAD in diagnosing TB, and (ii) the concordance between CUS, CXR, and CAD in identifying TB cases.

Data collection

Data collection will include demographic and clinical information (such as age, sex, symptoms and TB risk factors), and data from CUS, CXR and CAD. Data collection will be performed by previously trained data collectors. All data will be anonymized and stored into a dedicated, password-protected database.

Sample size

The sample size calculation is based on the anticipated sensitivity (0.80) and specificity (0.80) of the diagnostic modalities (CUS, CXD, CAD). A paired design will be used to test whether the sensibility (and specificity) of the experimental modality (CUS) is non-inferior to sensibility (and specificity) of the reference modalities (CXD and CAD separately), with a non-inferiority difference bound of −0.10. With a type I error of 5% and a power of 90%, 110 subjects are required to exclude a difference in favor of the reference group of more than 0.10. The final sample size is increased to 136 subjects to take into account the adjustment for multiple testing, both index cases and household contacts. The calculation was performed according to Liu

et al. (23) and was carried out using R 4.3 (R Foundation for Statistical Computing, Vienna, Austria) (24).

Statistical analysis

Two interim analyses are planned at 3 and 6 months of enrollment to check the assumptions on sensitivity and specificity of CUS, CXR and CAD in diagnosing TB. The interim analyses will not include any formal statistical testing. Adjustments to sample size and duration of enrolling period may be made according to the indications from the interim assessments. There are no stopping guidelines for harm and/or futility as none are expected. Categorical data will be summarized as absolute and relative frequencies. Numerical data will be summarized using mean and standard deviation (SD), or median and interquartile range (IQR). In accuracy investigation, the standard measures will be calculated (sensitivity, specificity, positive predictive value, negative predictive value). The non-inferiority hypothesis will be tested using a RMLE-based score test according to Liu et al. (23) Adjustment for multiple testing will be performed according to Benjamini-Hochberg procedure. Concordance between CUS and CXR, and between CUS and CAD will be assessed using Cohen's kappa and Gwet's AC1. Comparisons between variables will be performed with exploratory purpose using Pearson's or Spearman's correlation coefficients, Student's t-test, paired Student's t-test, Mann–Whitney test, Wilcoxon test, Chi Square test, or Fisher's test, as appropriate. Estimates will be reported with 95% confidence intervals where appropriate. Statistical significance will be set at 5%. The statistical analysis will be carried out using R 4.3 (R Foundation for Statistical Computing, Vienna, Austria) (24).

Patient and public involvement

Patients and public were not involved in the design and design, or conduct, or reporting of our research. Patients and public will be involved in the dissemination plans of our research.

Ethics and dissemination

The protocol was approved by the Oromia Health Bureau Research Ethics Committee (BFO/MBTFH/1–16/1908). This study will be conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Eligible subjects will be informed about the study before enrollment and participants will provide a written informed consent in an appropriate language (English/Oromifa). In case of illiteracy, a literature witness will sign, and the illiterate participant will provide his/her fingerprint. Participation in the study is voluntary and participants may withdraw at any time. All subjects will be informed that refusal to participate or withdrawal from the study will not affect their care.

All information obtained will be confidential, and all data will be anonymized and stored into a dedicated, password-protected database. Selected investigators will have access to the data, and international partners will sign a dedicated Data Protection Agreement.

The risks associated with participating in this study include minimal radiation exposure from CXR and potential discomfort during imaging procedures. However, the potential benefits of this study include contributing to the advancement of TB diagnostic strategies and early detection of TB cases, and indirectly contributing to improved patient outcome. There are no direct benefits to participants in this study.

The findings will be conveyed to the relevant stakeholders such as governmental health institutions, hospital management, healthcare staff, local community and decision-makers. The findings will be disseminated in scientific and community conferences, and will be reported in a peer-reviewed journal.

Ethics statement

The studies involving humans were approved by Oromia Health Bureau Research Ethics Committee. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

GG: Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology. WN: Investigation, Resources, Supervision, Writing – original draft, Writing – review & editing. SC: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. BK: Conceptualization, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. FB: Methodology, Supervision, Writing – original draft, Writing – review & editing. BG: Conceptualization, Investigation, Validation, Writing – original draft, Writing – review & editing. LP: Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. FM: Conceptualization, Validation, Writing – original draft, Writing – review & editing. MM: Investigation, Validation, Writing – original draft, Writing – review & editing. FC: Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – original draft, Writing – review & editing. SA: Conceptualization, Methodology, Validation, Writing – original draft, Writing – review & editing. GP: Project administration, Validation, Writing – original draft, Writing – review & editing. NV: Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. OT: Conceptualization, Validation, Writing – original draft, Writing – review & editing. FS: Funding acquisition, Supervision, Validation, Visualization, Writing – review & editing. AR: Investigation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. RI: Supervision, Validation, Visualization, Writing – review & editing. AT: Validation, Writing – original draft, Writing – review & editing. MB: Conceptualization, Supervision, Validation, Writing – original draft, Writing – review & editing. AS: Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. FG: Conceptualization, Funding acquisition, Investigation, Project administration,

Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1476866/full#supplementary-material

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Behavioural outcomes of “Model Family” SBC strategy implementation in the emergency context of Cabo Delgado, Mozambique

POSTER AND ORAL PRESENTATION

Conference
Ethiopian Health Education and Promotion Professionals Association (EHEPA). Social Behaviour Change SBC Summit

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Addis Abeba, Ethiopia

Presentation date
February 2024

Authors
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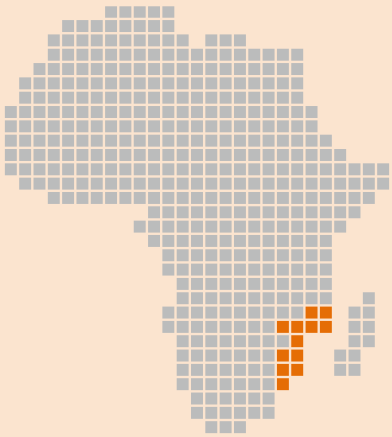
Focus country
Mozambique



L’antropologia medica applicata nella risposta all’epidemia di cholera in Mozambico. L’esperienza di Medici con l’Africa Cuamm

POSTER AND ORAL PRESENTATION

Conference
World Anthropology Day

Location
Milan, Italy

Presentation date
February 20243

Authors
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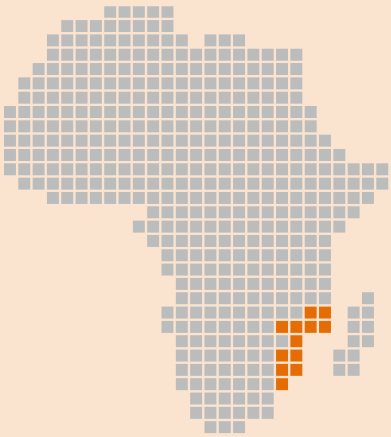
Focus country
Mozambique



Medical anthropology as a prism in the humanitarian response to the cholera epidemic in Mozambique EASA

POSTER AND ORAL PRESENTATION

Conference
European Association of Social Anthropologist. Doing and Undoing Anthropology

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Authors
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Focus country
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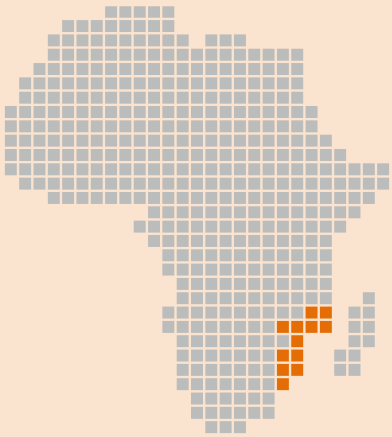

Chronic diseases

Protocol for an evaluation of the initiation of an integrated longitudinal outpatient care model for severe chronic non-communicable diseases (PEN-Plus) at secondary care facilities (district hospitals) in 10 lower-income countries

PAPER

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Protocol for an evaluation of the initiation of an integrated longitudinal outpatient care model for severe chronic non-communicable diseases (PEN-Plus) at secondary care facilities (district hospitals) in 10 lower-income countries

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ABSTRACT

Introduction The Package of Essential Noncommunicable Disease Interventions—Plus (PEN-Plus) is a strategy decentralising care for severe non-communicable diseases (NCDs) including type 1 diabetes, rheumatic heart disease and sickle cell disease, to increase access to care. In the PEN-Plus model, mid-level clinicians in intermediary facilities in low and lower middle income countries are trained to provide integrated care for conditions where services traditionally were only available at tertiary referral facilities. For the upcoming phase of activities, 18 first-level hospitals in 9 countries and 1 state in India were selected for PEN-Plus expansion and will treat a variety of severe NCDs. Over 3 years, the countries and state are expected to: (1) establish PEN-Plus clinics in one or two district hospitals, (2) support these clinics to mature into training sites in preparation for national or state-level scale-up, and (3) work with the national or state-level stakeholders to describe, measure and advocate for PEN-Plus to support development of a national operational plan for scale-up.

Methods and analysis Guided by Proctor outcomes for implementation research, we are conducting a mixed-method evaluation consisting of 10 components to understand outcomes in clinical implementation, training and policy development. Data will be collected through a mix of quantitative surveys, routine reporting, routine clinical data and qualitative interviews.

Ethics and dissemination This protocol has been considered exempt or covered by central and local institutional review boards. Findings will be disseminated throughout the project's course, including through quarterly M&E discussions, semiannual formative assessments, dashboard mapping of progress, quarterly newsletters, regular feedback loops with national stakeholders and publication in peer-reviewed journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a large prospective study carried out across 18 sites in 10 countries.
⇒ It has a comprehensive mixed-method design.
⇒ The main limitation is that it is an observational study with no control sites.

INTRODUCTION

Background

PEN-Plus (the Package of Essential Noncommunicable Disease Interventions—Plus) is a strategy to increase access to services and save lives by decentralising care for severe chronic non-communicable diseases (NCDs) in highly constrained health systems.[1 2] These

severe chronic NCDs (SC-NCDs) include conditions such as type 1 diabetes (T1D), rheumatic heart disease and sickle cell disease (SCD) that require services such as echocardiography, management of insulin and prescription of heart failure medications, anticoagulation and hydroxyurea that are rarely available at lower level health facilities in lower-income countries. PEN-Plus enables mid-level providers, such as nurses and clinical officers, to provide integrated care for a set of related conditions at intermediate care facilities such as district hospitals. PEN-Plus builds on and strengthens the WHO PEN strategy for decentralisation of care for common NCDs, such as hypertension, asthma and type 2 diabetes, at primary healthcare facilities.[3]

PEN-Plus was initially developed and scaled nationally in Rwanda.[4 5] PEN-Plus strategies have since been initiated in Haiti, Malawi and Liberia. Research has shown PEN-Plus to be affordable,[4] effective,[6] acceptable[7 8] and scalable,[5] but questions still remain about how to implement in new settings and how to scale up. PEN-Plus was identified by the Lancet Commission on Reframing NCDs and Injuries for the Poorest Billion (NCDI Poverty Commission) as a promising example of care through integrated teams. In 2019, WHO held a consultation to review a draft PEN-Plus strategy for the African Region.[3] In 2022, the WHO Regional Office of Africa adopted the PEN-Plus strategy as part of its Seventy-second Regional Committee Meeting.[9] In late 2020, the 21-country NCDI Poverty Network was launched to support implementation of the Lancet Commission's recommendation. The Center for Integration Science at Brigham and Women's Hospital serves as the Network's co-secretariat together with Mozambique's Universidade Eduardo Mondale. Increasing implementation of PEN-Plus is one of Network's strategic initiatives. Now, nine new countries and one state in India are initiating PEN-Plus programmes with support from the Network and other partners.

PEN-Plus expansion

A request for applications inviting countries to submit a letter of interest to apply for PEN-Plus implementation was posted and shared among partners in July 2020. Implementation organisations from countries that had previously completed a National NCDI Poverty Commission in partnership with the NCDI Poverty Network were eligible to apply. We received 21 applications from organisations in 11 countries. Following in-depth discussions and strategic planning from June to August 2021, 10 implementing partners were chosen to develop full proposals detailing implementation of a PEN-Plus package of clinical services at first-level hospitals.

Eighteen first-level hospitals in nine countries and one Indian state were selected for PEN-Plus expansion (table 1). The participating hospitals differ in the organisation of service delivery, training and overall systems in place. Based on these differing systems, we expect to have a range of approaches for different components of the implementation. In addition, we have a differing baseline knowledge of what existing services are. Where available, pre-existing services for NCDs are largely limited to primary care including screening and management of more common, less complex NCDs such as hypertension and type 2 diabetes, with little treatment for SC-NCDS that are the target of this work. Interventions contained in PEN-Plus vary based on local priorities (table 2), and existing Ministry of Health (MoH) initiatives. All PEN-Plus programmes involve training of midlevel providers and ensuring access to appropriate devices and medications for appropriate diagnosis and treatment of SC-NCDs.[2]

Over 3 years, these sites are expected to conduct the following activities:

1. Establish PEN-Plus clinics in one or two district hospitals, at least one of which must be rural. Clinics are expected to be staffed with trained staff and at a minimum provide chronic care for patients with severe or complex NCDs including type 1 and insulin-dependent diabetes, rheumatic and congenital heart disease and SCD. Based on sites-specific priorities, burden and other national resources, other conditions may be included as shown in online supplemental appendix 2. PEN-Plus clinics establishment may entail:
   a. Hiring, supervising and supporting clinical and auxiliary staff.
   b. Staff training and mentorship.
   c. Supplies and commodities procurement and distribution, with any needed supply chain support (eg, helping with projections, reporting on supplies).
   d. Supporting infrastructure where needed for clinic space.
   e. Systems development and support (eg, M&E).
2. Support the PEN-Plus clinics to mature into PEN-Plus training sites, in preparation for national or state-level scale-up. This would consist of readiness to host trainees that will be working to establish PEN-Plus clinics in other parts of the country.
3. Work with national MoH and other national stakeholders to describe, measure and advocate for PEN-Plus, ultimately supporting the development of a national PEN-Plus operational plan for scale-up following the grant period. This work includes assessing gaps in relevant clinical guidelines, formularies, clinical forms, regulations around scope of practice for mid-level providers such as nurses and clinical officers, and adaptation of training materials for national use in support of the MoH.

Implementation activities

Training

Training models for PEN-Plus will rely on many in-country contextual factors such as existing training programmes, specialist and other trainer availability, geography and certification processes. Thus, different models of PEN-Plus training, adjusted for context, are anticipated. For foundational PEN-Plus training, each implementing partner is planning on a set of didactics or classroom learning targeting the conditions in the initial proposed PEN-Plus

Table 1 PEN-Plus clinical sites

Country	Implementing partner	PEN-Plus clinical site	Facility type	Catchment population
Chhattisgarh State, India	Chhattisgarh NCD Plus Initiative	Surguja Government District Hospital, Surguja District (located at Ambikapur)	Public	840 352
		Surajpur Government District Hospital, Surajpur District	Public	900 198
Ethiopia	Mathiwos Wondu—Ye Ethiopia Cancer Society	Muketuri Primary Hospital, Oromia Region	Public	304 749
		Addis Zemen Primary Hospital, Amhara Region	Public	500 000
Kenya	NCD Alliance Kenya (NCDAK)	Hamisi Subcounty Hospital, Vihiga County	Public	176 264
		Kinna Health Center, Isiolo County	Public	115 533
Mozambique	Universidade Eduardo Mondlane (UEM) + Instituto Nacional de Saúde (INS) + CUAMM + Mozambique Institute for Health Education and Research (MIHER)	Hospital Rural de Nhamatanda, Nhamatanda District	Public	317 538
Nepal	Kathmandu Institute of Child Health (KIOCH)	Bardiya District Hospital, Bardiya District, Lumbini Province	Public	426 576
		Damak Hospital, Jhapa District, Province No. 1	Public	300 000
Sierra Leone	Partners In Health	Koidu Government Hospital, Kono District	Public	620 703
	CUAMM	Pujehun Hospital, Pujehun District	Public	406 931
Tanzania	National Institute for Medical Research (NIMR)	Kondoa District Hospital, Central Zone	Public	260 000
Uganda	Uganda Initiative for Integrated Management of Non-Communicable Diseases (UINCD)	Nakaseke General Hospital, Nakaseke District, Central Region	Public	300 000
		Atutur General Hospital, Kumi District, Eastern Region	Public	301 200
Zambia	Centre for Infectious Diseases Research in Zambia (CIDRZ)	Chibombo District Hospital (Mwachisompola), Chibombo District, Central Province	Public	421 315
		Matero Level 1 Hospital, Lusaka District	Public	478 710
Zimbabwe	SolidarMed+Clinton Health Access Initiative (CHAI)	Ndanga District Hospital, Zaka District	Public	194 739
		Mashoko Christian Hospital, Bikita District	Faith-based	174 068

PEN-Plus, Package of Essential Noncommunicable Disease Interventions—Plus.

Table 2 Evaluation components

Evaluation component	Research question	Timeline	Data collection lead	Proctor outcomes
Monitoring and evaluation	1,2	Quarterly	Site and Central	Implementation (adoption, feasibility, fidelity, penetration), service outcomes, client outcomes
Training indicators	2	Quarterly	Site and Central	Implementation (adoption, feasibility, fidelity, penetration)
Retrospective record reviews	1	2023, 2024	Site	Service outcomes (effectiveness), client outcomes
Baseline assessment	1	Q1 2022	Site	Implementation (adoption, fidelity, penetration), client outcomes
Qualitative formative assessments	1, 2, 3	Semiannual	Central	Implementation (acceptability, appropriateness, feasibility)
Midline assessment	1,2	2023	Site	Implementation (adoption, fidelity, penetration)
Endline assessment	1,2	2024–2025	Site	Implementation (adoption, fidelity, penetration),
Policy maker interviews	3	2022, 2024	Central	Implementation (acceptability, appropriateness, sustainability), health system
Cost analysis	1	Ongoing	Site and Central	Implementation (cost)
Monitoring of MoH activities	3	Ongoing	Central	Health system

package of care. Some countries may use e-learning or other digital innovations to support the didactic component of training. To complement classroom learning, each country will also incorporate practical or hands-on models of training where PEN-Plus trainees are clinically supervised by physician specialists or other expert cadres as they see patients, until trainees are deemed ready to see patients at PEN-Plus clinics independently. For example, in the most optimal setting, a country may already have specialists, who would come in weekly or biweekly to provide clinical supervision during PEN-Plus clinical encounters. However, this will not be the case for each type of condition or specialist in each setting, so a variety of approaches will be needed such as clinical experts travelling to be on-site for larger blocks of time, either from urban centres in-country or internationally.

We anticipate that most countries will have a hybrid combination of these models, as well as the potential for remote supervision via telemedicine and that systems will mature and advance over time. A large deliverable of the joint work across the 10 countries/states will involve articulating these different models, resources needed and best practices to ensure PEN-Plus trainees complete foundational training with competencies and skills needed to care for patients independently.

Trainees will initially be trained on basic competencies including an understanding of the pathophysiology of PEN-Plus conditions, knowledge of symptoms and diagnostic criteria, protocols for treatment, and counselling and education. Intermediate competencies will include knowledge of local and international epidemiology, atypical presentations of the disease, and, where relevant, new or advanced treatment techniques or updated protocols. Trainees will be evaluated using pre-training and post-training evaluations on condition-specific skills including screening, testing and treatment of PEN-Plus conditions like HBA1C testing, diabetes self-management education, echocardiology testing and peak flow spirometry.

Clinical implementation, community engagement and case finding

The PEN-Plus expansion work offers tremendous opportunity for learning across geographic contexts and clinical settings. Teams will tackle implementation questions such as staff supervision and mentorship, procedures for how patients flow through clinic, patient screening and linkage to care from a variety of clinical settings, long-term follow-up and missed visit tracking systems, incorporation of digital tools, research questions and more. The project will create several platforms for sharing of lessons, challenges and best practices to maximise cross-site learning including technical learning sessions, data review meetings, on-site visits and more.

Community engagement will be variable between sites, but examples may include engagement with community leaders, training of community health workers, social workers, radio campaigns, school campaigns and outreach.

For case finding, clinics initially will focus on identifying patients coming in for acute care (which primarily involves building links with inpatient care teams, emergency rooms and acute care outpatient clinics) and training providers to understand the initial signs of PEN-Plus conditions. Clinics are also strengthening links with referral hospitals to enable patients being seen at referral hospitals for conditions including T1D or SCD to be counter-referred to PEN-Plus clinics closer to their home. In later phases, after development of systems to identify the acutely ill patients, clinics will start to explore community case finding. This case finding varies in each setting and for each condition, but examples include school education around signs of T1D, community health worker education and radio outreach programmes.

Procurement

The PEN-Plus clinics will need a larger set of equipment available than is likely to be routinely found at first-level hospitals in these settings. This includes but is not limited to imaging capacity such as ultrasound machines with probes for echocardiography and other types of ultrasound scanning and laboratory capacity such as haemoglobin A1C, electrolytes, kidney and liver function, anticoagulation monitoring and sickle cell diagnostic tests. Most included sites are public MoH affiliated hospitals. Training, medications and equipment across the 10 countries are being externally financed through grants and donations. Implementation is occurring in partnership with local and central Ministries of Health to identify needs, gaps and public systems so that in the longer-term systems will be incorporated into national systems. Many of the countries will be able to acquire equipment in country or through international orders, and others will be supported for the initial PEN-Plus clinics by central procurement functions. Equipment models, pricing, procurement pathways, maintenance plans and ongoing planning for reagents and consumables will be closely tracked as part of the collective learning from PEN-Plus expansion to inform future scale-up and additional expansion and financing initiatives.

National planning

Each team will work through the MoH and relevant government officials to support the development of a national PEN-Plus operational plan. Building on the work of the national NCDI Poverty Commissions in each setting,[10] these operational plans will bring together key stakeholders to map out clear pathways for PEN-Plus expansion to first-level hospitals for national scale-up in the 10 years following initial pilot implementation of PEN-Plus. Each country will engage stakeholders across many realms including government, academic institutions, civil society and patient advocacy groups, clinical specialists, frontline healthcare workers, implementing partners and global and multilateral organisations. This process has already been conducted in Malawi, resulting in a national operational plan for PEN-Plus[11–13] as well

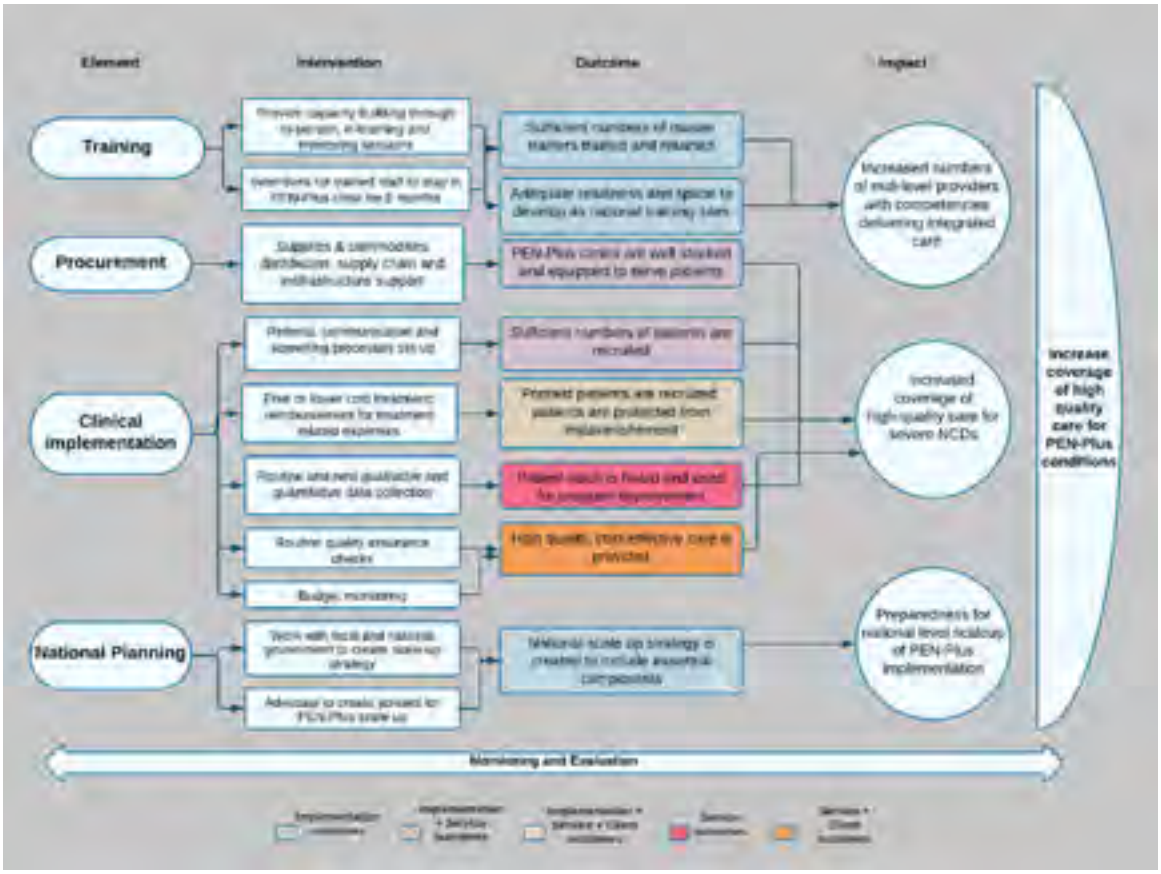

Figure 1 Theory of change. NCD, non-communicable diseases; PEN-Plus, Package of Essential Noncommunicable Disease Interventions—Plus.

as a national Steering Committee to steward and oversee national expansion.

