Field research

Papers, abstracts and posters from cooperation activities in Africa - 2018

MEDICI CON L'AFRICA CUAMM
Doctors with Africa

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Padua, February 2019

«We have to deal with emergency situations – wars, epidemics and refugee crises – but that's not all. The most dire problem we confront every day is persistent poverty. So solidarity means helping local communities find solutions to their problems today to make sure they will have a better tomorrow».

"Solidarity and Benefaction"
by ***Don Luigi Mazzucato***
in CUAMM News, Health and Development no. 2-3, May-December 1996, p. 76

RESEARCH FOR A HEALTHIER TOMORROW

"People have a big problem understanding the relationship between quality and systems". These are the words of Avedis Donabedian, probably the most authoritative figure in the field of medicine to work on the topic of quality in healthcare. Born a century ago in Beirut, Lebanon, after his family fled from the Armenian genocide, Donabedian, a Christian, grew up side by side with Jews and Palestinians, developing an approach to life characterized by a deep interest in dialogue, friendship, intellectual curiosity and poetry. The simple but powerful conceptual model he would go on to devise for evaluating the quality of health care was based on three measures: *structure* (the care delivery setting, including facilities, equipment and organizational methods), *process* (care delivery in terms of timeliness, appropriateness, completeness and continuity) and *outcome* (the effects of care on the health status of patients). This still valid framework later served as a basis for quality in healthcare research.

The first research conducted on Western healthcare systems revealed a huge divide between the services provided and their quality, underscoring the unjustifiable – and most importantly preventable – consequences of that divide in terms of morbidity and mortality, including suffering and disability, added social and institutional costs and a growing loss of public trust in healthcare systems. Numerous initiatives were subsequently undertaken in an attempt to close or at least narrow the divide, from health facility certification and accreditation processes, evidence-based medicine, continuous quality improvement and clinical governance to patient-centered care. Good results have been achieved and useful research conducted thus far, although Western healthcare systems continue to function in a precarious manner, burdened by challenges including the public's growing distrust in science and recourse to self-treatment.

Today the international focus on quality has shifted – and appropriately so – to low and middle income countries as well, with studies showing that the 8.6 million deaths there in 2015, representing a loss of approximately US$ 6 trillion, could have been prevented through healthcare. Six out of ten of these deaths were attributable to poor-quality care rather than to insufficient access to care. There were various aspects to the former, including poor adherence to guidelines, the unavailability of diagnostic and therapeutic means and a lack of focus on the centrality of patients. The data spoke loud and clear: two out of five pregnant women were examined more than an hour after delivering; just half of health workers followed guidelines correctly in the case of the clinical management of diarrhea in children, with that number falling in the case of malaria and anemia; 56% of women who underwent prenatal visits did not receive the minimum essential package of services; and glucometers and urine test strips were available in less than half of primary healthcare facilities. As for the centrality of patients, one third of the latter were found to have had poor experiences including long waiting times, inadequate communication and a lack of respect (including abusive behavior) by care providers. In addition, urgent, complex clinical situations were frequently left untreated due to a lack of continuity between services and assistance levels. Last but not least, with regard to equity and inequalities, it was the poor – individuals, families and communities – who accessed poor-quality care most frequently, suffering the consequences. The message underlying all this research is that it will be impossible to achieve universal health coverage if changes are not made in terms of policies, programs, data-gathering and the use of healthcare quality improvement research.