Monitoring and evaluation

This project involves gathering patient-level and visit-level data for each of the PEN-Plus conditions. Preliminary information suggest that most or all PEN-Plus clinics have paper-based data collection systems and will gradually progress to electronic medical records when sites are ready. M&E activities for the 10 sites were designed such that all 10 sites could complete them, regardless of their data system maturity. Specific activities will include:

- Collection of Quarterly Core Indicators and Narrative—a template with PEN-Plus core indicators and a quarterly narrative section will be completed by implementing partners each quarter (online supplemental appendix 1). PEN-Plus core indicators focus on basic patient counts (eg, numbers enrolled, active, loss to follow-up, and deaths). After being audited, these core indicators will feed into a cross-site dashboard. The quarterly narrative will prompt the clinical team to reflect on challenges and successes during the previous quarter.
- M&E based discussions/interactions—Central M&E staff will facilitate a quarterly discussion during the monthly PEN-Plus partners meeting. In order to promote shared learning in PEN-Plus, local M&E staff persons will also be invited to share interesting quality improvement cycles, challenges and other materials.

Additionally, a data dictionary has been developed to promote the standardised collection of clinical data across the 18 sites to the extent possible. To aid in the standardised collection of clinical data, a comprehensive data dictionary will be shared with clinical sites to help guide the development of clinical forms at PEN-Plus clinics.

As WHO-AFRO has endorsed PEN-Plus throughout the African region, PEN-Plus is expected to launch in many settings. As PEN-Plus is being expanded in a relatively short time period to 18 sites across 10 countries, it is imperative to understand implementation challenges and regional differences in the acceptability, adoption, implementation and sustainability of PEN-Plus. These lessons will aid

us in both ensuring best possible care at existing PEN-Plus sites, and ensuring optimal design for further expansion. This is a protocol describing the 10-component formative evaluation of the PEN-Plus initial programme of expansion into 10 new countries. The project will document and understand operational challenges to ensure best possible implementation at current implementation sites and inform further scale-up.

METHODS AND ANALYSIS

Research questions

This protocol is developed for a mixed methods evaluation based on the United Kingdom's Medical Research Council (MRC) framework for complex interventions[14] guided by the Proctor implementation framework.[15] The evaluation is designed to reflect overarching research questions across all sites, but also allows for the considerable variability in implementation practices and needs across the nine countries and one state. Here, we aim to understand:

1. Clinical implementation outcomes
   - Are PEN-Plus clinics enrolling sufficient numbers of patients, are these clinics concentrating on patients with severe chronic NCDs, particularly T1D, and are they reaching the poorest? (Sufficient numbers for each condition and clinic will be determined based on local prevalence in the catchment area, and other factors related to clinic capacity and accessibility).
   - Is the care being provided at these new clinics acceptable and comparable in quality to tertiary chronic care facilities in their country?
   - Are patients enrolled in these clinics being protected from further impoverishment?
   - What is the cost of providing these services?
2. Training outcomes
   - Over the course of the project, what is the readiness of the supported facilities to become national training centres for PEN-Plus?
   - How many midlevel providers have been prepared to become PEN-Plus master trainers including a sufficient period of clinical practice precepted by internal medicine specialists, paediatricians, cardiologists and endocrinologists?
   - Is the PEN-Plus clinic space adequate for a training facility?
   - What is the 6-month retention of these midlevel providers?
3. Policy outcomes
   - Has the MoH, together with its partners, begun to develop the policies and strategies needed to enable the implementation of PEN-Plus services at a national scale?
   - These policies and strategies include: disease management guidelines, medication formularies, patient medical record forms, health management information systems, training curricula and certification pathways for providers, national PEN-Plus operational plans and resource mobilisation plans.

Study design

This is a mixed-method evaluation consisting of 10 components (table 2). Data will be collected through a mix of quantitative surveys (baseline, midline and endline surveys), routine reporting (M&E and training indicators), routine clinical data (retrospective record reviews) and qualitative interviews.

Study area and study site selection

This evaluation will occur in the 18 sites in ten countries where PEN-Plus expansion is taking place: Chhattisgarh State, India, Ethiopia, Kenya, Mozambique, Nepal, Sierra Leone, Tanzania, Ugana, Zambia and Zimbabwe (table 1). First-level hospitals were selected by the MoH and implementation partners in each country. We provided guidance including a focus on the rural poor, and a catchment population typically between 100 000 and 50 000 people. Using those criteria, the MoH and partners chose hospitals based on contextualised factors including local MoH priorities, local political will and commitment, epidemiology and geography. These factors are expected to be typical and define challenges for PEN-Plus implantation across the region and into the future.

Study period

This research will be carried out over a 3-year period between 2022 and 2025 (table 2).

Sampling

No sampling will be conducted as all clinics initiating PEN-Plus during the 3-year period and all patients with PEN-Plus conditions will be included.

Evaluation framework

We will use the Proctor Implementation framework and Institute of Medicine (IOM) standards of care[16] to understand the implementation outcomes including acceptability, adoption, appropriateness, feasibility, fidelity, penetration and sustainability. In addition to the implementation outcomes, we will also assess changes to service and client outcomes, as noted below.

Theory of change

Following MRC guidance for the evaluation of complex interventions, we adapted the theory of change based on Proctor characteristics (figure 1).[15]

Evaluation components

Data collection

We will conduct both routine data collection and new data collection activities. We briefly describe both below (table 2, online supplemental appendix 3) Data collection will be done both centrally and at the site level, using paper-based forms, RedCap and excel spreadsheets.

Routine data collection

Routine monitoring and evaluation

Routine data collection will begin when the clinics are running. The M&E section of the PEN-Plus implementation involves quarterly review and reflection on collected information to inform formative strategic, evidence-based improvements to the implementation efforts. As site M&E teams submit collected data on indicators, the data will be checked for missingness, outliers and errors. The team will communicate with individual site teams to resolve questions related to data quality and completeness. Additionally, the team will meet with each site quarterly to discuss trends and identify and trouble-shoot issues related to data collection. These calls will also provide a space for implementers to share their on-the-ground experiences and reflections, and potential quality improvement cycles.

Indicators will include (by condition and health facility):

- Total patients ever enrolled.
- Total patients currently enrolled and active in care.
- Total patients <18 years old.
- Total patients who are female.
- Active patients who had a visit in last quarter.
- New patients enrolled in last quarter.
- Patients who have been lost to follow-up in last quarter.
- Patient deaths reported in last quarter.

Training

Training indicators will be collected quarterly with the goal of understanding the number of providers (by cadre) capable of providing PEN-Plus services. We will have a core set of quarterly indicators and will add other indicators as the systems mature. We will gather information including:

- Midlevel providers fully trained for PEN-Plus as per local definitions.
- Midlevel providers fully trained and currently working in PEN Plus clinic(s).
- Midlevel providers currently enrolled in classroom or didactic training.
- Midlevel providers currently enrolled in e-learning course.
- Midlevel providers currently enrolled in in-person didactic course.
- Mentorship visit days this quarter to the PEN-Plus clinic(s) by specialists (total).
- Trained providers working in PEN-Plus clinics 6 months post training.

Depending on the unique reporting structure of the individual sites, the person reporting may be a member of the training team, the in-person specialist, and/or the master trainer coordinating training.

Retrospective record reviews

We will document the site-specific patient cohorts using retrospective record reviews, or electronic record analysis (depending on site capability). Anticipating a majority of sites will begin with paper-based records; a retrospective review will be performed once during implementation and once at the end of the 3-year period. Retrospective record reviews will be conducted at the site level through manually inspecting routine patient records and collecting information on patient outcomes for key conditions.

Data from the patient cohort will include:

- Number of patients being treated.
- Costs to the patient.
- Availability of PEN-Plus to the poorest and sickest patients.
- Patient progress.
- Patient-centeredness.
- Clinical characteristics and outcomes.

New data collection

Baseline assessments

The baseline assessments is designed to understand the overall structure and function of the hospitals that will be part of PEN-Plus expansion. The baseline assessment was designed centrally with site base input, and consists of questions about hospital structure, staffing, infrastructure, data systems and the availability of medicines, diagnostics and equipment. We expect to administer the baseline survey in the first half of 2022. The baseline assessment is created in RedCap and sites will input data either directly into RedCap or using paper based forms. If paper base forms are used, then they will be enterered into RedCap manually centrally.

Qualitative formative assessments

Twice a year, the central team will conduct structured calls with members of the NCD team to understand any barriers and facilitators to PEN-Plus implementation. The calls will also provide an opportunity to work through issues and understand best practices to use for future scale-up. Topics will be kept open to enable us to explore early experiences, but are expected to cover perceived challenges, what has worked well, what has worked less well and any other issues that stakeholders have not had other opportunities to address.

Midline surveys

One year into the implementation, we will conduct an interim midline assessment that will consist of readministering a simplified version of the baseline survey to understand improvements to clinic structure, staffing, supply chain and infrastructure. Data collected at this time will be used to identify bottlenecks and allow for timely course correction. Forms will be created in RedCap, and individuals at the site level will input data either directly into RedCap or into paper-based forms. If paper base forms are used, then they will be enterered into RedCap manually centrally.

Endline survey

At the end of the initation project, we will conduct an endline assessment consisting of readministering a simplified version of the baseline assessment to understand

Table 3 Outcomes to research questions

Question	Implementation outcome(s)	Service outcome(s)	Client outcome(s)	Evaluation component
Clinical Implementation Outcomes				
Are PEN-Plus clinics enrolling sufficient numbers of patients largely with severe chronic non-communicable diseases, and particularly type 1 diabetes?	Fidelity Penetration	Effectiveness Equity		Retrospective record reviews
Is the care being provided at these new clinics acceptable and comparable in quality to tertiary chronic care facilities in their country?		Safety Effectiveness	Function Symptomatology Satisfaction	Formative assessments, M&E, published reports
Are patients enrolled in these clinics being protected from further impoverishment?		Equity	Access Financial burden	Retrospective record reviews
What is the cost of providing these services?	Costs			Cost analysis
Are patients' voices being heard?		Patient centeredness		Retrospective record reviews
Training outcomes				
What is the readiness of the supported facilities to become national training centres for PEN-Plus?	Adoption Appropriateness Feasibility Fidelity Penetration Sustainability			Baseline, M&E, Training, formative assessments, midline, endline, policy interviews
How many midlevel providers have been prepared to become PEN-Plus master trainers including a sufficient period of clinical practice precepted by internal medicine specialists, paediatricians, cardiologists and endocrinologists	Adoption Fidelity Penetration			M&E, Training
Is the PEN-Plus clinic space adequate for a training facility	Appropriateness Feasibility			Baseline, Midline, Endline
What is the 6-month retention of these midlevel providers?	Sustainability			Training
Policy outcomes				
Has the Ministry of Health (MoH), together with its partners, developed the policies and strategies needed to enable implementation of PEN-Plus services at a national scale?	Acceptability Adoption Penetration Sustainability			Policy interviews, Monitoring of MoH activities

institutional progress made to implementing PEN-Plus, and progress to becoming a national training site. Forms will be created in RedCap, and individuals at the site level will input data either directly into RedCap or into paper-based forms. If paper base forms are used, then they will be enterered into RedCap manually centrally

Policy interviews

Qualitative policy interviews will be conducted centrally twice; at the beginning if implementation and at the end of the the 3-year cycle with MoH officials and other national stakeholders active in agenda setting in NCDs at the national level. Informants will vary by country reflecting the unique makeup of the national policy space. Interviews will be conducted at the beginning of the project and after 3 years of implementation to understand local ownership and how early experiences have affected readiness and acceptability of national expansion of PEN-Plus. Questions will assess familiarity with PEN-Plus, perceptions of success, opportunities, dedication to training and barriers to successful scale-up. Qualitative data will be collected through interviews and may be conducted in person or via an online video platform such as zoom. Interviews will be conducted in English, or, if necessary, with the use of a translator. With consent, interviews will be recorded and transcribed.

Cost analysis

We will review payroll, budgets and other financial documentation available at each facility. Based on this information and to the extent possible, we will estimate the total annualised cost of services across all patients by summating estimated costs for several cost categories—including personnel, equipment, infrastructure and consumables. Coupled with outpatient and inpatient service volume, we will then generate an average cost per patient per visit for outpatient services and an average cost per patient per diem for inpatient services.

Outcomes

Our research questions span clinical and national levels. At the clinic level we are interested in (1) improvements

in *clinical implementation outcomes*, including correct diagnosis, initiation, and continuation of quality treatment for SC-NCDs; and (2) readiness and progress in *training outcomes*, including progress towards being national training centres. At the national level, we are interested in (3) *policy outcomes*, including sustainability and appetite for PEN-Plus scale-up at the national level.

For the purposes of this evaluation, we categorise our indicators into implementation, service and patient outcomes. Due to considerable heterogeneity across sites, progress will be measured differently based on local site characteristics. Outcomes mapped to the research question they pertain to and the evaluation component they are part of are found in table 3.

Study participants

The primary unit of analysis of this study will be the implementing first-level hospital, except for clinical outcomes where the patients will be the unit of analysis.

Data management

Data will be collected through paper-based forms or Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Mass General Brigham.[17 18] All data will be deidentified prior to data transfer. Data will be shared either through secure email or institutional Dropbox.[19] Data will be stored on secure Dropbox, and pooled non-identifiable indicator data will be uploaded into a shared cross-site dashboard powered by Microsoft Power BI.[20] All computers used to access data will be secure and password protected. Any paper data collection forms will be held in locked filing cabinets and will be stored for a maximum of 7 years, or end of research activities. All forms will be securely destroyed at the end of this period.

Data analysis

Baseline, Midline and Endline Assessments will be collected in RedCap. We will use excel to analyse descriptive statistics in order to understand trends and the evolution of clinic space, staffing, medicine and equipment availability and the clinics adequacy to become a training facility

Cost data will be collected on excel spreadsheets and simple descriptive statistics will be used to understand broad costs.

M&E and training data will be collected in Excel based sheets and used to enable timely reporting and understanding sites progress towards implementing PEN-Plus and ability to become regional training centres. We will examine trends over time and progress towards site-specific targets.

Retrospective record reviews will include patient numbers trends over time, and progress towards desirable patient outcomes for key conditions. Data will be collected in excel and analysed using descriptive statistics,

Qualitative data

After obtaining informed consent, interviews will be conducted virtually and, with permission, recorded. Qualitative data will be analysed in Dedoose[21] using a thematic analysis. Themes will be identified a priori and after initial coding based on these themes, we will expand our coding structure to encompass additional themes that emerged through the first step of analysis.

Data checking

Data will be checked for consistency and anomalous findings will be flagged and discussed with the local M&E or training teams.

Patient and public involvement

PEN-Plus is a programme aimed at improving care and the lives of people living with SC-NCDs, and was developed with the assistance of People living with SC-NCDs. Many of the authors and authorship group are either PLWSCNCDs or advocates. Patient advocates will be involved in dissemention activities.

ETHICS AND DISSEMINATION

This protocol has been considered exempt or covered by Mass General Brigham #2022P001390, Nepal Health Research Council 571/2022 P, National Institute for Medical Resarch (Tanzania) NIMR/Hq/R.8aVol. IX/4184, University of Zambia Biomedical Research Ethics Committee #3032-2022, Mulago Hospital Research and Ethics Committee MHREC 2022-74, Amhara Public Health Institute NoH/R/T/T/D/07/43 and Oromia Health Care Bureau BF/HBTFH/H6/2027.

Findings from routine data collection will be fed back to the local sites during quarterly M&E discussions and semi-annual formative assessments. Progress will be mapped on a dashboard that sites can access at any time. We will send quarterly newsletters to all the sites highlighting statistics, progress or successes including characteristics and predictors of compliance. We will have regular feedback loops with national stakeholders including members of the MoH. Finally, we will disseminate our findings and best practice through publications in open-access peer-reviewed journals.

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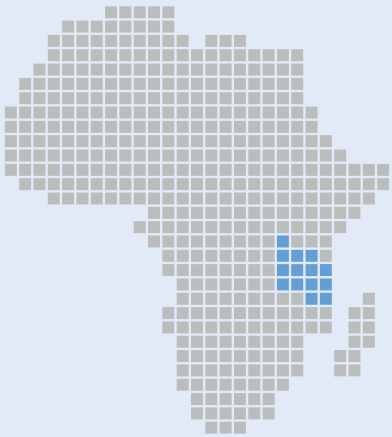

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RESEARCH ARTICLE

Multi-level barriers to early detection of breast cancer among rural midlife women in Tanzania: A qualitative case study

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Abstract

Background

Breast cancer is the second most common cause of cancer mortality among women in Tanzania and thus, early detection and treatment methods are central to improving breast cancer outcomes. However, in low- and middle-income countries in Sub-Saharan Africa, the survival rates remains low due to late presentation. Hence, a significant number of deaths could be prevented if barriers and facilitators to early detection are known.

Purpose

This qualitative case descriptive study explored the possible barriers to awareness and early breast cancer diagnostic services among midlife women in rural Tanzania.

Methods

Ten key informant interviews with health systems managers and community health workers and eight focus group discussions with women aged 40–65 years and their spouses were conducted to elicit the study data conducted from July to August 2021.

Results

The data revealed nine themes describing the barriers to early detection methods across five Socio-Ecological levels of influence, namely: 1) limited knowledge and 2) witchcraft beliefs (*individual level*); 3) limited male support (*interpersonal level*); 4) age and gender factors and 5) procrastination (*community level*) 6) limited availability of services 7) emphasis of curative over preventive care (*institutional level*); 8) poverty/inability to pay and 9) limitations of health insurance (*societal/policy level*).

Competing interests: The authors have declared that no competing interests exist.

Conclusions

The study findings suggest a need to further the design, implementation and evaluation of evidence-based community breast health awareness and education interventions to promote early detection of breast cancer in Tanzania. Specifically, the study highlights the need to address multiple level determinants of influence in breast cancer control as part of the country's Community Health Strategy.

Introduction

Breast cancer is a devastating global health problem, particularly in sub-Saharan Africa (SSA). Compared to high-income nations, Breast cancer mortality rates in Sub-Saharan Africa (SSA) are disproportionately high, despite the region's disease frequency appearing to be lower [1]. Although the disease incidence in SSA seems lower, mortality rates are disproportionately high in comparison to high-income countries. In Tanzania, Breast cancer is the second most common cancer, accounting for 14.4% of all newly diagnosed cancer patients [2]. It also ranks second in terms of cancer-related deaths among women. By 2030, an 82% increase in new instances of breast cancer is anticipated [2].

Globally, early detection and treatment methods are central to improving breast cancer outcomes. However, in low- and middle-income countries (LMICs) like those in Sub-Saharan Africa, the survival rates remain low due to late presentation that is attributed to inadequate or lack of access to early detection methods and treatment [3–6] such as mammography [7–9]. Thus, low cost, early detection strategies based on public health education related to awareness of risks, education about breast self-examination (BSE), clinical breast examination (CBE), and a well-trained health care workforce are considered the first line of control in improving breast cancer outcomes and survival rates [10–12]. In Tanzania, there are well-established health care system structures for health care provision from the least resourced community-level structures to specialized national hospitals. As of November, 2023, there were 7744 Dispensaries; 1115 Health Centers; 171 District Hospitals; 28 Regional Referral Hospitals; 5 Zonal Referral Hospitals; and 1 National Hospital [13]. In addition, Tanzania has **National Guidelines** for Early Diagnosis of Breast Cancer and Referral for Treatment [14]. However, due to shortage of skilled human resources and inadequacy/ absence of essential medical supplies for diagnosis and treatment of breast cancer, not all levels of health care perform as prescribed in the guidelines. The recent national assessment conducted in 2017 [15] revealed lower health facilities (from dispensaries to the district hospitals) lack patient information and do not perform routine clinical breast examination; while regional referral hospitals have some capacity for diagnosis and surgical management. On the other hand, Zonal consultant hospitals (for example, Bugando Medical Centre) and Muhimbili National Hospital are better equipped with facilities for diagnosis and surgical management of breast cancer. These higher-level hospitals do provide access to chemotherapy when available. A full range of cancer treatment is offered at Ocean Road Cancer Institute (ORCI), which is a National referral hospital specifically for treatment of cancer.

Absence of consistent breast cancer awareness [16] and early detection methods in the region [2], suggest that women themselves should be proactive to seek care from the primary health facilities and then follow the referral system, if so recommended, to the better equipped Zonal and National Hospitals. The earlier one starts the journey the better. However, geographic distance to services is a significant barrier to timely care, especially for rural

populations from which more than 80% of women with breast cancer are lately diagnosed [15]. To address this gap, intermittent efforts have been made to facilitate availability of early prevent methods through outreach services conducted by the Tanzania's Ministry of Health, and Clinical Breast Examination (CBE) campaigns conducted by Non-Governmental Organizations (NGOs) such as Tanzania's Medical Women Association (MEWATA). Unfortunately, most Tanzania women suffering from breast cancer continue to present with late diagnoses, suggesting existence of multiple barriers to early diagnosis and treatment [3–6]. Therefore, identifying the barriers and facilitators to early detection of breast cancer in LMICs [11] that cut across individual, interpersonal, organizational, community and health system barriers is needed for effective design and implementation of early detection methods [17]. However, few studies in the region have taken a multilevel approach to investigate barriers to early detection of breast cancer [17–19]. Thus, the goal of this qualitative descriptive study was to elucidate the possible multi-level barriers—herein defined as range of constraint/determinants to early access to breast cancer diagnostic services among women occurring at various level of influence (e.g. the individual, family and social supports, local community environment, health system, and national environments [17–19]. The purpose is to inform the development of a multilevel intervention in breast cancer awareness and early detection in rural Tanzania, where the risk for late detection of breast cancer is higher compared to their urban counterparts [20]. The current study addressed the following specific research question guided by the socio-ecological model [3]: What are the reported challenges/barriers to breast cancer awareness and early screening among midlife women aged 40–65 years old in rural Tanzania? We focused on midlife women as one of the most common affected age group in Tanzania [3].

Methods

Qualitative approach and research paradigm

The Standards for Reporting Qualitative Research (SRQR) were used to report findings from this qualitative case descriptive study.

The study was a result of a partnership between the faculty at a local public University in Tanzania and a public University in the U.S. The study allowed an in-depth and comprehensive exploration of multi-level barriers to early detection of breast cancer among rural midlife women using multiple methods and samples [21]. The collection of data and presentation of findings were guided by the Socio-Ecological model. Being qualitative in nature, the study took an interpretative paradigm [21]. That is, we studied barriers to a social action [prevention of breast cancer] in a specific context (mid-life women in a rural setting) by interpreting meanings behind the identified barriers.

Researcher characteristics and reflexivity

The interviews and focus group discussions were conducted by the first author who introduced himself as a public health faculty member with a background in nursing education from a Tanzania-based public university and an experienced researcher in conducting qualitative studies involving women's health. Prior to data collection, I was concerned about how the male gender was going to affect targeted key stakeholders' willingness to openly discuss the barriers to breast cancer awareness and early detection among mid-life women. However, this was not an issue after the introductions and relating with the male and female participants through shared experiences as a married man and public health professional.

Table 1. Summary of sources and methods of data collection.

		Number of Participants by Village		
Data Source	**Data Collection Method**	**Itumba**	**Isongole**	**Total**
Health system managers	Key informant interviews	4	1	5
Community Health Workers	Key informant interviews	3	2	5
Women	3 FGDs	18	12	30
Men	3 FGDs	10	18	28
Couples	2 FGDs	4 couples (8 participants)	4 Couples (8 participants)	16
Total		**45**	**39**	**84**

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Study setting and context

This study was conducted in two villages in Ileje District, Tanzania between July and August 2021. The district is in Songwe Region, which is second to Dar Es Salaam with respect cancer burden Nationally. The Ileje district was selected because it is the most remote rural setting in Songwe Region. This is because such areas are characterized by low household income, low educational achievement, and weak health system infrastructure.

Sampling strategy

The study employed a purposeful sampling strategy [22]. With assistance of Community leaders a total of 86 eligible participants (women aged 40–65 and their spouse) were identified, confirmed, and invited to participate in the study. However, 2 participants declined to participate in the study after being informed of what the study was all about. That is, the 2 did not consent. Thus, the data were collected from purposive samples [22] made of a) 10 *key informant interviews* (KII) with 5 health systems managers and 5 community health workers and b) 8 *focus group discussions (FDGs)*, (i.e., 3 groups with women only, 3 groups with men (spouses) only, and 2 couples-only groups), all of them with sum of 84 participants (see Table 1).

These categories of respondents—health system managers, community health workers (CHWs), and community members (women and men) were purposefully selected because they are potential key stakeholders in developing and implementing community-based programs for cancer prevention in Tanzania. Specifically, the purpose was to gather information that will facilitate future interventions that will involve CHWs as key players to mobilize individuals, families, community and raise awareness about breast cancer in Tanzania. Recruitment of the respondents stopped after reaching data saturation—the point in data collection and analysis when new information produced little or no change to the progression of theme identification. Using a community engagement approach [23], local [village] government leaders and the Ileje District Medical Officer served as the community field guides. They were notified about the criteria for recruitment and helped to identify the eligible study participants. Then, two Tanzania-based bilingual interviewers (i.e. TN, the study investigator and a study research assistant) validated eligibility of the prospective participants and carried out data collection.

Ethical issues pertaining to human subjects

The Muhimbili University of Health and Allied Sciences (MUHAS) Institutional Review Board approved and monitored this Wright State University-MUHAS collaborative study. The prospective interviewees and FGD participants were asked to take part in the study. The interviewer/moderator explained to the potential participants that their participation was

entirely voluntary before they gave their consent. Additionally, they were told that no names were necessary and that the data would be treated with the utmost confidentiality.

As a result, the authors did not have access to information that could identify individual participants during or after data collection.

Additionally, participants were asked to maintain confidence by not disclosing to those who were not participants any personal experiences that might be discussed. Finally, the option to decline participation was explained to each prospective participant. Ultimately, they gave their written consent.

Data collection methods

Data were collected using key informant interviews and focus group discussions (FGDs) that consisted of groups of 6–12 respondents. The data collection process was led by two facilitators: a moderator and a note taker (recorder). Participants completed a socio-demographic survey prior to the interviews and discussions.

Data collection instruments and technologies

Data were collected using interview and focus group discussion guides which were structured around a set of open-ended questions that explored midlife women's knowledge and experiences of breast cancer and breast examination as well as related barriers at multiple socio-ecological levels of influence (see Table 2 and S1 Appendix).

Units of study

A total 84 persons participated in the study (see Table 2)—of whom 10 were key informant interviews (health system managers and community health workers) and 74 were FGD participants whom 38 were women (see Table 1). Majority of the FGD participants were aged between 51–60 years (48.6%), had primary level of education (86.5%), and had monthly income of < USD 50 (78.5%) which is below the Anker Living Income reference for Rural Tanzania in 2020 of USD 200 per month [24]).

Data processing

The data were gathered in Kiswahili, followed by verbatim transcription and translation into English (see S2 Appendix).

Table 2. Interview and focus group discussion guide sample questions, by content area.

Content	Example questions
A: General health problems and their solutions	• What are the main health problems facing women aged 40–65 years in this community (hamlet/village) • For each main problem mentioned, what health programs deal with the problem at the family, facility and community levels?
B: Breast cancer and breast self-examination to see if there is any lump:	• What experience do you have about breast cancer to women aged 40–65 years in this community (hamlet/village). • What are the benefits of cancer early detection among women in this community? • What are the obstacles on breast cancer early detection among women in this community? • What methods can women in this community use to detect breast cancer early? • What does the concept of breast self-examination mean to women in this community? • What are the challenges of doing breast self-examination at the family, facility and community levels?

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Data analysis

The information in the transcripts was firstly unpacked and got organized in accordance to the levels of influence depicted by socio-ecological model—i.e individual factors, interpersonal factors, community factors, institutional factors, and societal factors. Then TN and RE independently reviewed and coded the transcripts using thematic analysis method [25]. The analysis was carried out in four stages [25, 26]: firstly, the line-by-line coding of field notes and transcripts; secondly, the in-depth examination and interpretation of the resultant codes and their categorization into descriptive themes; thirdly, synthesis of descriptive themes into more abstract analytical themes; and, fourthly, further condensation of analytical themes into the overarching theme.

Techniques to enhance trustworthiness

Limiting cultural bias and enhancing trustworthiness of the results was achieved through several ways, such as bracketing [27], prolonged engagement, member checks and peer debriefing [28]. Bracketing was employed by discussing and being aware of self-assumptions and preconceptions about the topic during the design and implementation of the FGD as well as synthesis of the findings. Regarding prolonged engagement, the data collection period was planned such that the data collection team (TN and the Research Assistant) had time for reflection with RE between field visits and were therefore able to conduct preliminary analyses that guided their subsequent data collection. Moreover, a member check technique was applied during key informant interviews and FGDs whereby the interviewer/ FGD moderator summarized the information from the respondent/ discussant to ensure that what was heard was in fact correct. Additionally, peer debriefing was done during data collection and analysis whereby TN and RE independently reviewed and coded the transcripts, shared the outputs, discussed the disparities to ensure that final themes were grounded in the data. Finally, the paper benefited from triangulation [28, 29], as data from multiple methods (interviews and FGDs and sources (health systems providers, community health workers, women and their spouses) were synthesized to develop a comprehensive understanding of the possible barriers to breast cancer awareness and early detection.

Results

The characteristics of study participants are shown in Table 3. The majority of the women and spouses (FGD participants) were aged 51–60 years old (48.6%), peasants (89.2%), had at least primary education (86.5%) and had a monthly income less than or equal to $50 (TZS 100,000) (78.4%). Other study participants (Key Informant interviewees) included 5 health systems managers (3 males and 2 females) at the district and health facility levels and 5 Community Health Workers (CHWs) (4 females and 1 male). On the education levels of the CHWs, 3 had primary level of education and only 2 had completed ordinary level secondary education.

Barriers to early detection of breast cancer among mid-life women

Nine main [analytical] themes describing barriers to early detection methods among mid-life women were identified across five socioecological levels of influence (see Table 4 - illustration of thematic analysis process).

Individual level factors

Limited knowledge about breast cancer and early detection. At the individual level, the majority of the women and their spouses indicated that they had heard of breast cancer. In

Table 3. Sociodemographic characteristics of the FGD participants.

Characteristics		Frequency (n = 74)	Percentage
Sex	Female	38	51.4
	Male	36	49.6
Age	40–50 years	28	37.8
	60 years	36	48.6
	> 60 years	10	13.5
Occupation	Peasant	66	89.2
	Small scale business	4	5.4
	Peasant and Pastoralist	1	1.4
	Government employee	1	1.4
	Artisan	1	1.4
	Pastor	1	1.4
Education	Never been to school	2	2.7
	Primary education but did not complete	2	2.7
	Primary education	64	86.5
	Secondary education but did not complete	3	4.1
	Secondary education—Form IV	3	4.1
Monthly Income	≤ 2TZS 100,000 (USD 50)	58	78.4
	> TZS 100,000 (USD 50)	16	21.6

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addition, some participants mentioned that they knew someone with or suspected of living with breast cancer who had a successful or unsuccessful story related to early or delayed treatment. As one woman noted:

> *People in the villages face many challenges but do not know how to overcome them. As women, our response is very positive because we do not want to suffer more consequences. Another thing is that, we just hear about breast cancer, a few days ago we heard that a student from Itumba Day [secondary school] had a painful breast that was bigger than the other. She is still getting treatment* (Woman, FGD participant, Itumba).

Many women attributed their awareness about breast cancer to a breast cancer awareness and screening campaign event that took place somewhat a while ago. In reference to the campaign, one woman stated, "*I learned about this disease when doctors from Dar es Salaam came to our district. It was a big campaign. We were informed about their presence at our district hospital. Many women went, they taught and examined us about breast cancer.*" (Woman, FGD participant, Isongole). This was also supported by one community health worker (CHW) who stated: "*More than five years ago, a group of experts came here. They were stationed at the District Hospital, and women from nearby villages went there for breast cancer investigations.*" (CHW, Isongole).

Despite reports on occasional breast cancer campaigns, all participants in the study admitted that limited knowledge was a major barrier to their uptake of breast cancer awareness and early detection strategies. As indicated by one of focus group discussion participants:

> *"We have no education. We do not know the causes of this disease [breast cancer] and its signs and symptoms. Consequently, it is difficult to practice preventive measures."* (Woman, FGD participant, Itumba).

Table 4. How analytical themes emerged.

Level	Selected quote/ text	Codes	Descriptive Themes	Analytical Themes	Overarching Theme
Individual Factors	People in the villages face a lot of challenges but don't know how to overcome them. As women, our response is very positive because we don't want to suffer more consequences. Another thing is that, we just hear about breast cancer, a few days ago we heard that a student from Itumba Day [secondary school] had one of her breasts that was bigger than the other. She is still getting treatment (Woman, FGD, Itumba).	Rural dwellers, A lot of challenges, Don't know how to overcome challenges, limited awareness about breast cancer, Just hear about breast cancer, Readiness of women, Suffer several social/ health problems Do not want suffer more consequences, Aware of women with breast problems	Rural women suffer from several social/ health problems Limited knowledge how to overcome challenges including breast cancer	Limited knowledge about breast cancer, including methods for early detection	Multi-level barriers to early detection of breast cancer among midlevel rural women in Tanzania
	"We have no education. We do not know the causes of this disease [breast cancer] and its signs and its symptoms. Consequently, it is difficult to practice preventive measures."	Do not have education about breast cancer, Do not know causes of breast cancer, Do not know signs of breast cancer, No practice of preventive measures	No knowledge about breast cancer Inability to practice measures for early detection of breast cancer		
Interpersonal Factors	*We have no education about this disease. We men are not involved when it comes to intervention targeting women's health problems. If we were knowledgeable we could have supported our spouses better, No man would want to see his spouse suffering*	Lack of knowledge about breast cancer Lack of men involvement Lack of knowledge constrains support Willingness of men to do something for the good of their wives' breast health.	Men lack knowledge about breast cancer Men are not involved in interventions *targeting women's health problems, including breast cancer*	Limited male partner support.	
Community Factors	*And our behavior, we Africans when we are not sick, we don't go to the hospital. That I just leave home, I am physically fit and I decide to leave in the morning and go to the hospital and say "let them examine me" aah I have never seen anyone do that aah I have never seen.*	Behavioral, Africans, Do not go to hospital, Unlikely to leave home when apparently okay.	Seeking medical checkup is a behavioral issue It is not African culture African women are unlikely to bother themselves with seeking medical checkup when apparently okay	Procrastination	
Institutional factors	The screening services we have are for cervical cancer, not breast cancer. For cervical cancer, we conduct outreach programs. However, when a woman presents with a complaint about her breast (s) she is attended to accordingly.	Screening services for cervical cancer No screening services for breast cancer Outreach program for cervical cancer Complaint about a problem in the breast Services rendered as per the complaints presented	There are no routine screening services for breast cancer There is no outreach program for breast cancer Services for breast health are curative	Limited availability of breast cancer screening services and resources Predominance of curative care at the expense of preventive care	
Societal Factors	*Life is difficult. It is not easy for a poor woman to spend money on healthcare when she does not feel endangered. She does not go to hospital for routine checkup and our economy is contributing to this fate. When you see you just feel okay, you eat, you are safe, you can't go. You just say God thank you. Because our rural economy is in shambles, deciding that I should be going for breast health checkup might be considered unnecessary expenditure.*	Life hardship, Poverty among women, Poor economic status *Unlikely to spend money for disease prevention on healthcare when she does not feel endangered* *Economic implications of breast checkup.*	Life hardship is a deterrent to practicing disease prevention A poor woman is *unlikely to spend money for breast cancer screening when she does not feel endangered*	Poverty	

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CHWs and health care providers also presented lack of knowledge as a barrier. As one CHW puts it: *"lack of knowledge about breast cancer is a challenge. Most women are not aware of what they need to do to avoid breast cancer." (CHW, Itumba)*. In terms of breast self-examination, the majority of women indicated a lack of knowledge and self-efficacy to complete the procedure: One FDG participant indicated: *"Most of us do not know and do not do breast self-examination. It could happen by chance when taking bath, one may notice something unusual in the breast; but deliberate attempts to do breast self-examination are almost nonexistent" (Woman, FGD participant, Isongole)*. Nevertheless, women knew that, if they noticed a change in their breasts, they should go to the hospital for further checkup and not to a traditional healer. Very few women and men were aware of mammography and its role in early diagnosis. Likewise, very few knew about clinical breast examination.

Witchcraft beliefs. Whereas the health care providers stressed the importance of early treatment in breast cancer control, beliefs such as witchcraft seemed to get in the way for some women, as expressed by one health care provider:

> *According to my knowledge, I only know about three people who suffer from cancer in this village. After asking them, some of them associated it with superstitious belief but since we are experts, we knew that it was not caused by superstition so if they would have been educated, they would be treated in the health facility*. (CHW, Isongole).

Interpersonal level factors

Limited male partner support. It was reported that support of the male partner in facilitating early diagnosis of breast cancer is limited, partly due to lack of knowledge about the disease. Male FGD participants attributed minimal knowledge to limited involvement of men in health campaigns. They cited an example of a breast health campaign that was carried about 5 or 7 years ago, [no one could remember the exact year]. One of the male FDG participant commented: *"We have no education about this disease. We men are not involved when it comes to intervention targeting women's health problems. If we were knowledgeable, we could have supported our spouses better. No man would want to see his spouse suffer." (Male FGD participant, Isongole)*.

Community level factors

Age and gender norms. While most women stated that they had no preference regarding the gender of the CHW who would conduct their screening, some participants indicated a potential concern, especially with male and younger CHW. For instance, one male FDG participant shared the concern as follows:

> *"It will be much easier for a female CHW especially if a woman is elderly. She might be an elderly woman aged 50. If a woman in her 50's comes to me, she will not be comfortable but a woman with a woman/grandmother it is okay. She will feel shy when I ask her to undress so that I can examine her breast. The same applies to me if I go to the hospital and find a young lady asking me to take off my clothes, I won't be comfortable. If you find a person of the same gender like yours, it is okay. There should be two genders so that if a person is not comfortable, they can just switch." (Male FGD participant, Itumba)*

Procrastination. Procrastination of health screening was a major factor that hindered breast cancer screenings for participants. Female participants cited that women in the village did not have a culture of routine check-up, they did not need to see a doctor if they are not

sick. That one would only go to a health facility when she feels unwell. One participant attributed this to low self-esteem (poor sense of self-value) as she said:

> *We women have tendency of saying to ourselves I am apparently healthy why get bothered. We ignore going to health facility for a check up before experiencing sign of disease. So the constraint I am seeing is low self-esteem. This is what torments us, we women we lookdown upon ourselves. (Female FGD participant, Itumba)*

This was corroborated by male respondents who also pointed out that not accessing clinical breast exams is a cultural issue, that people in Africa seek healthcare when they are troubled. Likewise, "apparently healthy" African women are less likely to go to the health facility for breast check-up when there is no obvious outward swelling and there is no pain whatsoever. One FGD participant thus said:

> *"And our behavior, we Africans when we are not sick, we don't go to the hospital. That I just leave home, I am physically fit and I decide to leave in the morning and go to the hospital and say "let them examine me" aah I have never seen anyone do that aah I have never seen." (Male FGD participant, Isongole).*

This corroborated by another participant who asserted that Africans tend to neglect signs especially when the have low knowledge about the impending consequences:

> *"I think it is lack of awareness, it is common for Africans not to take things seriously so whenever you see any sign you take it as a part of life. So, when the majority find something unusual, they take no action. They cannot do breast self-examination of the breast for something they do not know, even if has its negative effects. Only a few of them will see something unusual and seek medical attention. For the majority, one may ask herself 'why do I feel something hard in my breast during bath' but if she gets used to it, she will take it as normal." (Male FGD participant, Isongole).*

Institutional level factors

Limited availability of breast health services and resources. FGD participants pointed out that they were aware of services for cervical screening at the district hospital, but not for breast cancer. This was confirmed by health system managers who admitted that educational and diagnostic services for breast cancer were limited. That the district did not have an organized way of delivering information about breast cancer. During this study, the district had a specific program for early detection of cervical cancer, which did little or nothing about breast cancer. As described by one of the key informants at the district level:

> *"The screening services we have are for cervical cancer, not breast cancer. For cervical cancer, we conduct outreach programs. However, when a woman presents with a complaint about her breast(s) she is attended to accordingly."* (Health System Manager, Itumba).

Moreover, the district health management confirmed that the district did not have mammography screening services, adding that such services can only be found at the National Hospital in Dar es Salaam, about a thousand kilometers away.

Predominance of curative care at the expense of preventive care. The managers of health facilities in the study area admitted that they were not aware of existence of the *National*

Guidelines for Early Diagnosis of Breast Cancer and Referral for Treatment [14]. Moreover, there were reports on low priority to women's breast cancer in the community, which constitutes a hinderance to breast cancer control at the dispensary and community levels. Although it is known that early detection of breast cancer saves lives, it was gathered that efforts towards that direction are minimal. All managers of health facilities admitted that they did not have the current *National Guidelines for Early Diagnosis of Breast Cancer and Referral for Treatment* [14] for breast cancer care. They further admitted that breast healthcare at the health facilities within the district is mainly curative, that there is no routine breast checkup for early detection of breast cancer. One of the managers succinctly commented:

> *"We handle patients as per the complaints they come up with. If she does not report about abnormality in the breast, we do not examine it."* (Dispensary In-charge)

Besides, both women and men who participated in this study reported that the health system does not encourage people to engage in preventive practices against breast cancer. One CHW cited that: "*We have heard from media that breast cancer exists, but people are not encouraged/interested to go for breast cancer examination." (CHW, Isongole).*

Societal level factors

Poverty: Despair due to inability to pay. It was reported by both male and female FGD participants that women do not access clinical breast examination (CBE) because of despair associated with inability to pay. It is known that health services are not free and, because most women in the rural settings are poor, health checkup including CBE is not prioritized. The respondents argued that because of financial hardship women and most community members decide to seek healthcare and spend their meagre income when they fall sick:

> *"Life is difficult. It is not easy for a poor woman to spend money on healthcare when she does not feel endangered. She does not go to hospital for routine checkup and our economy is contributing to this fate. When you see you just feel okay, you eat, you are safe, you can't go. You just say God thank you. Because our rural economy is in shambles, deciding that I should be going for breast health checkup might be considered unnecessary expenditure." (Male FGD participant, Isongole).*

Limited health insurance scheme. It was reported by both male and female FGD participants that health insurance in the rural settings is failing to meet people's expectations of accessing "free" services, thereby demotivating them from seeking healthcare including breast health checkup. Some participants argued that there is a mismatch between what people are told when they are being incentivized to become members of the Community Health Fund (CHF) and what they actually experience when they become members. They are told that if they enroll in the CHF, they would not incur extra costs when they fall sick. To the contrary, after they enroll, they realize the CHF does not cover all their health care needs. For instance, the respondents expressed their disappointment on out of stock prescriptions in the district hospital that they had to buy from private pharmacies. As one, the FGD participants stated:

> *"It is true that people were very motivated to pay for insurance but even if you have insurance, you will often not get all the prescribed medicines. You get some and they tell you others are out of stock, you have to go and buy from the private pharmacy. The problem that I have seen is that when medicines are prescribed if they are 5, you will be given 2 and the rest you will be*

told to go and buy; and they even show you the shop/pharmacy. All these happen despite having health insurance." (Male FGD participant, Isongole).

Discussion

Overall, the study findings provide a better understanding of individual-level determinants for knowledge deficits about breast cancer awareness and early detection within a broader environmental context. For example, at the individual level, the findings on low risk perception about breast cancer align with previous studies conducted in the region [30], suggesting the importance to raise awareness regarding the risk and protective factors for breast cancer among women, especially in communities with low level of educational achievement, as evidenced by the majority of FGD participants (86.5%) in this study who had primary level of education. At the interpersonal level, the findings are corroborated by similar studies in other countries such as Ghana [31] and Saudi Arabia [32] on the importance of male partners' [spouses'] involvement. Moreover, the participant's culture of complacency on routine checkup seemed to be attributed to community level and institutional/systems/organization-level breast cancer-related health-seeking behaviors such as: 1) sheer negligence, 2) women's low risk perception due to limited or lack of knowledge and 3) nurturance by a less responsive health system characterized by long waiting times and payment requirements. This finding is consistent with findings conducted in Wakiso, Uganda [33].

Other determinants at the institutional level include the lack of educational services, routine clinical breast examination and continued access to a predominantly curative health care system. These factors have also been reported elsewhere by Philipo et al. [6]. The limited availability of institutional-based services for early diagnosis of breast cancer might be attributed to the delays in implementation of the recently approved *National Guidelines for Early Diagnosis of Breast Cancer and Referral for Treatment* [14]. Chao et al. [2] have reported comparable findings in the Northern region of Tanzania. At the societal/policy level, despair associated with inability to pay was identified as a factor that influenced the uptake of clinic-based clinical breast examination. This finding has also been reported in other studies in 15 low-income countries (Chad, Mali, Congo, Comoros, Laos, Zimbabwe, Burkina Faso, Nepal, Mauritania, Myanmar, Ghana, Kenya, Malawi, Ethiopia and Bangladesh) [34, 35]. Moreover, the health insurance schemes, such as iCHF and NHIF, in Tanzania, that take a curative approach in their coverage of expenses related to management of non-communicable diseases including breast cancer [34], continue to imply challenges related to preventive health care financing. [36, 37].

Limitations

First, the scope was limited to mid-life rural women, and second, the nature of the purposive sampling approach may provide missed opportunities for inclusive perspectives from community members and health care providers. Nonetheless, this is the first study that we are aware of that has collected and triangulated data from women and their spouses as well as health care providers to understand the multilevel barriers and facilitators of breast cancer awareness and early screening prior to the development of a multilevel intervention in the region.

Generalizability

This being a qualitative study, its goal was not to generalize but rather to provide a rich, contextualized understanding of barriers to early detection of breast cancer. Nevertheless, in the qualitative perspective, the study has achieved both analytic generazability and transferability

(reader generalizability) [38]. Regarding analytic generalizability, the authors developed conceptualizations of mid-life women's experiences through in-depth scrutiny and higher-order abstraction into themes. Moreover, on transferability, they have provided detailed descriptions that will allow readers to make inferences about applying the findings to other similar populations and settings.

Conclusion

This study has explored multi-level barriers to early detection of breast cancer among midlife women in Tanzania. They include: limited knowledge about breast cancer and early detection; witchcraft beliefs; limited male partner support; procrastination; limited availability of breast health services and resources; predominance of curative care at the expense of preventive care; despair due to inability to pay (poverty); and limited health insurance scheme. These study findings contribute to the accumulated exciting empirical support for the need to further the design, implementation and evaluation of evidence-based community breast health awareness and education interventions to promote early detection of breast cancer. Specifically, the study highlights the need to address the identified multiple level determinants of influence as part of the country's community health measures to mitigate the prevalence of delayed presentation of breast cancer among women in rural settings.

Supporting information

S1 Appendix. FGD guide.
(DOCX)

S2 Appendix. FGD transcript.
(DOCX)

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Management of insulin-dependent diabetes in low-resource countries: results from the chronic noncommunicable disease project in Iringa rural district of Tanzania

PAPER

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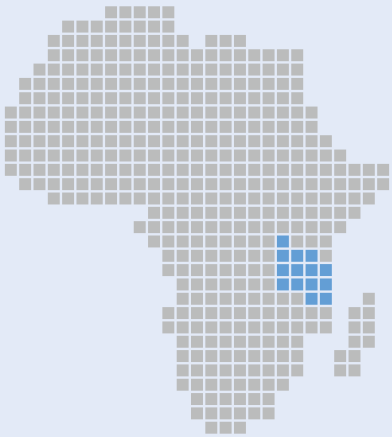

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Management of insulin-dependent diabetes in low-resource countries: results from the chronic non-communicable disease project in Iringa rural district of Tanzania

Gestione del diabete insulino-dipendente nei paesi a risorse limitate: risultati del progetto sulle malattie croniche non trasmissibili nel distretto rurale di Iringa in Tanzania

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Abstract

PURPOSE OF THE STUDY Chronic non-communicable diseases are experiencing a major growth in disease burden, especially in low-resource countries. Among them, diabetes represents a major challenge: its prevalence is growing exponentially in Africa, where scarcity of accessibility to care and resources make the issue even more burdensome. Insulin therapy in particular is very expensive and unwieldy. The aim of the study is to find answers to the emerging needs of people with diabetes in these settings

DESIGN AND METHODS A retrospective, prospective observational study of the diabetic population undergoing Premixed regular insulin/NPH 30/70 insulin treatment was carried out as part of CUAMM's chronic non-communicable diseases project in Tosamaganga Hospital in a rural area of Tanzania, a low- to middle-income country in sub-Saharan Africa. Data were extrapolated from the project database and from interviews with patients on active insulin treatment from March to August 2023.

RESULTS Improvement in blood glucose, glycated haemoglobin, and weight values over time; a reduction in the number of hospitalizations; a marked improvement in performance status; and a low rate of major hypoglycaemias were found. 83.1% of patients do not have health insurance, most have financial difficulties to support the cost of transportation to visit; counselling received on therapy and lifestyle is found to be very helpful and effective.

CONCLUSION Premixed regular insulin/NPH 30/70 insulin is effective and safe. Its low cost and increased manageability make its use desirable in low-resource countries due to issues of compliance and affordability. Increasing access to care and fostering qualified personnel is important to improve diabetes care in low-resource countries.

KEYWORDS low-resource countries; non-communicable disease; diabetes mellitus; insulin Premixed regular insulin/NPH 30/70.

Riassunto

INTRODUZIONE Le malattie croniche non trasmissibili stanno vivendo una importante crescita del carico di malattia, soprattutto nei paesi a basso e medio-basso reddito. Tra di esse il diabete rappresenta un'importante sfida: la prevalenza è in crescita esponenziale in Africa, dove scarsità di accessibilità alle cure e di risorse rendono la problematica ancor più gravosa. La terapia insulinica in particolare è molto costosa e poco maneggevole. L'obiettivo dello studio è quello di trovare risposte ai bisogni emergenti della popolazione diabetica in questi contesti.

MATERIALI E METODI È stato effettuato uno studio osservazionale retrospettivo e prospettico della popolazione diabetica in trattamento con insulina umana mista regolare/intermedia 30/70, nell'ambito del progetto *chronic non-communicable diseases* del CUAMM nell'ospedale di Tosamaganga in un'area rurale della Tanzania, paese a medio-basso reddito dell'Africa subsahariana. I dati sono stati estrapolati dal database del progetto e da interviste ai pazienti in trattamento insulinico attivo da marzo a agosto 2023.

RISULTATI Sono stati riscontrati un miglioramento dei valori di glicemia, emoglobina glicata e peso nel tempo; una riduzione del numero di ricoveri, un netto miglioramento del performance status e un basso tasso di ipoglicemie maggiori. L'83.1% dei pazienti non possiede una assicurazione sanitaria, la maggior parte ha difficoltà economiche a supportare i costi del trasporto per recarsi a visita; il counseling ricevuto su terapia e stile di vita è ritenuto molto utile ed efficace.

CONCLUSIONE L'insulina umana mista regolare/intermedia 30/70 è efficace e sicura. Il basso costo e la maggiore maneggevolezza ne rende auspicabile l'utilizzo nei paesi a basse risorse per questioni di compliance e disponibilità economiche. Incrementare l'accesso alle cure e favorire personale qualificato è importante per migliorare la cura del diabete in paesi a basse risorse.

PAROLE CHIAVE paesi a risorse limitate; malattie croniche non trasmissibili; diabete mellito; insulina umana mista regolare/intermedia 30/70.

Introduction and purpose of the study

Chronic non-communicable diseases (NCDs) are a serious public health issue worldwide: each year about 41 million deaths worldwide, accounting for 74% of global deaths, are caused by NCDs[1]. The number of deaths and the overall disease burden from these diseases has been steadily increasing since 1990[2–4]. Low-resource countries (low-and low-middle-income countries) have experienced a reduction in deaths from infectious and maternal-infant causes in recent decades, while experiencing a consistent growth in the burden of disease and deaths resulting from NCDs, thus representing a particular public health concern[3,5]. Among the NCDs, diabetes is the disease with the largest growth in disease burden, exceeding 80%[3,4,6]. It is widely prevalent in the global population with a prevalence of 10.5% among adults and about 1.2 million young people up to 19 years of age affected[7]. Prevalence is estimated to continue to rise globally, with the African continent experiencing the greatest increase. Africa also has the largest proportion of unaware, undiagnosed diabetics, and the issue of data collection and retrieval, especially regarding type 1 diabetes, is a huge problem[8]. In sub-Saharan Africa, as in all low-resource countries, poor health care infrastructure and accessibility to it, poor availability of means for diabetes diagnosis and monitoring, difficult availability of medications, shortage of trained health care workers, and poor education and disease awareness, all make diabetes management and treatment a major challenge in these countries; the challenge is even greater in rural areas where the poorest people live. Overall, barely 11% of diabetic patients in sub-Saharan Africa, receive the medicines they need for treatment[9]. In this landscape, insulin therapy deserves special mention, as the costs of the drug are very high and difficult to abate, due to the worldwide monopoly by three pharmaceutical companies[10]; the price of insulin analogues is significantly higher than human insulin in all sec-

tors both public and private[11]; sticks, lancets, and glucometers are needed for frequent blood glucose monitoring in addition to needles and syringes for drug injection; resources are needed to cope with complications and therapy of type 1 diabetes (hypoglycemia, diabetic ketoacidosis), so costs multiply. Finally, it turns out that self-administration of insulin is not easy, especially for uneducated people[9].

In Tosamaganga Hospital, in the rural area of Iringa district in Tanzania, the Non-Governative-Organization Doctors with Africa CUAMM, has launched a project dedicated to NCDs, in collaboration with local authorities. Tanzania is a low-middle-income sub-Saharan African country with a pyramidal and predominantly private health care system and very few health care providers[12,13]. It represents the first African country by prevalence of diabetes in adults[7]. Overall, it is estimated that just 6% of Tanzanians diagnosed with diabetes are properly treated and have controlled blood glucose values; moreover, accessibility to care is lower in rural areas than in urban areas, which represent a minority in Tanzania[14]. The CUAMM NCDs clinic is the only clinic located in a rural area throughout Tanzania, seeking to address this health issue where care is most lacking. Special attention is given to diabetic patients on insulin therapy, to whom a special day called "Insulin Day" is dedicated. It is held every 50 days: patients are educated about diabetes, insulin management, and receive the necessary therapy and tools for glycemic monitoring free of charge. The insulin administered is Premixed regular insulin/NPH 30/70 insulin, consisting entirely of human insulin in a ratio of 30/70 regular insulin/insulin intermediate neutral protamine hagedorn (NPH)[15].

Our study stems from the need to overcome critical issues related to the care of diabetic patients who need insulin in a rural setting of low- and low-middle-income countries. The endpoints are to describe the diabetic population in the rural district of Iringa in Tanzania and to evaluate the impact of the proposed management model on the health of patients undergoing treatment.

Materials and methods

An observational study was carried out. Two groups of patients were identified: group 1 consisting of patients who had taken insulin at least once and systematically entered into the management database of the CUAMM NCDs project from February 2019 to August 2023; group 2 consisting of patients on active follow-up and in insulin therapy during the period from March to August 2023. For the first group, data were retrospectively extrapolated from the database, obtaining information on anagraphic data, type of diabetes, nutritional status (expressed by body mass index - BMI), socioeconomic status and accessibility to the care (identified through possession of health insurance and type of work and peripheral health centre of origin), and glycemic control (through fasting blood glucose, glycated haemoglobin - HbA1c - values). Patients in Group 2 were interviewed on targeted topics, through which data were obtained on: anagraphic data, diabetes and related social issues, socioeconomic status and education, accessibility to care, ability to manage insulin therapy, adherence to treatment, relevance of NCDs clinic, number of hospitalizations for any cause (except childbirth and trauma), episodes of major and minor hypoglycemia and reported ability to work. Statistical analysis was performed using Epiinfo 7 and Excel 2007 programs.

Results

General features of the study population

Group 1

Since the project began, out of a total of 2020 patients attending the outpatient clinic, 59 patients have been recorded to have taken insulin at least once (2.9%). Of these, 50.9% were females and 49.1% were males **(Table 1)**. Considering only the diabetic population (521 patients), the number of patients on insulin therapy represents a minority (11.3%) and they are predominantly young: all but 22 are younger than 40 years old; among them, 17 are under 25 years of age. The proportion of patients with type 1 and type 2 diabetes is similar (47.5% and 45.8%, respectively), of the 6.7% no classification was made. Predominantly patients are normal weight (49.1%), however a large proportion are underweight (20.3%) and as many patients are overweight or obese (10.2% respectively) **(Table 1)**.

Considering the type of diabetes stratified by age and BMI, no patients younger than 25 years of age were classified as having type 2 diabetes, while patients over 40 years old were mainly classified as type 2 diabetes except one patient, considered type 1, and three patients unassigned. Two patients who were underweight at the first visit were

classified as having type 2 diabetes, and virtually all overweight or obese patients were classified as type 2 **(Table 1)**. Among patients aged 25-40 years, 45% (9 of 20) were classified as having type 2 diabetes; only two were obese at the first visit and one underweight, the others were normal weight. Of these, 66.7% had a BMI at the lower limits of normal weight (BMI<21).

Regarding socio-health indexes and accessibility of care 45.8% of patients are farmers, 8 patients (13.6%) are students; 83.1% of patients do not have health insurance. Moreover, 64.4% of patients are from the Tosamaganga area, which is the area strictly surrounding the hospital **(Table 1)**. On average, the distance travelled by patients to reach Tosamaganga is 42.9 km and the most frequently travelled distance is 27 km (median).

At the first visit, fasting blood glucose values averaged 15.7 mmol/L (282.6 mg/dL) and glycated haemoglobin values averaged 11.9%. Blood pressure values are within normal range. The main chronic complication of diabetes objectifiable at the time of the first visit is chronic renal failure. Very common is the issue of decreased visual acuity, reported by 27 patients (45.9% of the tested population) **(Table 1)**. However, the nature and extent of this disorder could not be determined due to lack of diagnostic means and specialised personnel.

Group 2

The second group consists of 33 patients in active follow-up from March to August 2023, interviewed during insulin days. The patients are 54.5% male and the majority are between the ages of 15 and 40 years. 39.4% of patients report disease onset at less than 25 years of age and only 24.2% above 40 years of age. Mainly patients are normal weight (54.4%), a high percentage are underweight (21.2%) the rest are overweight (12.1%) and to a lesser extent obese (9.1%). Patients were mostly classified as type 2 diabetes (48%) and to a lesser extent as type 1 (45%) however 6% were not assigned. All patients with age at diagnosis less than 25 years were classified as having type 1 diabetes, all patients with age at diagnosis greater than 40 years were framed as having type 2 diabetes **(Table 2)**. Among patients aged 25-40 years, 66.7% (n=8) were classified as having type 2; only one had an obese condition at the time of the first visit, one was underweighted and the others were normal weight; however, among normal weight, half had a BMI at the lower limits (BMI 19-20).

Almost all patients had at least one hospitalization due to diabetes (87.9%). Although 90.9% of patients are able to read, most attended only first-grade schools, defined as "Standard 1-7" (51.5%); only two people attended college or university. Most patients work as farmers (54.5%) while 15.2% have no occupation at all;

Table 1 | General features of Group 1 patients.

GROUP 1	Total patients (n=59)	Diabetes type 1 (n=28)	Diabetes type 2 (n=27)
Age			
- <15	- 3 (5.1%)	- 3 (10.7%)	- 0 (0)
- 15-24	- 14 (23.7%)	- 14 (50%)	- 0 (0)
- 25-40	- 20 (33.9%)	- 10 (35.7%)	- 9 (33.3%)
- >40	- 22 (37.3%)	- 1 (3.6%)	- 18 (66.7%)
Sex			
- Female	- 30 (50.9%)	-	-
- Male	- 29 (49.1%)	-	-
BMI			
- <18	- 12 (20.3%)	- 9 (32.1%)	- 2 (7.4%)
- 18-24	- 29 (49.1%)	- 14 (50%)	- 14 (51.8%)
- 25-29	- 6 (10.2%)	- 1 (3.6%)	- 4 (14.8%)
- ≥30	- 6 (10.2%)	- 0 (0%)	- 5 (18.5%)
- Not known	- 6 (10.2%)	- 4 (14.3%)	- 2 (7.4%)
Diabetes			
- Type1	- 28 (47.5%)	-	-
- Type2	- 27 (45.8%)	-	-
- Unspecified	- 4 (6.7%)	-	-
Farmer			
- Yes	- 27 (45.8%)	-	-
- No	- 30 (50.8%)	-	-
- Unspecified	- 2 (3.4%)	-	-
Health insurance			
- Yes	- 10 (16.9%)	- 3 (10.7%)	- 6 (22.2%)
- No	- 49 (83.1%)	- 25 (89.3%)	- 21 (77.8%)
Health center of origin			
- Idodi	- 1 (1.7%)	-	-
- Ifunda	- 3 (5.1%)	-	-
- Isimani	- 2 (3.4%)	-	-
- Kimande	- 1 (1.7%)	-	-
- Kiponzelo	- 3 (5.1%)	-	-
- Mgama	- 3 (5.1%)	-	-
- Mlowa	- 2 (3.4%)	-	-
- Nzihi	- 4 (6.8%)	-	-
- Tosamaganga	- 38 (64.4%)	-	-
- Wenda	- 2 (3.4%)	-	-
Complications			
- Previous stroke	- 1 (1.7%)	-	-
- Previous AMI	- 0 (0%)	-	-
- Chronic heart failure	- 2 (3.4%)	-	-
- Diabetic foot	- 2 (3.4%)	-	-
- Lower limb amputation	- 1 (1.7%)	-	-
- CKD stage > IIIa	- 7 (11.9%)	-	-
- Visual impairment	- 27 (45.9%)	-	-

BMI = Body Mass Index; AMI = Acute Myocardial Infarction; CKD = Chronic Kidney Disease.

Table 2 | General features of Group 2 patients.

Group 2			
Total patients (n=33)		**Total patients (n=33)**	
Age		Socio-economic conditions	
- <15	- 1 (3%)	- Farmer	- 18 (54.5%)
- 15-24	- 12 (36.4%)	- No occupation	- 5 (15.2%)
- 25-40	- 12 (36.4%)	- No source of income in the household	- 3 (9.1%)
- >40	- 8 (24.2%)	- 1 source of income in the household	- 17 (51.5%)
Sex		- > 1 source of income in the household	- 13 (39.4%)
- Female	- 15 (45.5%)	- Health insurance	- 5 (15.2%)
- Male	- 18 (54.5%)	- Difficulty in supporting transportation costs to travel to checkup	- 22 (66.7%)
BMI		Accessibility to care	
- <18	- 7 (21.1%)	- Time to visit < 1 hour	- 3 (9.1%)
- 18-24	- 18 (54.5%)	- Reaching the outpatient clinic on foot	- 1 (3%)
- 25-29	- 4 (12.1%)	- Reaching the outpatient clinic by public transportation	- 26 (78.8%)
- ≥30	- 3 (9.1%)	- No logistical difficulties in transportation	- 4 (12.1%)
- Not known	- 1 (3%)	- Presence of other points of care near one's home	- 13 (39.4%)
Diabetes		Therapy issues	
- Type1	- 15 (45%)	- Consultation of a traditional healer	- 9 (27.3%)
- Type2	- 16 (48%)	- No help with therapy	- 16 (48.5%)
- Unspecified type	- 2 (6%)	- Help in handling insulin and/or managing nutrition	- 17 (51.5%)
- Mean age at diagnosis	- 32	- Perception of stress or fear in injecting insulin	- 2 (6.1%)
- Perception of good health at diagnosis	- 1 (3%)	- Sense of shame in injecting insulin in front of other people	- 4 (12.1%)
- Familiarity for diabetes	- 11 (33.3%)	- Storage of insulin in the refrigerator	- 9 (27.3%)
- ≥ 1 hospitalization for diabetes	- 29 (87.9%)	- Injecting insulin changes lifestyle habits	- 13 (39.4%)
- ≥ 1hospitalization for diabetes after diagnosis	- 26 (72.7%)	Treatment adherence	
- No oral hypoglycemic drugs before starting insulin	- 11 (33.3%)	- Failure to inject insulin >5 times in the past month	- 13 (39.4%)
- Perception of stigma because of diabetes	- 12 (36.4%)	- Failure to inject insulin due to hypoglycemia	- 19 (57.6%)
Awareness of illness		- Consumption of rice ≥ 2 times per week	- 1 (3%)
- Knowledge of diabetes before diagnosis	- 10 (30.3%)	- Consumption of whole-grain ugali	- 29 (87.9%)
- Full knowledge of the need for treatment and complications	- 11 (33.3%)	- Quantity of vegetables eaten per meal greater than the amount of ugali	- 22 (66.7%)
Comorbidities		- Consumption of whole grain bread or oatmeal for breakfast	- 27 (81.8%)
- No	- 22 (66.7%)	- Consumption of corn > 1 time per week	- 3 (9.1%)
- Hypertension	- 3 (9.1%)	- No alcohol consumption	- 29 (87.9%)
- HIV	- 2 (6.1%)	- No consumption of soda	- 30 (90.1%)
- Other	- 5 (15.2%)	- No physical activity	- 0 (0%)
- Hepatic steatosis	- 6 (18.2%)	- Physical activity 1-2 times per week	- 9 (27.3%)
- Vaccinated for HBV	- 1 (3%)	- Physical activity ≥ 3 times per week	- 23 (69.7%)
Education		- Time devoted to physical activity each session ≥ 1 hour	- 14 (42.4%)
- Ability to read	- 30 (90.9%)	- Time devoted to physical activity each session 30 minutes	- 18 (54.5%)
- Did not go to school	- 1 (3%)	Relevance of the NCDs outpatient clinic	
- Standard 1-7	- 17 (51.6%)	- No possibility of treatment in the absence of the NCDs clinic.	- 27 (81.8%)
- Basic vocational	- 1 (3%)	- People previously in care elsewhere	- 12 (36.4%)
- Forms 1-4	- 12 (36.4%)	- Counselling about diet carried out in the NCDs clinic is very helpful	- 33 (100%)
- College/University	- 2 (6.1%)		
Living conditions			
- Inhabitants with > 5 people	- 10 (30.3%)		
- Inhabitants with 2-5 people	- 22 (66.7%)		
- Electrical connection	- 16 (48.5%)		
- Mud and/or sheet metal houses	- 12 (36.4%)		

BMI = Body Mass Index; HIV = Human immunodeficiency virus; HBV = Hepatitis B virus; NCDs = chronic non-communicable diseases.

most families have only one source of income (51.5%) and 3 patients live in families with no income. Only 5 people (15.2%) possess health insurance **(Table 2)**.

Fewer than half of the patients (39.4%) have an alternative facility available to the NCDs at Tosamaganga Hospital that is capable of delivering

care and is in close proximity to their homes. Only 9.1% of patients take less than an hour to reach the NCDs clinic, most (60.6%) take between one and two hours. Moreover, 78.8% reach the hospital by using public transportation, and 66.7% find it difficult to support the cost of transportation to go for follow-up visits. Only 4 people (12.1%) reported no logistical difficulties in transportation (Table 2), where the main problems are instead, in order of frequency, poor roads, rain, and low availability of public transportation.

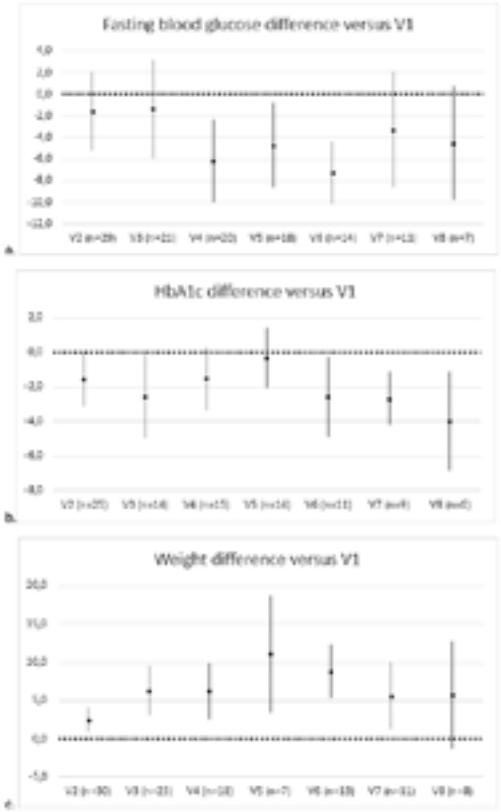
For 39.4% of patients, the beginning of insulin therapy resulted in a change in lifestyle habits: 12.1% experience shame in injecting insulin in front of other people; 51.5% are helped in the management of therapy; the support basically consists of handling insulin and/or following a proper diet. Among patients who receive support, 29.4% receive it relative to insulin, 29.4% receive it with feeding, and 41.2% receive it with both. Only a minority of patients, 27.3%, have the ability to properly store insulin in the refrigerator (Table 2).

In addition, 39.4% of patients in the month prior to the interview skipped insulin injection more than 5 times, 46.4% skipped it a maximum of 5 times; 24.2% always administered insulin; 76% of those who did not administer insulin report glycemic values below 5 mmol/L or presence of symptoms of hypoglycaemia as reasons (Table 2). It was observed that 69.2% (9/13) of those who missed injection more than 5 times in the month had a maximum education level up to "Standard 1-7" grades, namely a low level of schooling.

Nearly all patients (89.7%) consume whole-wheat ugali (local flour polenta) almost every day, preferring this lower glycemic index carbohydrate to non-whole-wheat ugali; for 66.7% of patients, the amount of vegetables consumed each day is greater than that of ugali. Furthermore, 87.9% of patients deny consuming alcohol and 90.1% deny consuming sodas. All patients engage in regular physical activity at least once a week for at least 30 minutes a day, while 69.7% practice it at least three times a week and 42.4% at least one hour per session (Table 2).

Nearly all patients (81.8%) stated that they would have no way of treatment at the present time in the absence of the NCDs clinic. The counselling carried out by the experienced nursing and nutritionist staff of the outpatient clinic regarding nutrition and diet to be followed is considered very helpful by all patients.

Figure 1 | Trends of fasting blood glucose (a), glycated haemoglobin (b) and weight over time (c).



V = visit; HbA1c = glycated haemoglobin.

Clinical outcomes

Group 1

Looking at the trend in fasting blood glucose and HbA1c over time (Figure 1a and 1b), there is an improving trend between the first visit (V1) and the subsequent six-monthly checkups. There is a significant average decrease of up to 7.3 mmol/L (131.5 mg/dL) in blood glucose and up to 2.6 percentage points in HbA1c after two and a half years (V6) of treatment in the NCDs clinic. Significant weight gain is observed for all patients as early as the six-month follow-up, which is maintained at subsequent visits with significant average weight gain up to 8.8 kg after two and a half years (V6) from the first visit (Figure 1c).

Group 2

Hospitalizations: following enrolment in the project, the number of hospitalizations per patient for any cause dropped dramatically. Out of 33 people surveyed, 28 reported that they had gone through at least one hospitalization before starting treatment in Tosamaganga; of these, 82.1% did not undergo further hospitalizations thereafter (Figure 2).

Major hypoglycemia: 78.8% of patients presented no episodes in the month prior to the interview, 15.2% experienced one or two episodes (Figure 2).

Minor hypoglycemia: 72.2% of patients experienced at least one minor hypoglycemia in the month prior to the interview. Most frequently, there were three hypoglycemic episodes per patient. Mainly hypoglycemia occurred in the morning (58.3%) and only 12.5% occurred in the evening (Figure 2). Among those with a lower level of education (not going to school, "standard 1-7" schools or "basic vocational" schools), the number of observed hypoglycemic episodes tended to be 3 times higher than among those with a higher level of education (from "forms 1-4" schools to college).

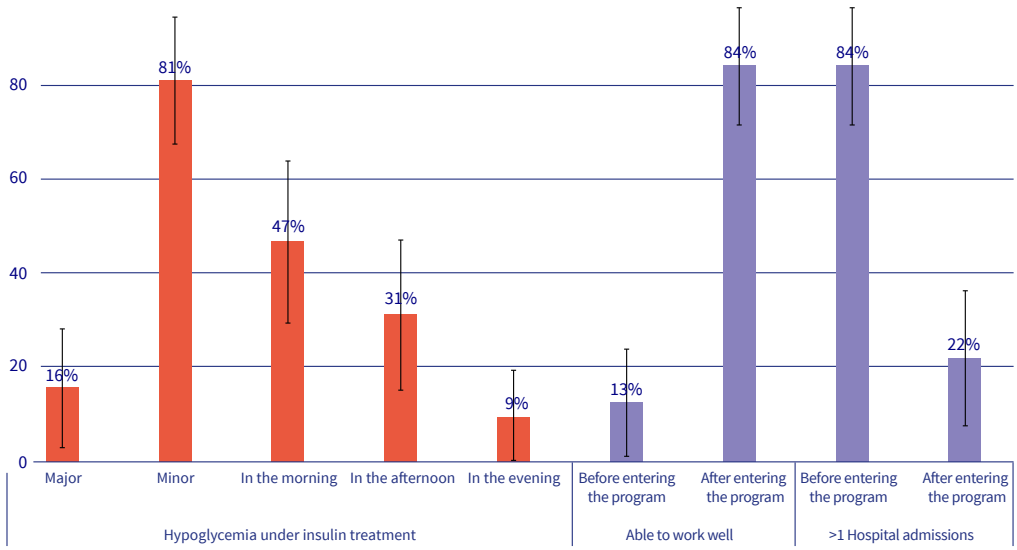
Working capacity: out of 33 patients surveyed, 32 are working or studying; among the latter, 87.5% reported difficulty in performing their daily work or study activities before the start of insulin therapy. Specifically, 34.4% continued to work with reduced performance, while 53.1% had to stop their activities completely due to the disease. All but one of the patients resumed or perform better in their activities subsequent to taking assignment from the NCDs clinic (Figure 2).

Discussion

In low-resource countries with low or low-middle income, diabetes management presents a daunting challenge. A large proportion of the population is poor and lives in rural areas far from health facilities, which are poorly represented on the ground and often lack the tools and drugs needed to manage the disease; they also lack health personnel with adequate diabetes training. The difficulties are even greater for the management of insulin therapy, which is considerably expensive, unavailable and difficult to handle, especially for people who are poorly educated, have difficulty reading and have an irregular diet. This study represents a picture of the critical issues encountered in the management of diabetic patients on insulin therapy, in a rural area of a low-middle-income country such as Tanzania.

Insulin therapy is mainly needed by patients with type 1 diabetes, largely young due to onset in childhood/youth, and used by patients with type 2 diabetes who no longer respond to oral therapy at a more advan-

Figure 2. Description of events index of clinical outcomes: hospitalization, hypoglycemia and performance status.



ced stage of disease[16,17]. In agreement with what has been reported, the patients examined in our study are predominantly young people, 62.7% being under 40 years of age. However, against expectations, 45.8% of patients are classified in the dataset as type 2. This could be due to the diagnostic difficulties found in low-resource countries, especially in rural areas, where diagnosis is based solely on clinical history, age of disease onset and BMI at onset. Especially in the age range of 25 to 40 years, straddling adulthood and youth, these patterns can generate misclassifications. In group 1 in this age group, 45% of the patients are labelled as type 2 diabetes, however, only 2 are obese and frankly belong to this category; the others were normal weight and among these, most had a BMI at the lower limits of normal weight. Similarly in group 2, more than half are classified as type 2 but only one is obese, and among the normal-weight half have a BMI at the lower limits of normal. The proportion of patients whose type of diabetes is not specified at the first visit is a further indication of the diagnostic difficulty encountered. It would be interesting to be able to investigate this question further to see whether, in these doubtful cases, we are actually dealing with type 1 diabetes, particular forms of diabetes prevalent in Africa such as that related to malnutrition, or even whether the low weight is due to glycemic decompensation in type 2 as well.

In our cohort, patients on insulin therapy are 49.1% male and among patients in active follow-up males are 54.5%. This male sex proportion is unusual: NCDs clinics in Tanzania are mainly attended by women, with a small number of men on treatment, due to a social and cultural factor[18–20]. Probably the extent of symptomatology due to diabetes also prompts men to seek health care help to deal with the problem. In fact, almost all the patients interviewed, prior to starting treatment, had either gone through hospitalisation or perceived a state of poor health with marked weakness and asthenia, so much so that they were unable to work in a performant manner or dropped out of work or study completely. In addition, most patients do not have a family history of diabetes or particular comorbidities, so there are few opportunities for contact with health care facilities, except for women who, in the maternal and child health setting, are more accustomed to frequenting health care environments; therefore, it is not surprising that for many patients the diagnosis is generally made in conjunction with an episode of diabetic ketoacidosis[21].

From the socio-economic status indices, it appears that patients predominantly present a poor substratum. This can be deduced from the significant number of mud or sheet metal dwellings, poor availability of electric light (present in less than half of the houses), living in large families (often at least 5 people), and low economic income per family, amounting to only one source of income in 51.5% of cases. In addition, the main occupation is farming, and 15.2% of the patients surveyed have no occupation; more than 80% of patients have not passed the elementary school level ("Standard 1-7"), and do not have health insurance; nearly 70% face economic difficulties in supporting transportation costs to travel to check-up in Tosamaganga. The economic component is undoubtedly a major factor in influencing the origin of patients from different peripheral health centres, so much so that the Tosamaganga area is the most represented (64.4%). However, the economic-geographical factor is not the only one influencing accessibility to care: poorly travelled roads, long distances, rainfall, and scarcity of public transportation are major obstacles to continuity of care. Therefore, it is highlighted that decentralisation of care and accessibility to diabetes services at the grassroots level is vital. Lack of services on the ground generates health inequity, making continuum of care accessible only to the wealthier population.

Insulin therapy is certainly the most expensive of all diabetes therapies, both because of the cost of insulin itself, but also because of the need for close monitoring several times a day of blood glucose values through test strips and glucometer. Together with needles and the syringes required to inject the drug, they represent an added cost to the overall budget per person. To limit health inequities as much as possible, Doctors with Africa CUAMM's NCDs project offers free treatment to patients on insulin. Considering that the cost of the cheapest insulin regimen is equal to about four salaries of an early-career nurse, in the absence of health insurance, it becomes extremely difficult to meet this expense. Hence, predictably, 81.8% of the patients surveyed said they would have no way to treat themselves in the absence of the Tosamaganga insulin clinic.

All guidelines, from high-income countries as well as lower-income countries, indicate diet and physical activity as an integral part of care. For this reason, the NCDs clinic has a nutritionist who conducts counselling. Such counselling was found to be very

helpful by all patients interviewed. High dietary adherence is found: consumption of carbohydrates is low and whole-grain carbohydrates are preferred; consumption of alcoholic and sugary beverages such as sodas is exceptional, in contrast to what is usually seen in the general population. In addition, most patients reported that they engage in regular physical activity. Our study demonstrates how qualified health personnel can make a difference and how it is critically important that all services enjoy the presence of these specialised figures.

About half of the patients surveyed (51.5%) said they need help handling insulin and/or following proper nutrition. Overall, 70.6% of them need support in handling insulin; for example, many patients have visual impairment and cannot read the small numbers written on the syringe by themselves so that they can independently inject themselves with the correct number of insulin units. Some perceive shame in injecting themselves with insulin in front of other people or experience stress and fear about injecting and more than 1 in 3 people perceive social stigma due to their disease. The insulin regimen used is the Premixed regular insulin/NPH 30/70 30/70 insulin regimen with two daily administrations (breakfast and dinner). Existing literature data report a higher rate of hypoglycemias with the premixed regimen and human insulin, compared with the basal bolus regimen with insulin analogs[22]. In the study population, reported hypoglycemias are numerous; however, major hypoglycemias, which are more dangerous, occurred in a minority of patients (15.2%), in no more than two per patient in a month. In contrast, symptomatic minor hypoglycemias are very prevalent in almost 8 in 10 people , frequently occurring in numbers of at least three per month. They occur mainly in the morning, after prolonged fasting at night. A survey regarding the regularity of diet and the amount of food taken at each meal could help to understand whether there is any margin to reduce these hypoglycemias through modification of eating habits. In addition, the number of hypoglycemic episodes observed tended to be higher in those with a lower level of education, which also accounts for the majority share of the study population. A higher degree of education would probably allow for more careful handling of insulin, without confusion in counting the units to be injected, and is associated with higher economic status, which allows for a more regular diet without skipping meals or reducing quantities. In this context, counselling by health care professionals to recognize symptoms of hypoglycemia early and resolve them without complications is crucial.

It is indicative of the effectiveness of the medical intervention that patients followed by the NCDs clinic reported a significant benefit on the other clinical outcomes considered. In fact, an improvement in blood glucose, glycated haemoglobin, and weight values over time was observed, although without reaching the target. The number of hospitalizations for any cause excluding childbirth and trauma decreased dramatically after patients were enrolled in the NCDs clinic: more than 80% no more experienced hospitalization. Performance status improved dramatically: almost all patients resumed and improved their work ability following the initiation of insulin therapy.

Limitations of the study include: the limited sample size, which is largely related to the very epidemiology of type 1 diabetes and the tendency to procrastinate, as much as possible, the initiation of insulin therapy in patients with type 2 diabetes. The difficult data collection in the described setting for several reasons: it is not easy to obtain clear information about the medical history and medications taken, sometimes even the age of the patients themselves is difficult to define; in addition, sometimes the reagents made available for haematochemical tests become out of stock and the results are not always reliable; patients often get lost at follow-up or miss scheduled checkups.

In conclusion, there are many challenges to be faced in a low-middle-income country like Tanzania, especially in a rural setting. Increased access to treatment at the grassroots level and training of qualified personnel would be appropriate to improve disease control and reduce the dangerous adverse effects represented by hypoglycemia. Spreading awareness of the problem, currently rather small, so that interest in it develops at the community level is a winning strategy to spark new initiatives and achieve tangible and lasting goals over time. All outcomes considered improve with the proposed management model, the medical intervention described, and the counseling performed. Based on the results obtained from this study, Doctors with Africa CUAMM promotes the use of the insulin regimen with pre-mixed 30/70 insulin. Compared with basal-bolus, because of only two daily administrations, it is less expensive and more manageable for patients. In this way adherence to treatment as well as cost sustainability to support as many patients as possible

are promoted. It results in important clinical improvements related to performance status and reduced hospitalizations, in the presence of an otherwise limited number of major hypoglycemia and improved glycemic control over time. In a setting such as the one described, the use of Premixed regular insulin/NPH 30/70 insulin is therefore desirable.

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Assessing the impact of a community-based psychodrama intervention on mental health promotion of adolescents and young adults in Mozambique: A mixed-methods study

PAPER

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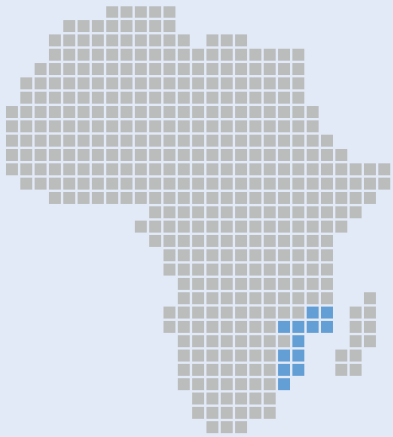

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PAPERS

Assessing the impact of a community-based psychodrama intervention on mental health promotion of adolescents and young adults in Mozambique: A mixed-methods study

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Background While mental health is an emerging issue in low-income countries, its promotion remains poor, with little context-oriented evidence available. Here we aimed to assess the impact and acceptability/feasibility of a community-based psychodrama intervention involving both adolescents and young adults (AYA) living with HIV (AYALHIV) and without HIV (AYAHIV–).

Methods We used a mixed-methods approach, where the quantitative part was based on pre/post questionnaires and the qualitative one on content analysis of semi-structured interviews. Trained community health care workers delivered psychodrama sessions involving AYAs aged 15–24 years once a week between July and August 2023 in Beira, Mozambique. The baseline assessment involved a sociodemographic and three mental health questionnaires: the Mental Health Knowledge Schedule (MAKS), Community Attitudes toward People with Mental Illness (CAMI27), and the Toronto Alexithymia Scale (TAS). We repeated all questionnaires after the intervention and conducted semi-structured interviews.

Results We enrolled 354 AYAs (50.8% female, 45.5% AYALHIV) at baseline; 315 (89.0%) attended the sessions, with a mean participation rate of 94.4%. Overall, 281 (89.2%) completed the post-intervention assessment. MAKS score improved from 44.5 (95% confidence interval (CI) = 44.0–45.0) to 47.1 (95% CI = 46.4–47.7, $P < 0.001$). Total CAMI27 score showed no significant variation ($P = 0.855$). Total TAS score decreased from 57.3 (95% CI = 56.1–58.5) to 54.3 (95% CI = 53.0–55.6, $P < 0.001$). We found no statistically significant interactions between time and sex, age, or HIV serostatus in all questionnaires. For the qualitative part of the study, we analysed 37 semi-structured interviews (43.2% with females, 40.5% with AYALHIV). We identified four areas of intervention impact: peer-to-peer support (30.3%), social empowerment (24.7%), resilience (23.0%), and emotional skills (21.9%). Regarding acceptability/feasibility, perceived scalability (37.2%) and affective attitude (34.5%) were the sub-areas most frequently retrieved in the SSIs.

Conclusions The community-based psychodrama intervention proved to be an effective tool in AYAs' mental health promotion, increasing knowledge and improving emotional awareness through group experience and interpersonal learning. The intervention also showed good acceptability and feasibility in the context of our study.

Like most sub-Saharan African (SSA) countries, the population of Mozambique mainly comprises adolescents and young adults (AYA), with 22.4% being aged between 15 and 24 years [1]. This period of life, characterised by psychophysical and social changes and challenges, brings a high risk for the onset of mental health illness; for example, up to half of all mental health disorders start before the age of 14, while suicide is the third leading cause of death in adolescents aged 15–19-year-old [2,3].

Mozambique is particularly affected by mental health problems. It has an estimated suicide rate of 13.7 per 100 000 population, more than double the average for the African region (6.0 per 100 000 population), and is the sixth country with the highest suicide rate in the African region [4]. Data from 2018 on mental health diseases in Mozambique show a prevalence of 54% of AYAs being positive on at least one screening tool for anxiety, depression, PTSD, or drug-alcohol abuse [5]. Notably, Mozambique also has the eighth highest HIV prevalence globally [5]. HIV has been recognised as a major risk factor for the development of mental health problems, with the prevalence of positive screening for mental health disorders increasing to 73% in the group living with HIV [5].

While it is well recognised that adolescence is a period of vulnerability, the World Health Organization (WHO) points out that this age also offers great potential for mental health promotion and prevention [6,7]. Such activities could enable AYAs to realise their potential and participate meaningfully in their communities [6]. Among the main targets of the WHO Guidelines on mental health promotive and preventive interventions for adolescents are psychosocial interventions aimed at helping AYAs develop skills that may positively influence their behaviour, thoughts, feelings, and social interactions [7]. Fostering socioemotional competencies and improving mental health knowledge has been shown to be one of the most effective approaches to reducing stigma around mental health problems and promoting help-seeking behaviours, making it a key strategy for preventing mental disorders, risky behaviour, and suicide [8-10].

Community-based interventions in low- and middle-income countries (LMICs) have proved to be effective in improving mental health and reducing violence and substance use in AYAs [11]. Among the interventions implemented to promote psychological well-being of individuals and communities, psychodrama has widely been used in diverse settings and for various issues, including stress related to HIV-positive diagnosis [12]. Created by Jacob Levy Moreno in 1921, psychodrama is a group format therapeutic model with deep roots in theatre, psychology, and sociology [13]. It offers participants the opportunity to explore feelings, thoughts, and behaviours through actions rather than words alone [14]. Psychodrama aligns with positive psychology by focussing on promoting people's capacities to actively participate in healing themselves and thriving, both as individuals and as a society [15]. Although psychodrama has proven to be an effective tool in both therapeutic and educational settings, few studies evaluated the effectiveness of related interventions among AYAs in the context of resource-limited countries [15]. Thus, we aimed to assess the impact of a community-based psychodrama intervention on AYAs' knowledge and attitudes towards mental health, and their emotional consciousness and skills, as well as to consider possible differences in this impact based on the HIV serostatus. Our secondary objectives were to evaluate the acceptability and feasibility of this intervention and to describe the baseline level of mental health knowledge and attitudes of AYAs living with (AYALHIV) and without HIV (AYAHIV–). We hypothesised that a community psychodrama intervention could be associated with increased knowledge about mental health and improved social-emotional skills of AYAs being equally effective in AYALHIV and AYAHIV– working in mixed groups.

METHODS

Ethical approval

We performed this study per the 1964 Declaration of Helsinki, and we received approval from the Comité Interinstitucional de Bioética para Saúde (CIBS) – Sofala on the 21 July 2023 (protocol number 007/CIBS/2023).

Study design, setting, and population

This was a mixed-methods study, where the quantitative analysis was based on data from pre-post questionnaires, and the qualitative one on semi-structured interviews. We carried out this study in the Beira, province of Sofala, Mozambique, between July and September 2023.

We recruited AYAs at the community level in four neighbourhoods, and AYALHIV specifically from the adolescents' and youths' friendly service (*serviço amigo dos adolescentes e jovens* (*SAAJ*)) of the four health

centres within these neighbourhoods. These services provide education, prevention, primary care support, and HIV treatment for target population aged between 10 and 24 years.

We considered all persons aged between 15 and 24 years living in the four neighbourhoods or accessing the *SAAJ* during the study period as eligible for inclusion. For AYALHIV, we excluded those who had been diagnosed less than three months before the study period. We otherwise excluded AYAs attending less than five (65%) sessions.

Participant and public involvement

We involved local health authorities and key stakeholders at the community level in setting priorities for the scope of action and planning the intervention. We otherwise sought the participants' personal feedback on the intervention in the qualitative part of our study.

Psychodrama intervention

This intervention encompassed three phases. First, we provided training for eight community health workers (CHW) from a local cooperative. It started with a five-day intensive course; two days were dedicated to theory, to give the participants basic knowledge on mental health, while three days were focussed on experience-oriented training to let them experience a psychodrama session and acquiring the most important psychodrama-related principles and techniques.

Second, we created AYA groups. Here, the CHWs were divided into four pairs, each active in a different neighbourhood. They recruited AYAs for the baseline assessment and enrolled them in a list for subsequent group formation. After the baseline assessment, the CHWs called up the AYAs and formed groups with those available, resulting in 30 groups each ranging from 8 to 13 AYAs.

Third, we implemented the psychodrama sessions themselves and provided ongoing training for the CHWs. For eight consecutive weeks, the CHWs took part in a weekly training, actively exploring the specific themes and techniques of each session they were going to have with the AYAs during the week. Eight weekly psychodrama sessions were conducted for each group in total. Psychodrama techniques were applied across all sessions to promote emotional self-awareness, empathy, and conflicts mediation (**Figure 1**).

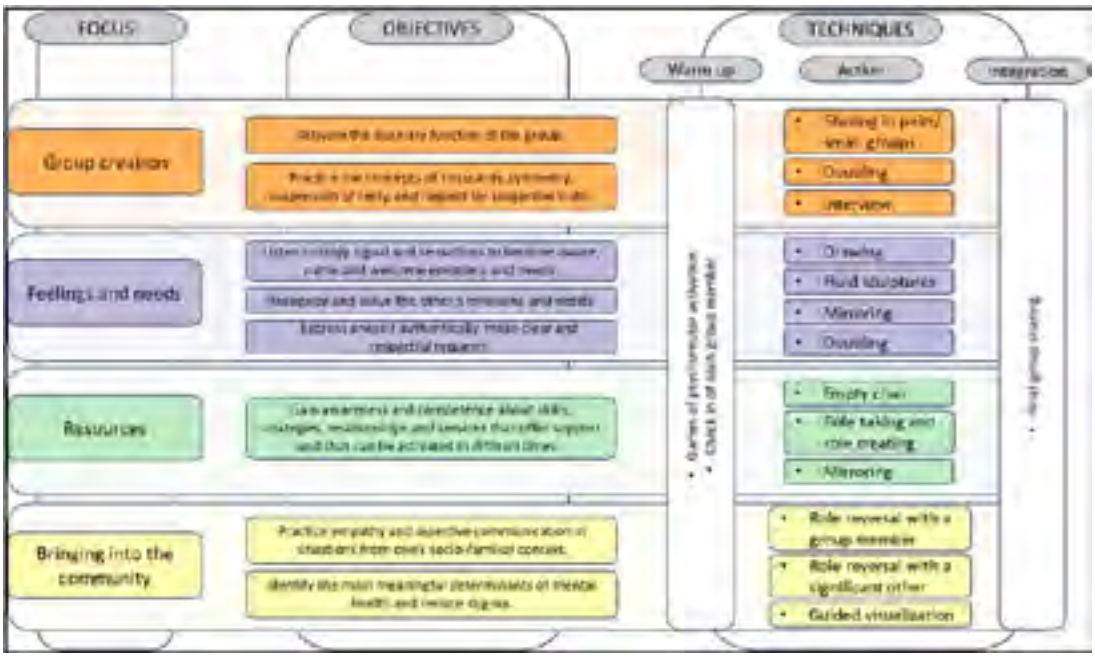

Figure 1. Framework of the psychodrama intervention implemented in the study.

Sample size

For the pre-post questionnaire, we calculated that we needed a minimum sample of 315 with the following formula: $(Z_{\alpha/2} + Z\beta)^2 / d^2$, with α and β set at 0.05 and 0.2, respectively, and the effect size (d) set at 0.17, expressing a small effect size, and considering a lost to follow-up rate of 15% [16].

There is no consensus in literature on sample size estimation for qualitative analyses, although some authors suggest that 6 interviews would correspond to an 80% saturation of topics or 12 to a higher saturation rate [17]. To better represent our sample, we collected two interviews from each psychodrama group, resulting in a total of 60 interviews. We selected the two participants in each group randomly, drawing a number from a container corresponding to each participant (simple random sampling) from those present in the last session.

Questionnaires

We used two questionnaires to assess knowledge and attitude towards mental health, respectively. The Mental Health Knowledge Schedule (MAKS) has 12 items constructed on a 5-point Likert scale, with a maximum total score of 60 points. A score above 35 gives a good level of mental health knowledge [18]. In turn, the 27-item's version of the Community Attitudes toward People with Mental Illness (CAMI27) has a two factors structure: 'prejudices and exclusion' and 'tolerance and support in the community.' It has a 5-point Likert scale response scheme with a maximum total score of 135 points. Both MAKS and CAMI27 have been previously validated in Portuguese and in LMIC settings [19–21].

We used the Toronto Alexithymia Scale (TAS) to assess the impact of the psychodrama intervention on participants' perceptions about expressing and describing their emotions. It includes 20 items with a 5-point Likert scale divided into three factors: 'identifying feeling,' 'describing feelings,' and 'externally-oriented thinking.' The total score ranges from 20 to 100 points, with a higher score suggesting a higher level of alexithymia (cut-off: 20–51 for non-alexithymia, 52–60 for possible alexithymia, 61–100 for alexithymia) [22]. A Portuguese validated version of the TAS questionnaire is available [23].

Data collection

At baseline, we asked all participants to complete an informed consent form; we obtained consent from parents or legal guardians if they were underaged. We administered a sociodemographic questionnaire (**Online Supplementary Document**) along with the MAKS, CAMI27, and TAS. Two CHWs and a child and adolescent neuropsychiatry resident supervised the baseline assessment to ensure that participants understood the questions and to address any problems. To ensure privacy and to match the pre- and post-tests, we anonymised the participants' data through a numeric alpha code.

We then repeated the MAKS, CAMI27, and TAS questionnaires after the psychodrama intervention. On the same day that the post-test was applied, a single CHW who had received training in the interview methodology carried out on the semi-structured interview in the local language (Portuguese) using a question guide (**Online Supplementary Document**). The interviews were recorded and transcribed, with the transcripts analysed in Portuguese and only select quotes translated into English for presentation here in the manuscript.

Content analysis

We performed an inductive content analysis to identify themes in the interview and codify them. First, we obtained a full overview of the transcripts, reading it repeatedly, after which we highlighted the parts of the text that may capture a theme of interest. We then reread the transcripts and labelled the themes, proceeding to group the labels that referred to similar concepts into categories. We then repeatedly continued this process of reading the transcripts and labelling/grouping the themes, until all highlighted themes were grouped into categories. Lastly, we organised the retrieved categories into a hierarchical structure (identifying areas and eventual sub-areas) based on the relationship between them, only to finally develop definitions and codes for each area and subarea.

Two researchers (CM and AS) applied these steps to six semi-structured interviews to identify possible themes and code them into areas and sub-areas. They discussed all potential classifications with a third researcher (RB) to obtain a consensus. Then, we created a classification index code which we tested on four more interview transcripts (**Online Supplementary Document**). Using this classification, two researchers (CM and AS) independently assessed and coded the remaining transcripts, with codes and excerpts presented below in this manuscript. We discussed discrepancies in the coding process and resolved them by involving a third rater (RB).

Statistical analysis

We first conducted a descriptive analysis, where we described categorical variables through frequencies and percentages and continuous variables through means and standard deviations (SDs) or medians and interquartile ranges (IQRs). We assessed for differences in the participants' sociodemographic characteristics through the χ^2 test, Fisher exact test, and Wilcoxon-signed-rank test. We used the Shapiro-Wilk test to test the normality of the distribution of the included variables.

We measured the participants' socioeconomic status (SES) by considering household factors based on the available literature [24,25]. Afterwards, we built an SES index using principal component analyses of the abovementioned variables, categorised into wealth tertile (low, middle, high) [26].

We explored the association between baseline score of the MAKS, CAMI27, and TAS and sociodemographic characteristics using the analysis of covariance (ANCOVA) test. To assess the change in the total score of the three questionnaires, we used the repeated-measures analysis of variance (RMANOVA) test, imputing one within-subject factor (time pre/post) and three between-subject factors (sex, age, and HIV serostatus). We otherwise used multivariate analysis of variance (MANOVA) with repeated measure to assess differences in the scores of the two and three factors of the CAMI27 and TAS questionnaires, respectively.

Table 1. Sociodemographic characteristics and questionnaire descriptive statistics of the adolescents and young adults involved in the baseline assessment distinguished by HIV serostatus

	AYAHIV– (n = 193)	AYALHIV (n = 161)	Overall (n = 354)
Sex			
Female	99 (51.3%)	81 (50.3%)	180 (50.8%)
Male	94 (48.7%)	80 (49.7%)	174 (49.2%)
Age group			
Adolescent (15–19 y)	108 (56.0%)	80 (49.7%)	188 (53.1%)
Young adult (20–24 y)	85 (44.0%)	81 (50.3%)	166 (46.9%)
School (N/A = 1)			
None	7 (3.6%)	8 (5.0%)	15 (4.2%)
Primary	2 (1.0%)	5 (3.1%)	7 (2.0%)
Secondary	161 (83.4%)	133 (82.6%)	294 (83.1%)
Secondary technical	15 (7.8%)	5 (3.1%)	20 (5.6%)
University	8 (4.1%)	9 (5.6%)	17 (4.8%)
Job (N/A = 4)			
None	171 (88.6%)	133 (82.6%)	304 (85.9%)
Farmer	1 (0.5%)	3 (1.9%)	4 (1.1%)
Self-employment	11 (5.7%)	15 (9.3%)	26 (7.3%)
Employee	2 (1.0%)	4 (2.5%)	6 (1.7%)
Public employee	6 (3.1%)	4 (2.5%)	10 (2.8%)
SES group			
Low	69 (35.8%)	49 (30.4%)	118 (33.3%)
Middle	59 (30.6%)	59 (36.6%)	118 (33.3%)
High	65 (33.7%)	53 (32.9%)	118 (33.3%)
MAKS score, $\bar{x}$ (SD)	44.1 (5.1)	44.9 (4.5)	44.5 (4.8)
CAMI27 score, $\bar{x}$ (SD)			
Overall	88.6 (8.3)	90.3 (8.6)	89.4 (8.5)
Factor 1	47.8 (7.0)	47.7 (6.9)	47.8 (7.0)
Factor 2	40.8 (7.9)	42.6 (7.9)	41.6 (7.9)
TAS score, $\bar{x}$ (SD)			
Overall	57.7 (9.6)	56.8 (10.5)	57.3 (10.0)
Factor 1	19.8 (5.7)	20.0 (6.2)	19.9 (5.9)
Factor 2	15.2 (3.7)	14.8 (3.9)	15.1 (3.8)
Factor 3	22.6 (4.1)	21.9 (4.7)	22.3 (4.4)

AYAHIV– – adolescents and young adults without HIV, AYALHIV – adolescents and young adults living with HIV, CAMI – Community Attitudes toward People with Mental Illness, MAKS – Mental Health Knowledge Schedule, SD – standard deviation, SES – socioeconomic status, TAS – Toronto Alexithymia Scale, $\bar{x}$ – mean

To identify the issues the participants' discussed more frequently, we performed a frequency count of all areas and sub-areas retrieved in interviews. We calculated Cohen's kappa values to assess the agreement between the two raters on the four SSIs used to test the classification index code, where agreement was considered satisfactory if the values ranged between 0.61 and 1.00 (from moderate to almost perfect level of agreement) [27]. We used the χ^2 test to assess differences in the frequency of the different areas according to sex, age, and HIV serostatus.

A *P*-value <0.05 denoted statistical significance. We performed all analyses in R, version 4.1.1 (R Core Team, Vienna, Austria).

RESULTS

Baseline assessment

Overall, 354 AYAs attended the baseline assessment; 188 (53.1%) were adolescent (aged between 15 and 19 years) and 180 (50.8%) were females. There were 161 AYALHIV (45.5%), with no differences based on sex (*P* = 0.87), age (*P* = 0.10), educational level (*P* = 0.07), or SES group (*P* = 0.30) compared to AYAHIV– (**Table 1**).

The mean scores on the MAKS and CAMI27 questionnaires were 44.5 (SD = 4.8) and 89.4 (SD = 8.5), respectively. Eighty-nine (25.1%) AYAs had good knowledge of mental health, while most (n = 265, 74.9%) had a suboptimal level. The mean score at the TAS questionnaire was 57.3 (SD = 10.0); 70 (19.8%) AYAs had a score suggestive of alexithymia, while most (n = 160, 45.2%) scored negative.

We found no statistical differences in the MAKS score at baseline based on sex (*P* = 0.55), age (*P* = 0.21), HIV serostatus (*P* = 0.14), educational level (*P* = 0.15), or SES group (*P* = 0.59). Baseline CAMI27 score was higher in AYALHIV compared to AYAHIV– (*P* = 0.041), in those with higher educational level (*P* < 0.001), or in the higher SES group (*P* = 0.042). Men had a lower total TAS score than women (*P* = 0.002), as did young adults (YAs) compared to adolescents (*P* = 0.048).

Post-intervention evaluation

Of the 354 AYAs enrolled, 315 participated in the psychodrama sessions, with an average participation rate of 94.4% sessions (average of 7.5 sessions, SD = 0.9). After applying our exclusion criteria, we included 281 AYAs in the post-intervention assessment (Figure S1 in the **Online Supplementary Document**). Overall, the mean scores on the MAKS, CAMI27, and TAS after the intervention were 47.1 (SD = 5.3), 88.9 (SD = 10.7), and 54.4 (SD = 11.4), respectively.

In the RMANOVA model, the MAKS score significantly improved from baseline (44.5; 95% CI = 44.0–45.0) to post-intervention (47.1; 95% CI = 46.4–47.7, $P < 0.001$), without statistically significant differences based on sex, age, or HIV serostatus (**Figure 2**, **Table 2**).

The CAMI27 score showed no significant variation from pre-intervention (89.1; 95% CI = 88.1–90.1) to post-intervention (88.9; 95% CI = 87.7–90.2, $P = 0.86$), nor based on the between-subject factors (**Table 2**). Considering the two factors of the CAMI27, the first ('tolerance and support in the community') decreased from 47.5 (95% CI = 46.7–48.2) to 33.2 (95% CI = 32.5–33.8, $P < 0.001$). Conversely, factor 2 ('prejudices and exclusion') significantly increased from 41.6 (95% CI = 40.7–42.5) to 55.8 (95% CI = 54.8–56.7, $P < 0.001$). We saw no differences in the two factor pre- and post-intervention based on sex ($P = 0.39$), age ($P = 0.45$), or HIV serostatus ($P = 0.89$).

The total TAS score decreased from 57.3 (95% CI = 56.1–58.5) at baseline to 54.3 (95% CI = 53.0–55.6, $P < 0.001$) in the post-intervention evaluation. We also confirmed the difference found at baseline by sex, with men having lower TAS scores overall. We found no statistically significant interactions between time and sex, age, or HIV serostatus (**Table 2**). Considering the three factors of the TAS questionnaire, the first factor ('difficulty identifying feelings') and second ('difficulty describing feelings') contributed to the decrease ($P = 0.021$ and $P = 0.015$, respectively), while the third ('externally-oriented thinking') showed no statistically significant changes ($P = 0.15$).

f2

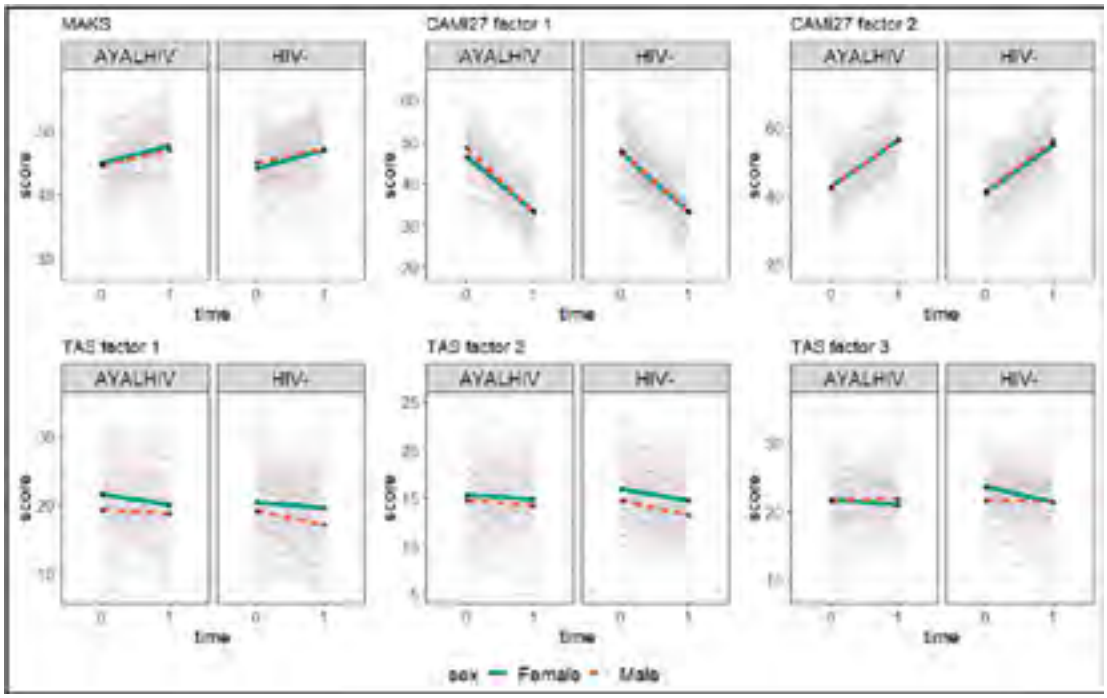

Figure 2. Mean scores for the MAKS, for factors 1 and 2 of the CAMI27, and at factors 1, 2, and 3 of the TAS in the baseline (time = 0) and in the post-intervention assessment (time = 1), as well as stratified by HIV serostatus and sex. The grey lines represent the individual values. AYALHIV – adolescents and young adults living with HIV.

Table 2. Descriptive and test statistics from the three repeated measure ANOVA model, with total MAKS, CAMI27, and TAS scores as dependent variables and with one within-subject factor (time) and three between-subject factors (sex, age, and HIV serostatus)

		Descriptive statistics				Test statitsics		
Sex	HIV serostatus	Age	Time	n	Mean (95% CI)	ANOVA-type statistic	Test statistic	*P*-value
MAKS questionnaire								
Woman	Negative	adol	pre	45	43.9 (39.8–48.0)	sex	0.030	0.86
Woman	Negative	adol	post	45	47.5 (43.2–51.9)	HIV	0.304	0.58
Woman	Negative	YA	pre	32	44.0 (38.2–49.9)	sex:HIV	1.799	0.18
Woman	Negative	YA	post	32	45.9 (38.6–53.3)	age	0.889	0.35
Woman	Positive	adol	pre	29	45.3 (40.1–50.5)	sex:age	1.158	0.28
Woman	Positive	adol	post	29	48.1 (42.2–54.0)	HIV:age	0.797	0.37
Woman	Positive	YA	pre	33	44.4 (39.9–48.9)	sex:HIV:age	1.510	0.22
Woman	Positive	YA	post	33	46.9 (42–51.8.0)	time	37.588	<0.001
Man	Negative	adol	pre	38	44.8 (40.8–48.9)	sex:time	0.299	0.59
Man	Negative	adol	post	38	48.1 (43.8–52.4)	HIV:time	0.001	0.98
Man	Negative	YA	pre	39	45.0 (41.7–48.2)	sex:HIV:time	0.008	0.93
Man	Negative	YA	post	39	46.2 (42.4–50.0)	age:time	0.637	0.43
Man	Positive	adol	pre	33	44.4 (40–48.80)	sex:age:time	0.232	0.63
Man	Positive	adol	post	33	46.0 (40.6–51.3)	HIV:age:time	2.230	0.14
Man	Positive	YA	pre	32	44.7 (39.6–49.7)	sex:HIV:age:time	0.385	0.54
Man	Positive	YA	post	32	47.7 (42.1–53.2)			
CAMI27 questionnaire								
Woman	Negative	adol	pre	45	88.2 (81.8–94.5)	sex	1.228	0.27
Woman	Negative	adol	post	45	87.2 (80.0–94.4)	HIV	1.309	0.25
Woman	Negative	YA	pre	32	88.2 (80.6–95.7)	sex:HIV	0.007	0.93
Woman	Negative	YA	post	32	88.8 (78.7–98.9)	age	1.911	0.17
Woman	Positive	adol	pre	29	87.5 (77.8–97.3)	sex:age	0.317	0.57
Woman	Positive	adol	post	29	87.9 (72.6–103.1)	HIV:age	3.272	0.07
Woman	Positive	YA	pre	33	90.0 (81.1–98.8)	sex:HIV:age	0.594	0.44
Woman	Positive	YA	post	33	90.8 (81.4–100.1)	time	0.033	0.86
Man	Negative	adol	pre	38	88.9 (81.7–96.1)	sex:time	0.203	0.65
Man	Negative	adol	post	38	90.7 (81–100.3)	HIV:time	0.208	0.65
Man	Negative	YA	pre	39	88.5 (79.7–97.3)	sex:HIV:time	0.942	0.33
Man	Negative	YA	post	39	87.9 (78.4–97.4)	age:time	0.005	0.94
Man	Positive	adol	pre	33	89.3 (81.2–97.4)	sex:age:time	0.585	0.45
Man	Positive	adol	post	33	87.8 (76.5–99.1)	HIV:age:time	0.036	0.85
Man	Positive	YA	pre	32	92.4 (83.6–101.3)	sex:HIV:age:time	0.337	0.56
Man	Positive	YA	post	32	77.8 (65.0–90.7)			
TAS questionnaire								
Woman	Negative	adol	pre	45	56.9 (49.4–64.5)	sex	8.399	0.004
Woman	Negative	adol	post	45	51.6 (43.1–60.1)	HIV	0.493	0.48
Woman	Negative	YA	pre	32	51.9 (45.2–58.6)	sex:HIV	0.913	0.34
Woman	Negative	YA	post	32	49 (38.2–59.7)	age	3.334	0.07
Woman	Positive	adol	pre	29	54.5 (41.7–67.3)	sex:age	0.141	0.71
Woman	Positive	adol	post	29	50.4 (34.8–66)	HIV:age	0.068	0.79
Woman	Positive	YA	pre	33	52.4 (43.1–61.7)	sex:HIV:age	3.232	0.07
Woman	Positive	YA	post	33	51.2 (41.3–61)	time	13.678	<0.001
Man	Negative	adol	pre	38	50.6 (41.1–60.2)	sex:time	0.480	0.49
Man	Negative	adol	post	38	45.6 (35.1–56)	HIV:time	1.896	0.17
Man	Negative	YA	pre	39	49.9 (41.8–58)	sex:HIV:time	0.182	0.67
Man	Negative	YA	post	39	47.5 (36.7–58.4)	age:time	1.803	0.18
Man	Positive	adol	pre	33	52.5 (42.6–62.3)	sex:age:time	0.139	0.71
Man	Positive	adol	post	33	51.4 (41.3–61.5)	HIV:age:time	0.091	0.76
Man	Positive	YA	pre	32	48.7 (35.5–61.9)	sex:HIV:age:time	0.214	0.64
Man	Positive	YA	post	32	47.9 (35.2–60.7)			

adol – adolescent, ANOVA – analysis of variance, CAMI – Community Attitudes toward Mental Illness, MAKS – Mental Health Knowledge Schedule, TAS – Toronto Alexithymia Scale, YA – young adult

Semi-structured interview analysis

We analysed thirty-seven semi-structured interviews with 16 women (43.2%) and 15 AYALHIV (40.5%). The median age was 20 years (IQR = 15–22). The interviews lasted between 20 and 35 minutes.

We coded 472 themes that we found to be relevant; 356 (75.4%) were related to the impact of the intervention and 116 (24.6%) to acceptability/feasibility. The interrater agreement over the main area was very good (α = 0.85; 95% CI = 0.73–0.96), while the agreement over sub-areas was good (α = 0.71; 95% CI = 0.52–0.90) (Table 3).

The most frequent retrieved area was 'Peer-to-peer support' (30.3%). We found no statistically significant differences in the frequency of the four main area based on sex ($P = 0.10$), age ($P = 0.69$), or HIV serostatus ($P = 0.13$). In this area, 'sharing and self-expression' and 'belonging and trust' were the two more frequently reported sub-areas. They referred to the intimate bond between group members created by sharing personal stories and to the empowerment resulting from being able to express hidden parts of one's inner world in a group atmosphere characterised by acceptance and appreciation of each member.

> *I used to be someone who didn't know how to share my own personal stories with others, I didn't like to share the problems I have in my life, and I've learnt to share my problems with other people.* – Woman, YAHIV–.

> *For me, being part of this group has been a privilege. Since then, I've learnt a lot of good things and before I was afraid and sad, now I feel accepted.* – Woman, YAHIV–.

The group-based method was also important because it gave AYA the possibility to gain new insights through the process of interaction with others and to discover that one's own experience may be shared by many other group members.

> *That's when we had the face-to-face game where we told each other about what we were going through and I discovered that in the group there was someone who was going through the same situation as me, and when we saw each other, we realized that we were going through the same thing. I was very touched and realized that I'm not alone.* – Woman, AHIV–.

The second area we identified was 'social empowerment' (24.7%). It encompassed the sub-areas of 'communication skill' and 'prosocial attitude,' referring to increasing skills in positive relationship building, group cooperation, and empathic communication.

Table 3. Frequency of the main areas and sub-areas retrieved in the inductive content analysis of the semi-structured interviews, distinguished by HIV serostatus, sex, and age group*

	AYAHIV– (n = 302)	AYALHIV (n = 170)	Woman (n = 198)	Man (n = 274)	Adolescent (n = 187)	YA (n = 285)	Overall (n = 472)
Peer-to-peer support	69 (30.7)	39 (29.8)	39 (25.2)	69 (34.3)	41 (29.1)	67 (31.2)	108 (30.3)
Sharing and self-expression	30 (13.3)	16 (12.2)	17 (11.0)	29 (14.4)	19 (13.5)	27 (12.6)	46 (12.9)
Belonging and trust	21 (9.3)	19 (14.5)	14 (9.0)	26 (12.9)	16 (11.3)	24 (11.2)	40 (11.2)
Interpersonal learning	18 (8.0)	4 (3.1)	8 (5.2)	14 (7.0)	6 (4.3)	16 (7.4)	22 (6.2)
Social empowerment	50 (22.2)	38 (29.0)	36 (23.2)	52 (25.9)	37 (26.2)	51 (23.7)	88 (24.7)
Communication skills	22 (9.8)	19 (14.5)	15 (9.7)	26 (12.9)	18 (12.8)	23 (10.7)	41 (11.5)
Mental health awareness	15 (6.7)	17 (13.0)	17 (11.0)	15 (7.5)	11 (7.8)	21 (9.8)	32 (9.0)
Prosocial attitude	13 (5.8)	2 (1.5)	4 (2.6)	11 (5.5)	8 (5.7)	7 (3.3)	15 (4.2)
Resilience	60 (26.7)	22 (16.8)	38 (24.5)	44 (21.9)	29 (20.6)	53 (24.7)	82 (23.0)
Coping	30 (13.3)	9 (6.9)	19 (12.3)	20 (10.0)	16 (11.3)	23 (10.7)	39 (11.0)
Breaking habits	20 (8.9)	6 (4.6)	12 (7.7)	14 (7.0)	12 (8.5)	14 (6.5)	26 (7.3)
Self-efficacy	10 (4.4)	7 (5.3)	7 (4.5)	10 (5.0)	1 (0.7)	16 (7.4)	17 (4.8)
Emotional skills	46 (20.4)	32 (24.4)	42 (27.1)	36 (17.9)	34 (24.1)	44 (20.5)	78 (21.9)
Empathic listening	20 (8.9)	11 (8.4)	18 (11.6)	13 (6.5)	12 (8.5)	19 (8.8)	31 (8.7)
Emotional intelligence	18 (8.0)	12 (9.2)	19 (12.3)	11 (5.5)	16 (11.3)	14 (6.5)	30 (8.4)
Perspective taking	8 (3.6)	9 (6.9)	5 (3.2)	12 (6.0)	6 (4.3)	11 (5.1)	17 (4.8)
Acceptability/feasibility	n = 77	n = 39	n = 43	n = 73	n = 46	n = 70	n = 116
Perceived scalability	26 (33.8)	17 (43.6)	13 (30.2)	30 (41.1)	18 (39.1)	25 (35.7)	43 (37.1)
Affective attitude	28 (36.4)	12 (30.8)	19 (44.2)	21 (28.8)	18 (39.1)	22 (31.4)	40 (34.5)
Practicality	13 (16.9)	6 (15.4)	6 (14.0)	13 (17.8)	6 (13.0)	13 (18.6)	19 (16.4)
Burden	10 (13.0)	4 (10.3)	5 (11.6)	9 (12.3)	4 (8.7)	10 (14.3)	14 (12.1)

AYAHIV– – adolescents and young adults without HIV, YA – young adult, AYALHIV –adolescents and young adults living with HIV
*Presented as n (%) unless specified otherwise.

Looking at it with the knowledge I have now, my actions would be different: in fact, I could get close to the person and listen to them and know how to be there for them, not keep them at a distance, but make them understand that they can be sincere and upfront. – Woman, YAHIV–.

Another important subarea in this area was 'mental health awareness,' expressing how the AYAs involved in the sessions gained increased awareness about the importance of mental health as an integral component of human well-being, alongside knowledge on both protective and risk factors in mental health. This also allowed them to develop a non-stigmatising attitude towards people suffering from mental illness.

What I would do at the moment would be to talk to the person and understand what they are feeling, and then I would recommend psychological counselling. – Woman, YAHIV–.

Empathise with people suffering from mental disorders: they too are people and deserve love, and I would not want them to be victims of bad behaviour. – Man, YAHIV.

The 'resilience' area expressed how the intervention helped AYAs improve their capacity for self-regulation and self-care in difficult situations by giving them a better ability to recognise and activate one's own resources, namely 'coping' (11.0%), 'breaking habits' (7.3%) and 'self-efficacy' (4.8%). In particular, 'breaking habits' referred to stepping out of one's stereotyped way of acting and thinking in order to develop new and more appropriate ways of handling situations and conflicts.

Before I started taking part in this psychodrama in the past, I had many frustrations and I didn't know how to deal with my emotions and I easily lost hope in believing and living, unlike today when I know how to manage my emotions. – Woman, ALHIV.

When I started coming here, I began to open up and I changed my way of being and seeing things a lot and I realized that I am very important myself and I deserve to be good with myself. – Woman, ALHIV.

In the 'Emotional skills' area, the two most represented were 'emotional intelligence' and 'empathic listening.' The first included the process of recognising one's own and others emotional state and of using language as a tool to express feelings; the second referred to a mindful, non-judgemental, quality listening aimed at truly understanding what another person is experiencing.

The difference is that if you look around the neighbourhood and within the family, people don't have the spirit of listening, sometimes people judge us without realizing the root cause of why we're acting the way we are. I've learned that you need to be someone who is caring, someone who is ready to listen to the other person's situation so that you can help, there's no way you can help without listening to the people. – Woman, YAHIV–.

I have the right to express my emotions and my needs. – Man, ALHIV.

Regarding acceptability and feasibility, 14 (37.8%) and 19 (51.4%) AYAs did not report any difficulties nor anything to improve, respectively. Among the experienced difficulties, 14 (12.1%) were classified as a 'burden' and concerned the problem of transport for the AYAs who lived more distant or had financial difficulties in paying for it. The 'practicality' sub-area was retrieved in 19 (16.4%) themes and related mainly to the initial difficulty in talking about oneself and in getting into another person's point of view.

The 'perceived scalability' was mentioned 43 times (37.1%) and referred to both to the willingness to continue the sessions and to extend the intervention to other groups involving more AYAs. In 38 of 40 (95.05%) themes, a positive 'affective attitude' was stated, while 29 (78.4%) of the respondents did not express any discomfort during the sessions.

DISCUSSION

In this study, we assessed the impact and acceptability/feasibility of a community-based psychodrama intervention on AYAs. Both the total MAKS (measuring knowledge on mental health) and TAS scores (measuring level of alexithymia) significantly improved after the intervention, as did the 'prejudices and exclusion' factor of the CAMI27. These effects remained significant even when adjusting for sex, age, and HIV serostatus, showing that this intervention can be useful in these at-risk populations. The AYAs found the intervention a useful and pleasant experience; they would have continued it afterwards and would like it to be extended to more people. Adherence to the psychodrama sessions was very good, with more than 94% of participants attending. The main difficulty they mentioned was transportation and its cost for people coming from farther away.

The available scientific literature describes psychodrama interventions carried out in Europe, North America, South America, and Asia [28]. This method has shown its effectiveness and positive impact on mental

health in a wide range of applications, ranging from therapy groups with clinical and subclinical patients suffering from different psychological disorders to community-based mental health care programmes, or to personal development plans aimed at, for example, improving socio-emotional skills or changing attitudes. The heterogeneity of the applications and issues addressed indicates that psychodrama can improve the symptoms associated with a wide range of problems and that it is suitable for adaptation to different cultural and social contexts.

Community-based interventions are a key pillar to delivering mental health promotion, prevention, and care. As outlined in WHO's Community Toolkit mhGAP, it is low-cost and can reach many people at their places of residence and work, providing a full spectrum of mental health interventions and reducing stigma [29]. Despite only limited studies, especially for LMICs, there is some evidence that community-based interventions can improve emotional health and mental health literacy [30]. Compared to most psychoeducational intervention methods implemented in the context of LMICs, which are primarily based on frontal lecture modes, the use of psychodrama techniques and group dynamics allows AYAs to get involved directly and personally, thus enabling an experiential learning process and a constructive change in the person's perceptions and functioning. Compared to interventions carried out within hospitals or psychology and psychiatry units, community-based interventions make it possible to precisely reach those people who suffer most from barriers related to stigma, cultural preconceptions, and economic status.

The results of this study showed that mental health knowledge and attitudes improved significantly after the intervention, along with the participants' ability to identify and express emotions. Surprisingly, we found the 'tolerance and support in the community' factor of the CAMI27 to be worse after the intervention. This could be related to the fact that it contains some items related to the medicalisation of patients with mental illness and that the psychodrama sessions emphasised the importance of seeking help from mental health professionals in health centres, which may have led to this counterintuitive result. In a setting where stigma and the use of traditional medicine practices remain widespread, proper information and fostering help-seeking by specialised personnel (i.e. psychologists and psychiatrists) is still a necessary focus [31]. Moreover, in the 'mental health awareness' sub-area of our semi-structured interview analysis, the AYAs showed a greater sensitivity and sense of inclusion toward people with mental illness that was paralleled by an understanding that it is important to counsel them or refer them to seek professional support at health units. With a treatment gap estimated at 85% in LMIC, promoting dialogue about mental health (thereby reducing stigma), alongside increasing help-seeking behaviour, community ownership, and responsibility for good mental health, are key steps to improving the mental health of the community itself [32].

Many factors contribute to the promotion of mental health; among them, social and emotional learning is recognised to be pivotal in adolescents [33]. Indeed, this age period is characterised by major hormonal and physical changes that are coupled with a substantial change in the social environment. In this context, the peer network plays a crucial role in the adolescent's life and well-being [34]. The need to improve social and emotional learning is also recognised by adolescents themselves in LMICs; in a focus group study, adolescents identified developing social-emotional skills, especially in interpersonal relationships, as their main need toward good mental health [35].

In this context, psychodrama proved to be a useful approach to improve social and emotional learning. In the semi-structured interviews, AYAs stated that the participation in these sessions enhanced their sharing and self-expression ability and communication skills, resulting in two main areas – peer-to-peer support and social empowerment. Considering the 12 sub-areas we identified in our content analysis, they fall within the society-level actions required by the 'helping adolescents thrive toolkit' proposed by WHO to improve adolescent mental health [7]. These are interpersonal, emotional regulation, and higher-order thinking skills (e.g. decision-making, problem-solving), self-esteem, and coping. According to the sub-areas found in the semi-structured interviews, psychodrama sessions influenced all of the above dimensions. These dimensions act in the outermost level of the social-ecological system according to Bronfenbrenner's theory, meaning on the individual as they are embedded in a specific sociocultural environment. This can create an environment that enables promotion and prevention in mental health, leading to the concept of 'community mental health competence' [36]. Mental health is indeed a shared resource promoted by a competent community. These psychodrama sessions enabled AYAs to gain knowledge, practical skills, and empowerment in actively taking care of their own mental health and in creating relational contexts in their community that promote it. Through this intervention, we intended to promote AYAs as actors taking an active role in promoting their mental health and that of their community. Indeed, the empowerment of adolescents is recognised as fundamental to their mental health and resilience, and it promotes social inclusion and harmony [28]. Available evidence supports the role of community-based psychodrama

in improving personal skills such as empathy, self-awareness, increasing social skills, and understanding one's strengths and weaknesses, thus fostering emotional and cognitive integrity [37]. Furthermore, psychodrama has been found to address well-being and hopelessness, with a positive effect on both. Hopelessness is a particularly important aspect to consider in Mozambique, which is among countries with the highest incidence of suicide deaths in sub-Saharan Africa, as it is believed to be one of the predictors of suicide [38]. Improving social and emotional learning is one of the most effective strategies recognised globally for suicide prevention and suicide risk reduction at community level [8,39].

We found no differences in the effect of the psychodrama intervention based on HIV serostatus. Increased self-connection and emotional awareness and the creation of a group feeling free from judgement (and thus stigma) is particularly helpful for AYALHIV, as it creates a feeling of acceptance within themselves and by others [40]. Furthermore, integrating mental health interventions into those for HIV has been shown to have mutually beneficial effects both on mental health itself and on improving adherence to antiretroviral therapy with better quality of life [41].

The psychodrama intervention proposed here was well-accepted by the participants, with a high participation rate (approx. 94%). The greatest burden was related to transport and its cost for those who lived far away. The early difficulties in practising some techniques, such as the double and the role reversal, were overcome over time, and the interviews suggested that AYAs were willing to continue the course and extend it to other AYAs because of its positive effect on the community. The challenge of adopting an intervention model developed in a different cultural context was also overcome through the sessions being held by the CHWs. This made it possible to have group leaders embedded in the local sociocultural background and to reach more AYAs at a lower cost. The employment of CHWs is a key strategy for the large-scale implementation of culturally oriented mental health interventions [30].

This study has some limitations. First, it was monocentric, conducted only in the city of Beira, so it is not representative of the whole national context. Second, although all three questionnaires have been previously used in sub-Saharan Africa and LMICs, no cultural validation was conducted in Mozambique, so some of the items may not be fully appropriate for this setting. Moreover, the absence of a control group does not allow the entire effect observed to be attributed to the intervention. Finally, the open-ended nature of semi-structured interviews may lead the interviewer to steer the questions, with consequent observer bias, while the respondents may attempt to answer in the way they think is acceptable, leading to a social desirability bias. However, the use of a mixed methodological approach was useful in limiting the biases arising from both the use of the questionnaires and the qualitative content analysis of the interviews.

The use of psychodrama and action methods is effective in raising awareness about mental health. Through specific strategies based on group dynamics work and participatory methods, AYAs can improve their socioemotional functioning and empower their resilience and coping strategies toward major mental health stressors. These kinds of interventions can be well accepted and well-integrated into the LMIC context thanks to a culturally oriented approach and the involvement of the community.

CONCLUSIONS

This psychodrama intervention proved to be effective in enabling AYAs with better knowledge about mental health and improving their ability to recognise and describe emotions. This may improve related outcomes in AYAs and spread a positive culture towards mental health. The intervention was equally effective in AYALHIV or AYAHIV–, making it useful for promoting mental health in such an at-risk group. The use of CHWs helped us culturally adapt the intervention method developed in a different context, resulting in good acceptability and feasibility. Consequently, the AYAs showed willingness to continue the sessions and extend them to more people. It is important to continue to foster community interventions that address the social and emotional learning of the AYAs to create a competent community that can promote mental health and care for its members by serving as an additional preventive instrument for related disorders and suicidal risk.

PAPERS

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Ethics statement: This study was approved by the Inter-institutional Bioethics Committee for Health of Sofala (ComitéInterinstitucional de Bioética para Saúde, CIBS – Sofala) on the 21 of July 2023 (protocol number 007/CIBS/2023). Written informed consent was provided by all the participants.

Data availability: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authorship contributions: RB, AS, MG, and CM conceptualised and designed the study. RB and CM made substantial contributions to original writing. RB was responsible for the data analysis. AS and CM contributed to qualitative data analysis. HC, IC, and CA contributed to data collection. GP and DD supervised the study phases. AZ, GB, CG, and MG reviewed the study critically and contributed to data interpretation. All authors critically reviewed the study.

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Additional material
Online Supplementary Document

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Effectiveness of the Hypertension Screening Corner in Enhancing the Cascade of Care at Primary Healthcare Center Level: Evidence from Zambezia, Mozambique

PAPER

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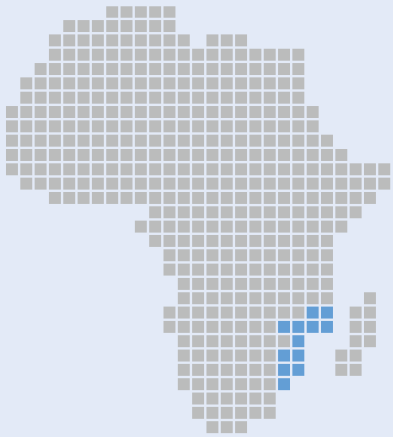

Effectiveness of the Hypertension Screening Corner in Enhancing the Cascade of Care at Primary Healthcare Center Level: Evidence from Zambezia, Mozambique

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ABSTRACT

Background: Hypertension is the leading cause of cardiovascular disease, whose death burden is dramatically increasing in sub-Saharan Africa. To curb its effects, early diagnosis and effective follow-up are essential. Therefore, this study aims to evaluate the impact of a hypertension screening corner on the hypertension care cascade at the primary healthcare level.

Methods: A prospective cohort study was conducted between October 2022 and March 2023 in two PHCCs in Zambezia (Mozambique). The study involved a demographic and socioeconomic status (SES) questionnaire for those screened. Patients with blood pressure (BP) ≥ 140/90 mmHg were given a follow-up questionnaire regarding the care cascade. The four cascade steps were: medical visit, diagnosis confirmation, follow-up visit, and recalling the follow-up appointment. The odds ratio (OR) of reaching each step of the cascade was assessed by binomial logistic regression.

Results: Patients with BP ≥ 140/90 mmHg were 454, and 370 (86.0%) completed both study phases. Individuals attending the medical visit were 225 (60.8%). Those with low SES had a higher probability of visit attendance than those with middle (OR = 0.46, 0.95CI[0.23–0.88] p = 0.020) and high (OR = 0.21 0.95CI[0.10–0.42], p < 0.001). Hypertension diagnosis was confirmed in 181 (80.4%), with higher probability in the low SES group compared to the middle (OR = 0.24 IC95[0.08–0.66], p = 0.007) and high (OR = 0.23, IC95[0.07–0.74], p = 0.016) groups. The OR to complete step 1 and step 2 were higher for older age groups. A follow-up appointment was received and recalled by 166 (91.7%) and 162 (97.6%) patients, respectively.

Conclusions: The hypertension corner proved to be a useful tool for effective screening of hypertension with satisfactory retention in care, especially for people with lower socio-economic status.

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INTRODUCTION

Noncommunicable diseases (NCDs) are responsible for 41 million deaths every year, accounting for 74% of all deaths globally. Of these, 77% occur in low- and middle-income countries (LMIC) [1]. Cardiovascular disease (CVD) is the leading cause of death among NCDs, and hypertension is one of its major causes [2]. According to data from the Global Burden of Disease 2019, between 1990 and 2019, disability-adjusted life years (DALYs) due to high systolic blood pressure decreased by 34% in high-income countries, while it increased by 24% in low- and middle-income countries (LMICs) [3].

The burden of NCDs in the African region is mainly due to the epidemiological transition linked to globalization and lifestyle changes, with an increased prevalence of risk factors such as unhealthy diets, insufficient exercise, dyslipidemia, and obesity [4]. Moreover, other risk factors such as pollution and urbanization are emerging [4]. In addition, systemic factors such as the lack of services and human and material resources, as well as socio-economic factors, make sub-Saharan Africa one of the areas with the lowest rate of access to care and consequently with a higher risk of CVD death [5].

The prevalence of hypertension is rising globally, and the WHO reports a prevalence of hypertension of 27% in the African region [6]. In Mozambique, despite the population being very young (63.3% under 24 years) [7], a prevalence of hypertension between 14.1% and 25.2% has been reported [8, 9]. Although older age is a known risk factor for hypertension, it was found that in Mozambique, blood pressure measurement and diagnosis is more common among younger age groups (36.2% and 13.6% respectively in those aged 20–30 years) than older ones (23.3% and 5.8% in those over 60 years) [9].

There are numerous studies on the prevalence and determinants of hypertension in sub-Saharan Africa (SSA), but information on hypertension awareness, treatment, and control is limited [10, 11]. Low awareness contributes to low treatment and control rates, influenced by a poor network of public health facilities, poor distribution of essential drugs, and poor access to care [12]. Key actions in the response to NCDs include primary prevention, early diagnosis, and appropriate treatment. Despite an increase in the NCD visits in LMICs, access to healthcare for chronic disease remains low with primary healthcare centers (PHCC) playing a pivotal role in disease control and prevention [13]. Screening campaigns can help increase awareness of the risks associated with hypertension and the benefits of early diagnosis and management [14].

In Mozambique, a new approach was tested introducing the *hypertension corner* (HC), a suitably equipped space at the entrance to the PHCCs. At the HC a trained community healthcare worker invites and measures blood pressure (BP) to all adults consenting to do so, using an automatic BP machine. If the BP is higher than 140/90 mmHg in two subsequent measurements, the person is referred to the appropriate outpatient clinic. A pilot study reported a significant increase in the number of new hypertensive patients diagnosed by the health center in 6 months after the introduction of the HC [15].

The cascade of care, or continuum of care, is a model used to assess patient retention through the sequential steps of care required to achieve a positive outcome. The cascade is used to identify areas where there are gaps in care delivery and to implement improvement interventions. It can be used to assess the effectiveness of a population screening intervention. In LMICs, it has been suggested that the care cascade should also include the screened population, in addition to those connected to quality care and those adhering to prescribed treatment, allowing for a better measurement of the coverage and performance of health systems [16].

Therefore, the primary objective of this study is to evaluate how the screening strategy implemented in Zambezia, Mozambique, through the hypertension corner, influences the cascade of care for patients with high blood pressure. Secondary objectives are the description of the beneficiaries of the hypertension corner and the evaluation of sociodemographic and socioeconomic factors that may influence each step of the cascade of care.

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METHODS

STUDY DESIGN

A prospective cohort study was conducted to assess the impact of the *hypertension corner* on the hypertension cascade of care from October 2022 to March 2023 in Quelimane, province of Zambezia, Mozambique.

POPULATION AND SETTING

The study was conducted in two PHCCs in the city of Quelimane, namely the "17 de Setembro" PHCC and the "Coalane" PHCC, where the hypertension corner was active.

Mozambique is a country in south-eastern Africa and is divided into ten provinces. Quelimane is the capital city of Zambezia, a region in the north of Mozambique. It has an estimated population of 350,000 inhabitants, 36,7% of whom are over 25 years of age [17].

Individuals aged 25 years or older who accessed the PHCC were considered eligible for this study. Before being enrolled in the cohort, they were asked by a community health worker (CHW) located in the hypertension corner to sign an informed consent to participate. The exclusion criteria were declining to participate, not being able to give informed consent, and already being treated for chronic diseases (i.e., diabetes, cardiovascular diseases, chronic respiratory diseases, thyroid diseases, and neoplastic diseases).

DATA COLLECTION

The study recruitment took place in the HC located at the PHCC and consisted of two phases. First, people underwent blood pressure measurements by a trained CHW on a voluntary basis and, if their blood pressure was equal or above 140/90 mmHg after the second measurement, they were asked to participate in the study; if they agreed, they signed the informed consent and were given a questionnaire. The following information was collected: socio-demographic characteristics, household and individual socioeconomic factors, and knowledge and habits regarding hypertension **(Annex 1)**. Subsequently, all patients with high BP were referred to the chronic diseases outpatient clinic to confirm hypertension. Phase two of the study consisted of a second questionnaire on the management and treatment of hypertension. The second questionnaire **(Annex 2)** was either filled out at the health unit after the medical examination or by telephone two weeks after the positive screening by the same trained CHW.

STEPS OF THE CASCADE OF CARE

The treatment cascade for hypertension consisted of five steps:

- **Stage 0: Positive screening**. After PHCC access and hypertension screening, subjects who tested positive for hypertension screening were referred for specialist consultation.
- **Stage 1: Underwent the medical visit**. Patients could go to the specialist outpatient clinic on the same day as the screening or within the following 15 days.
- **Step 2: Confirmed diagnosis**. If the diagnosis was confirmed after a third BP measure, the doctor explained the hypertension disease to the patient and prescribed the necessary treatment.
- **Stage 3: Received a follow-up appointment**. The patient with hypertension received an appointment for a follow-up visit to monitor symptoms and check the treatment.
- **Stage 4: Recalled the follow-up appointment**. The patient can recall the follow-up appointment date.

VARIABLE DEFINITION

Hypertension was defined as a blood pressure measurement equal to or higher than 140 mmHg for systolic and 90 mmHg for diastolic in two 5-minute repeated measurements. The CHW was trained accordingly to the WHO guidelines using an automated BP machine with an adequate cuff size [18].

Socioeconomic status (SES) was measured based on the available literature (papers from research conducted in LMICs dealing with the creation of an SES index were included),

considering household and individual factors, such as education and employment [19, 20]. Education and employment were assessed according to International Standard Classifications [21, 22]. The most common jobs in Mozambique have been included and ordered according to the relative rank and income of each occupation [19]. The SES index was built using principal component analyses (PCA) of the abovementioned variables, and then categorized into wealth tertile (low, medium, high) [23].

Basic knowledge of hypertension and its risk factors was assessed by asking each individual what the most common symptoms of hypertension were (i.e., headaches and dizziness) and how important a low-salt diet was. The index ranged from 0 to 4.

STATISTICAL ANALYSIS

The descriptive analysis of the sample used frequencies and proportions for qualitative variables; means and standard deviation, or medians and quartiles for quantitative variables.

Differences in sample distribution were tested with the t-test or Mann-Whitney test for continuous variables and the χ^2 or Fisher's exact test for categorical variables, as appropriate.

The multivariable association between individual characteristics and the steps of the cascade of care was explored using binomial logistic regression, including all variables. The response variables were medical consultation (yes/no), confirmed diagnosis (yes/no), follow-up appointment (yes/no), and recalling the appointment (yes/no). Independent variables were age, sex, and SES index categories. Results were presented as odds ratio (OR) with 0.95 confidential interval (CI). Post-hoc pairwise comparison between SES index and age groups in the logistic regressions was carried out through Tukey's test.

A p-value < 0.05 was considered significant. All analyses were performed using the R software (version 4.1.1).

ETHICS

The inclusion of a patient in this protocol did not require any additional exams or invasive medical procedure besides those normally needed for clinical routine. The research was performed following the ethical standards of the 1964 Declaration of Helsinki and was approved by the Institutional Bioethics Committee for Health (Comité Institucional de Bioética para a Saúde, CIBS) – Zambezia, on September 9, 2022 (protocol number 97/CIBS-Z/22).

RESULTS

SAMPLE CHARACTERISTICS

In the study period, 6,659 individuals were BP screened and 454 (6.8%) presented a blood pressure ≥140/90 mmHg. After applying the inclusion/exclusion criteria, 430 individuals were included in the study (Figure 1).

Of these, 275 (64.0%) were female. The descriptive data of the sample are summarized in Table 1.

Females had a significantly higher prevalence of SES index low, (47.2% vs. 15.2%). Indeed, women were more likely to be illiterate (40.7% vs. 14.3%) and had a higher prevalence of subsistence farming as the main household income (63.3% vs. 26.0%).

The mean knowledge index score was 2.02 (SD = 0.77), i.e., most individuals considered a low-salt diet to be relevant (n = 365, 84.9%). However, few have been able to correctly identify at least one symptom of hypertension (n = 81, 18.8%). In the study sample, knowledge of hypertension differed significantly according to SES index, being higher in the high group than in both the low and middle groups ($p < 0.001$).

There were no differences according to sex ($p = 0.627$) and age ($p = 0.175$).

Of the 430 people who tested positive for hypertension, 329 (76.5%) were asymptomatic, 72 (52.5%) had already taken antihypertensive drugs in the past, 137 (31.8%) were aware of their condition, and 150 (34.9%) had never had their blood pressure measured. There were no significant differences between those who had and those who had not had their blood pressure measured by sex ($p = 0.213$), age ($p = 0.423$), or SES index ($p = 0.470$).

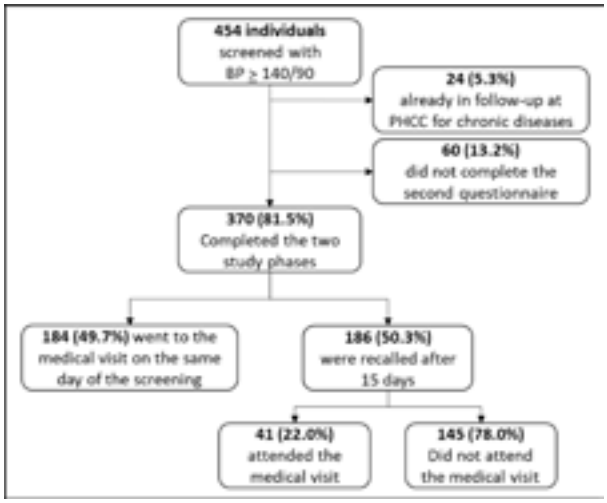

Figure 1 Flowchart of study inclusion criteria. BP = Blood pressure, PHCC = Primary Health Care Center.

Table 1 Number and frequencies of the socioeconomic status (SES) index group and variable included in SES index estimation distinguished by sex.

	FEMALES (n = 275)	MALES (n = 154)	OVERALL (n = 430)
SES index (NA = 81)			
Low	107 (38.9)	16 (10.4)	123 (29.6)
Medium	79 (28.7)	27 (17.5)	106 (28.6)
High	50 (18.2)	70 (45.4)	120 (27.9)
Education (NA = 1)			
Illiterate	112 (40.7)	22 (14.3)	134 (31.2)
Primary school	67 (24.4)	39 (25.3)	107 (24.9)
Middle school	54 (19.6)	39 (25.3)	93 (21.6)
High school	29 (10.5)	36 (23.4)	65 (15.1)
University or higher	13 (4.7)	18 (11.7)	31 (7.2)
Employment (NA = 35)			
Subsistence agriculture	22 (8.0)	22 (17.5)	203 (47.2)
Self-occupied	175 (63.6)	27 (26.0)	65 (15.1)
Formal paid work	25 (9.1)	40 (15.6)	80 (18.6)
Unemployed	30 (10.9)	50 (12.3)	44 (10.2)
Household variables			
Non-perishable ceiling (NA = 2): yes	233 (84.7)	144 (93.5)	377 (87.7)
Washable floor (NA = 3): yes	133 (48.4)	90 (58.4)	223 (51.9)
Telephone (NA = 1): yes	176 (64.0)	137 (89.0)	313 (72.8)
Television (NA = 2): yes	170 (61.8)	113 (73.4)	283 (65.8)
Electricity (NA = 9): yes	244 (88.7)	138 (89.6)	373 (86.7)
Running water (NA = 1): yes	190 (69.1)	129 (83.8)	319 (74.2)
Toilet (NA = 2)			
With a washable floor	68 (24.7)	27 (17.5)	95 (22.1)
With perishable ceiling	191 (69.5)	124 (80.5)	315 (73.2)
None	15 (5.5)	2 (1.3)	17 (3.9)
Means of transport (NA = 16)			
None	188 (68.4)	68 (44.2)	256 (59.5)
Motorbike	42 (15.3)	50 (32.5)	92 (21.4)
Moto	44 (16.0)	39 (25.3)	83 (19.3)
Car	8 (2.9)	9 (5.8)	17 (3.9)

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THE CASCADE OF CARE

The two phases of the study were completed by 370 (86.0%). There were significant differences between the group of those who completed the study and those who did not, according to sex and SES index (Table S1). Of those who completed the study, the majority were women (62.0%, p = 0.041) and from the middle (34.4%) and high (33.8%) SES index categories (p < 0.001). No differences were found between the two groups according to age (p = 0.423).

STEP 1: UNDERWENT THE MEDICAL VISIT

After the positive screening, 225 (60.8%) underwent the recommended medical examination (Figure 2). Reported barriers to accessing healthcare were lack of time (n = 89, 61.4%), lack of recommendations (n = 30, 20.7%), lack of symptoms (n = 17, 11.7%), lack of willingness (n = 8, 5.5%), and reported inability to locate the healthcare unit (n = 1, 0.7%).

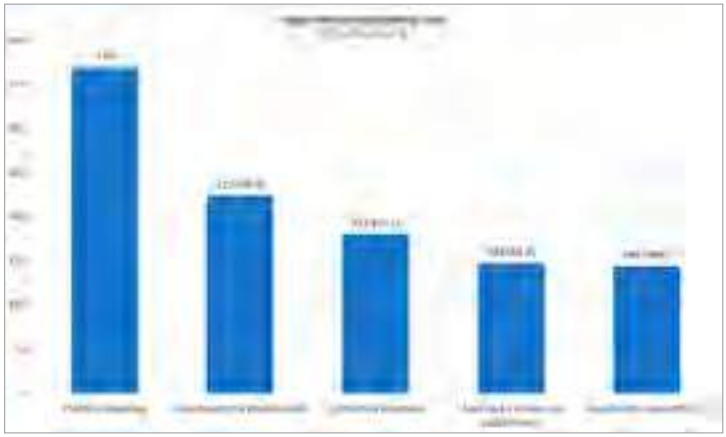

Figure 2 Number and percentage of patients meeting the inclusion criteria distinguished according to each step of the hypertension care cascade.

The probability of attending the visit was influenced by age and SES (Figure 3). Individuals aged over 35 years were more likely to attend the visit than those in the 25–34 age group (Table 2). The probability of attending the visit was lower for those from the high SES group compared to both middle (OR = 0.35, 0.95CI 0.16–0.76 p = 0.004 and low (OR = 0.21, 0.95CI 0.09–0.49, p < 0.001). No differences were found based on sex (p = 0.140).

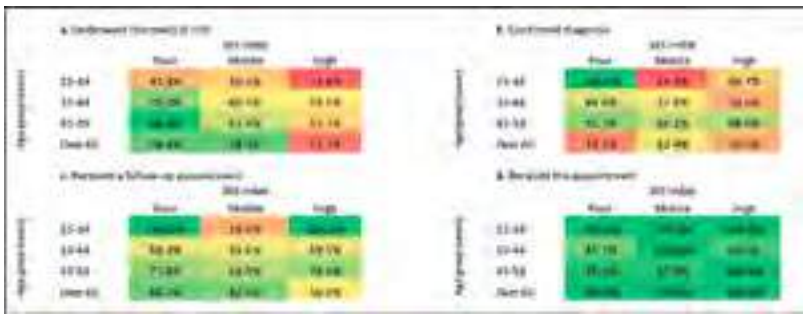

Figure 3 Proportion of participants with hypertension-positive screening who fulfilled each cascade step, stratified by age group, and SES index group. The color scale ranges from red (0.0%) to green (100%).

STEP 2: CONFIRMED DIAGNOSIS

A total of 181 out of 225 (80.4%) persons had the diagnosis of hypertension confirmed and 107 (59.1%) reported being informed about the diagnosis during the visit. The probability of having a hypertension diagnosis confirmed was influenced by age and SES, but not sex (p = 0.487).

The age group 45–59 years had a higher probability of a confirmed diagnosis than those aged between 25–45 years (Table 2). The probability of having the hypertension diagnoses confirmed was lower for both middle (OR = 0.28, IC95 0.08–1.02, p = 0.054) and high (OR = 0.21, 0.95CI 0.05–0.87, p = 0.027) SES groups compared to the low SES group.

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	OR	0.95CI	p-VALUE
1 step – Underwent medical consultation			
Age groups (years)			
AG2 – AG1	4.43	1.41–13.88	0.005
AG3 – AG1	3.95	1.41–11.03	0.003
AG4 – AG1	3.41	1.08–10.77	0.032
AG3 – AG2	0.89	0.38–2.11	0.986
AG4 – AG2	0.77	0.27–2.17	0.915
AG4 – AG3	0.86	0.35–2.11	0.974
Sex(Female)			
Male	1.56	0.87–2.23	0.140
SES index			
Middle – Low	0.59	0.26–1.32	0.270
High – Low	0.21	0.09–0.49	<0.001
High – Low	0.35	0.16–0.76	0.004
2 step – Confirmed diagnosis			
Age groups (years)			
AG2 – AG1	2.39	0.41–14.02	0.585
AG3 – AG1	9.34	1.61–54.24	0.006
AG4 – AG1	5.54	0.84–36.77	0.092
AG3 – AG2	3.91	1.08–14.15	0.033
AG4 – AG2	2.32	0.49–11.08	0.507
AG4 – AG3	0.59	0.13–0.74	0.816
Sex(Female)			
Male	1.37	0.58–3.39	0.487
SES index			
Middle – Low	0.28	0.08–1.02	0.054
High – Low	0.21	0.05–0.87	0.027
High – Low	0.75	0.23–2.43	0.831
3 step – Received a follow-up appointment			
Age groups (years)			
AG2 – AG1	0.73	0.13–4.01	0.964
AG3 – AG1	1.64	0.33–8.22	0.856
AG4 – AG1	2.81	0.47–16.90	0.449
AG3 – AG2	2.25	0.78–6.50	0.201
AG4 – AG2	3.84	0.98–15.03	0.055
AG4 – AG3	1.71	0.50–5.77	0.670
Sex(Female)			
Male	0.91	0.43–1.92	0.794
SES index			
Middle – Low	0.56	0.21–1.47	0.336
High – Low	0.92	0.30–2.80	0.981
High – Low	1.64	0.57–4.67	0.511

(Contd.)

	OR	0.95CI	p-VALUE
4 step – Recalled the appointment			
Age groups (years)			
AG2 – AG1	0.00	0–inf	1.000
AG3 – AG1	0.00	0–inf	1.000
AG4 – AG1	1.20	0–inf	1.000
AG3 – AG2	3.00	0.23–38.69	0.668
AG4 – AG2	$1.09e^{8}$	0–inf	1.000
AG4 – AG3	$3.64e^{7}$	0–inf	1.000
Sex(Female)			
Male	0.33	0.03–3.26	0.997
SES index			
Middle – Low	2.17	0.10–47.13	0.824
High – Low	4.31	0.18–100.68	0.522
High – Low	1.98	0.06–62.15	0.887

Table 2 Results of the logistic regression models fitted on the four hypertension care cascade steps (yes/no) as dependent variables and age class, sex, and socioeconomic status (SES) index group as potential determinants. Post-hoc pairwise comparison was carried out through Tukey's test. AG1 = 25–34 years, AG2 = 35–44 years, AG3 = 45–59 years, AG4 = over 60 years.

STEP 3: RECEIVED A FOLLOW-UP APPOINTMENT

Individuals who reported receiving a follow-up appointment were 148 (81.8%). This probability was not influenced by sex, age nor SES (Table 2).

STEP 4: RECALLED THE FOLLOW-UP APPOINTMENT

Of the 148 patients who stated that they had a scheduled follow-up visit, only 3 (2.0%) could not remember the date. The next visits were scheduled after one month for 114 (78.6%) patients and the following week for 31 (21.4%). The probability of remembering the exact date of the follow-up was not influenced by sex, age, or SES group (Table 2).

DISCUSSION

MAIN FINDINGS

Through the analysis of the hypertension care cascade, this study evaluated the impact of a hypertension screening strategy (namely "hypertension corner") implemented in two PHCCs in Quelimane, Mozambique. The first step (undergoing the recommended medical visit) was completed by 60.8% of individuals screened positive and 80.4% were confirmed with a diagnosis of hypertension (second step). The last two steps (receiving a follow-up appointment and recalling the appointment) were fulfilled by 81.8% and 98.0% of the patients in the previous step, respectively.

HYPERTENSION BURDEN AND SCREENING STRATEGIES IN LMICs

Implementing new screening strategies for hypertension is crucial in LMICs, where chronic diseases are steadily increasing. In 2020, approximately 19.1 million deaths were attributed to CVD globally, with SSA being one of the regions with the highest mortality rates (345.8 to 475.7 per 100,000) [24, 25]. Moreover, the African region is the WHO region with the highest prevalence of hypertension, at 27% [6]. In Mozambique, the prevalence of hypertension in young adults (aged 18–25) was 14.1% and 21.0% in women and men, respectively [8]. In the general population (aged over 20), a prevalence of 15.7% in women and 16.1% in men was observed [9].

The burden of hypertension on a vulnerable healthcare system is increased by the long-time hypertension can remain asymptomatic before presenting symptoms and complications. To decrease the burden of hypertension in these settings, it is essential to increase the rates of diagnosis, treatment, and disease control. The proposed targets for 2025 in Africa are to achieve

a hypertension diagnosis rate of 80%, a treatment rate among diagnosed patients of 80%, and a disease control rate among treated patients of 80% [26]. The Hypertension Corner was effective in increasing the number of people the PHCC was able to include in the care cascade and in approaching the first two objectives mentioned above, as 60.8% of people with positive screening for hypertension went to the recommended visit and of these, 80.4% confirmed the diagnosis of hypertension.

By implementing different screening strategies, it is possible to reach wider segments of the population and increase awareness of hypertensive disease. A nationwide study conducted in Mozambique in 2015 found an awareness rate of hypertension of 14.5%, a treatment rate of 50.1%, and a control rate of 44.5% of treated patients [27]. Awareness in our sample was 38.5%; consisting of people who had been previously diagnosed with hypertension but were no longer under treatment at the time of the study. In addition, 34.9% of people had never had their blood pressure measured. Among the barriers to access to care reported in our study, those with the most striking support from the literature are the distance from health centers, lack of resources, and lack of adequate knowledge [28]. The implementation of awareness-raising interventions helps to increase treatment and control rates and to spread awareness of chronic diseases such as hypertension among the population [12].

HYPERTENSION CASCADE OF CARE

In the first step of the care cascade, 60.8% of individuals with high blood pressure underwent the recommended medical examination. Previous studies in SSA have shown that population-based interventions for hypertension screening are an effective tool for improving mid-term outcomes in low-resource settings. [29]. The probability of undergoing the recommended visit was influenced by socioeconomic factors, with individuals with a lower SES being more likely to attend. This is an interesting finding, as higher SES is generally associated with greater access to care. Previous studies have shown that barriers to accessing screening for cervical and breast cancer in SSA include socioeconomic factors, such as low education, low income, and poor access to services [28, 30]. The presence of a hypertension screening point at PHCC such as the HC could be a useful strategy to reach a disadvantaged population, i.e., those with low SES, who need tailored interventions to improve retention in care, as they are most at risk of not accessing health services.

Despite no differences being found based on sex, females are one of the populations most at risk regarding health provision and access. Indeed, in our sample, there were significant differences in SES between females and males the first having a lower level of education and lower-paying occupations. In sub-Saharan Africa, access to treatment is low for women, at 23% in East African states, resulting in females being disproportionately affected by CVD in terms of mortality, with a 15% excess of CVD deaths [31, 32].

Individuals with a positive screening for hypertension were sent for a medical visit to the same PHCC where they were screened. Of the individuals who underwent the suggested examination, 80.4% were confirmed as having hypertension. The probability of diagnosis confirmation was lower for the “medium” and “high” SES categories than for the “low” category, and increased with age. Both age and socio-economic status are well-known risk factors in the literature [33]. Lower SES is associated with a higher risk of hypertension and higher blood pressure in LMICs, although some regional differences were found [34, 35]. In particular, the greatest influence of SES on hypertension was due to the education level (pooled OR = 2.02, 0.95CI 1.55–2.63) and its burden was higher in women [36].

Once an individual enters the hypertension care cascade, it is crucial that they receive information about their condition and promote their retention in care. This is necessary to maintain high rates of adherence to therapy and, consequently, disease control. This approach contributes to reducing the long-term complications of the disease and its burden on one’s life and the health care system [37]. In our sample, 91.7% of patients with a confirmed diagnosis of hypertension received a follow-up appointment. This figure shows the possibility of healthcare providers to effectively attend to patients seen in the outpatient clinic and the PHCC’s capability to support these visits. In the last step of the care cascade, almost all those who had been scheduled for a follow-up visit remembered the visit date.

Access to care in Mozambique is also influenced by the geographical distribution of PHCC, as up to 66.7% of the population is underserved by these health services [38]. Therefore, investing in primary health care is key to ensuring universal health coverage. This can be done through continuous monitoring and evaluation of the PHC system [39].

STUDY LIMITATIONS

The study has some limitations. First, the study was carried out in only two PHCCs in the city of Quelimane. Subsequent studies involving more facilities and different areas could strengthen the result and expand its generalizability Secondly, the group that completed the two phases of study differed from those lost to follow-up in terms of SES. This could result in selection bias. However, the three categories of SES identified were equally represented in the final sample. Lastly, data on follow-up visits and clinical outcomes were not collected so to better assess the effectiveness of this intervention future studies should include also these endpoints.

CONCLUSIONS

Hypertension screening is critical in sub-Saharan Africa to address the increasing prevalence of hypertension, increase awareness and education about the disease, improve access to health services, and ultimately reduce the burden of cardiovascular diseases and their complications on individuals and societies. The hypertension corner, a screening tool for the health center-attending population, has proven to be a useful tool for effective hypertension screening with satisfactory retention in care, especially for people with lower socio-economic status. Nevertheless, given the low prevalence of hypertension found, future studies should conduct a cost-effectiveness analysis of this screening strategy. A screening point at the PHCC level can increase diagnosis and treatment rates and ultimately reduce the burden of non-communicable diseases on the health care system, reaching a vulnerable population at higher risk for NCDs and its complications.

DATA ACCESSIBILITY STATEMENT

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

ADDITIONAL FILE

The additional file for this article can be found as follows:

- **Annexs.** Annex 1 and Annex 2. DOI: https://doi.org/10.5334/gh.1339.s1

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

AS and RB made substantial contributions to data interpretation and analysis and to original writing. LR contributed to study conceptualization and design and to data interpretation. AM and FK contributed to data collection. AR and EM reviewed the study critically. PM and NJ contributed to study design and data collection. GP supervised the study phases AD contributed to study conceptualization and design and to data interpretation. All authors reviewed the study critically.

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Septic cardioembolic stroke secondary to infective endocarditis in a young patient with rheumatic heart disease: a case report

PAPER

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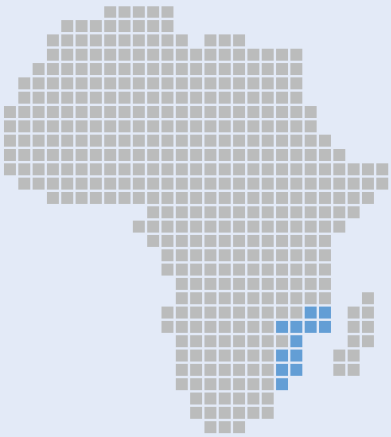

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Case Report

Septic cardioembolic stroke secondary to infective endocarditis in a young patient with rheumatic heart disease: a case report

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Abstract

The risk of stroke due to infective endocarditis is particularly high during the first week. Moreover, in low-resource settings where imaging access is limited, and diagnostic pathways are inaccurate the risk further increases. In addition to antibiotic therapy, treatment may include intravenous thrombolysis, with high risk of hemorrhagic complications in patients with infective endocarditis or mechanical thrombectomy. We report here a case of a 24-year-old male with rheumatic heart disease presenting a septic cardioembolic stroke secondary to infective endocarditis that was successfully treated in a low-resource setting.

Keywords: infectious diseases and tropical medicine; cardiology and cardiovascular systems

Introduction

Cerebral ischemic events are among the most common presenting symptoms and a main cause of death of infective endocarditis, although stroke secondary to infections remain a rare condition [1]. Although the increase access to advanced neuroimaging allows the detection of silent early-stage cerebral embolism, clinically manifest stroke remains the classic presentation especially in low-resource settings where the imaging access is limited and diagnostic pathway often inaccurate [2]. Moreover, it is estimated that the risk of stroke due to infective endocarditis remains high (4.8/1000 patient-days) during the first week of antibiotic therapy and then declines rapidly [3]. Stroke secondary to infections is likely a result of embolism by migration of fragments vegetation and/or mycotic aneurysm rupture [1]. The main cerebrovascular complications include meningitis, intracerebral abscess, encephalopathy, hemorrhage and aneurysms with consequent high risk for intracranial bleeding [4]. In infective endocarditis the higher rate of cerebral embolic events are associated with *Staphylococcus aureus* when the anterior leaflet of the mitral valve is affected [5]. Interestingly, the most common location of ischemic events is the middle cerebral artery although also multifocal or distal ischemic events may occur [5]. Based on clinical and functional presentation and health general status, in addition to antibiotic therapy, treatment may include intravenous thrombolysis or mechanical thrombectomy [5].

We report here a case of a 24-year-old male with rheumatic heart disease presenting a septic cardioembolic stroke secondary to infective endocarditis that was successfully treated in a low-resource setting.

Case report

A 24-year-old male presented with sudden onset of muscle strength loss in the left hemi body, found fallen early in the morning, complaining of intense holocranial headache and fever, followed by drowsiness and hypo-responsiveness. He reported that he was attending outpatient follow-ups at the local health center for two months due to epigastric pain diagnosed as gastritis. He was previously healthy, with no smoking or alcohol habits, nor chronic diseases. He was not taking corticosteroids or other immunosuppressive medications. The examination showed drowsiness, clear and coherent speech, with gaze diverted to the right, mydriatic pupils reactive to light, deviation of the lip commissure to the left and facial asymmetry with facial paralysis to the left. Gait not assessable, with muscle strength at 1/5, with neck stiffness and preserved sensitivity. His body temperature was 38.9°C, blood pressure 90/55 mmHg, heart rate 90 bpm. A 5/6 murmur was detected in the 2nd and 5th intercostal space in the left mid-clavicular line, with thrill throughout the precordial area. Biochemistry revealed leukocytosis with neutrophilic predominance, moderate anemia,

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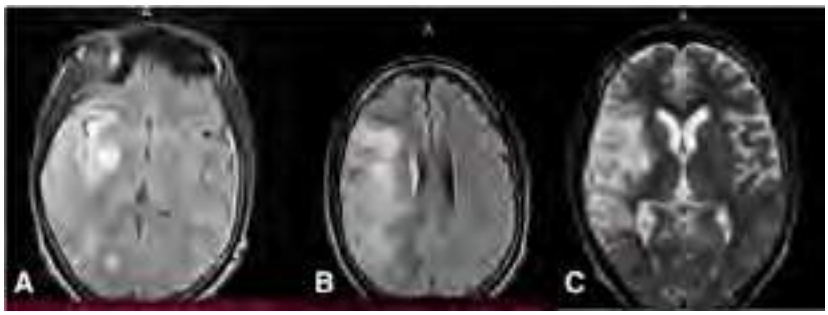

Figure 1. Magnetic resonance showing the cerebral lesion at admission (**A**) and after 14 (**B**) and 33 (**C**) days.

mild hyponatremia and hypochloremia. Malaria, HIV and Covid-19 tests were negative, but he had a positive blood culture for *S. aureus*, sensitive to Ceftriaxone. Cardiac ultrasound revealed carditis with vegetations on the mitral and aortic valves. Magnetic resonance imaging (MRI) showed an extensive lesion in the area of the right middle cerebral artery and occipital with extensive perilesional edema (Fig. 1A). He was first treated with Ceftiaxone 2 g twice per day, Gentamicin 160 mg/day, Mannitol 20% 80 ml each four hour, lactate ringer 2 l/day, Aspirin 100 mg/day, Simvastantin 20 mg/night, Lisinopril 5 mg/day, Paracetamol 1 g each six hours and Omeprazole 20 mg/day.

After 5 days of treatment, there was a clinical improvement, he was awake, cooperative, apyretic, with no neck stiffness or headache; The focal neurological deficit with left hemiparesis persisted and he started physiotherapy. On the 14th day, he had improvement in muscle strength with 3/5 in the upper limb and 2/5 in the lower limb. Control MRI showed edema reduction with areas of cerebritis. (Fig. 1B). Ultrasound confirmed chronic rheumatic heart disease with severe mitral insufficiency and mild to moderate aortic insufficiency. Ceftriaxone was suspended and ciprofloxacin 500 mg twice per day was started for 14 days. On the 33rd day MRI showed hypersignal in the territory of the middle cerebral artery, with rediffusion and without cerebral edema (Fig. 1C). On the 35th day he was discharged with outpatient follow-up.

Discussion

The most important factor in managing cardioembolic stroke secondary to infective endocarditis is timing in terms of proper diagnosis and adequate treatment. In particular, the early administration of effective intravenous antibiotics allows to reduce mortality and morbidity from embolic complications and heart failure [5]. In the present case, the patient presented a full-blown symptomatic stroke including sudden and complete hemiparesis associated with fever, neck stiffness, altered level of consciousness and heart murmur. Such presentation raised the suspicion of cardiac involvement and, as expected, diagnosed, with subsequent MRI confirmation, a cardioembolic stroke secondary to infective endocarditis likely developed during previous weeks based on reported clinical history. On the one hand, this reiterates the lack of adequate tools for diagnosis, the lack of trained medical professionals and the absence of an effective referral system in low-resource settings. On the other hand, it significantly reduced the chances of a favorable outcome for the prognosis. In this case, ultrasound played a crucial role in diagnosis orientation, in line with previous evidence on the versatility of this diagnostic tool that can be easily employed in extremely resource-limited settings where radiological and microbiological investigations are scarce [6]. Moreover, the patient presented with large vessel occlusion and, at the time of writing, there is no consensus on the gold standard management for similar cases. Indeed, for in-patients with acute ischemic stroke treatment with intravenous thrombolysis is suggested; in patients with infective endocarditis particular attention must be paid due to the high risk of hemorrhagic complications [7]. An option to be considered for these patients could be a mechanical thrombectomy [7]. While the first option was not performed by choice, there was no possibility to consider the second option due to lack of equipment. In low-resource settings, limited equipment is common, reducing favorable prognosis [8]. Immediately, even before having confirmation of positive culture for *S. aureus*, the patient commenced an intravenous antibiotic therapy with Ceftriaxone and Gentamicin which proved to be lifesaving in this case. Indeed, the patient conditions improved significantly after 4–5 days of therapy institution and no complication such as heart failure or valve rupture developed.

This successful case highlights on one hand the proper management of such complicated and late-stage condition, and on the other hand the necessity to continuously train and support health professionals across low-resource settings. Onsite healthcare workers training is crucial to avoid "brain drain" as well as to avoid training on different standards of practice and ultimately to encourage a sense of belonging and professional growth. In particular, for this specific condition, a recent history of strep infection or rheumatic fever is the key to hypothesize the diagnosis of rheumatic heart disease. Moreover, symptoms of rheumatic fever vary and typically begin one to six weeks after a bout of strep throat and, in some cases, the infection may have been too mild to have been recognized, or it may be gone by the time the person sees a medical practitioner. These considerations reinforce the importance of appropriate training for health professionals especially in remote areas and make mandatory a call to action to all involved institutions to improve and increase the efforts to achieve universal health care coverage.

Conflict of interest

All authors declare no conflict of interest.

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Ethical approval

No approval is required.

Consent

Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images.

Guarantor

Evangelina Namburete.

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Nutrition

The challenge of tuberculosis diagnosis in malnourished children: employing clinical scores in Tosamaganga Hospita

POSTER AND ORAL PRESENTATION

Conference
European Congress of clinical microbiology and infectious diseases

Location
Barcelona, Spain

Presentation date
April 2024

Authors
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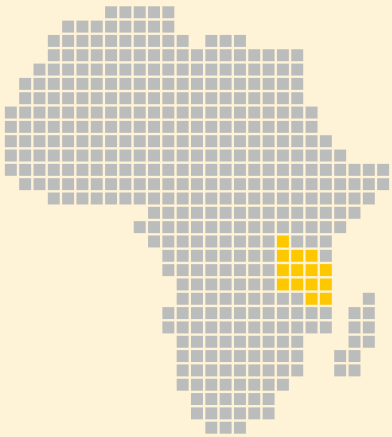
Focus country
Tanzania



Children with Special Healthcare Needs among malnourished pediatric patients: a challenge for healthcare personnel to provide tailored and holistic care

POSTER AND ORAL PRESENTATION

Conference
National Human Resources for Health (HRH) Conference

Location
Dar es Salaam, Tanzania

Presentation date
July 2024

Authors
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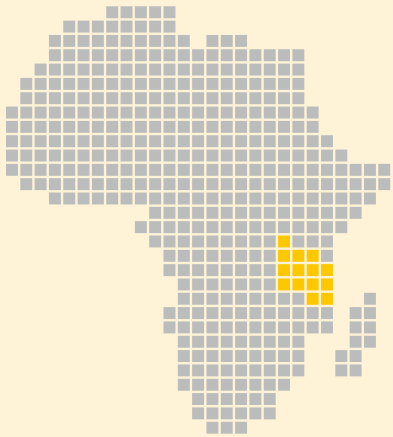
Focus country
Tanzania



Children with special healthcare needs in the population of severe acute malnourished at Tosamaganga regional referral hospital, rural Tanzania: characteristics, anthropmetrics and outcomes

POSTER AND ORAL PRESENTATION

Conference
UNICEF: Building brighter futures: Evidence for children

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Presentation date
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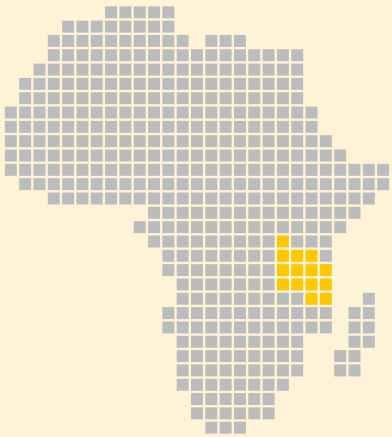
Focus country
Tanzania



Children with Special Healthcare Needs nella popolazione di pazienti trattati per malnutrizione acuta presso l'ospedale di Tosamaganga, Tanzania: studio retrospettivo di caratteristiche, antropometria

POSTER AND ORAL PRESENTATION

Conference
SIP - 79esimo Congresso Italiano di Pediatria

Location
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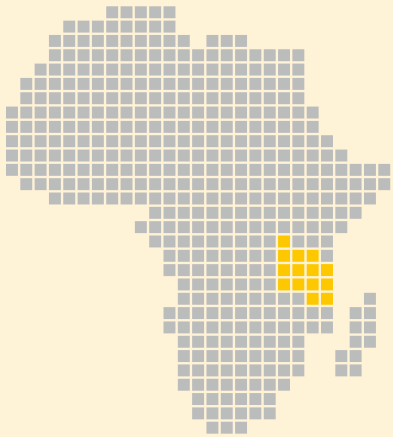
Focus country
Tanzania



Children with Special Healthcare Needs among patients admitted for acute malnutrition in rural Tanzania: retrospective analysis of population characteristics and outcomes

POSTER AND ORAL PRESENTATION

Conference
Tanzania Health Summit

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Zanzibar, Tanzania

Presentation date
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Authors
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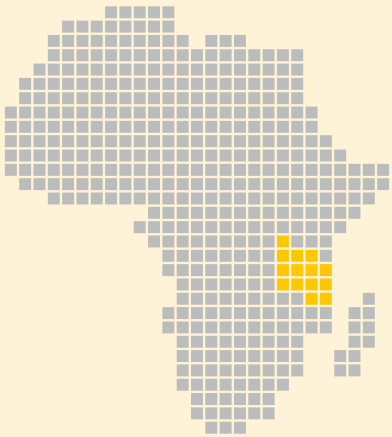
Focus country
Tanzania



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Focus country
Italy

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Focus country
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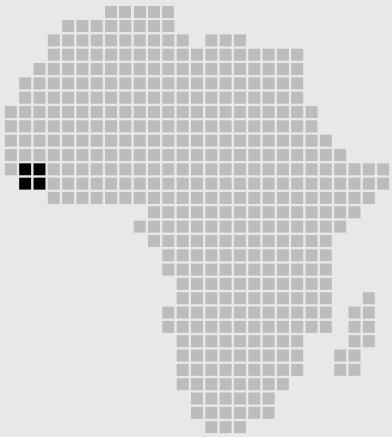

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“While predictive models can provide possible scenarios with respect to climate change and epidemics, there has been little research thus far on the ability of local communities to adapt to and mitigate these impacts.”

“Modelli predittivi sul clima e le epidemie ci possono dire molto sugli scenari possibili, tuttavia rimane poco studiato l’aspetto legato alle comunità locali e al modo in cui riescono ad adattarsi e a mitigare gli effetti di questi cambiamenti”.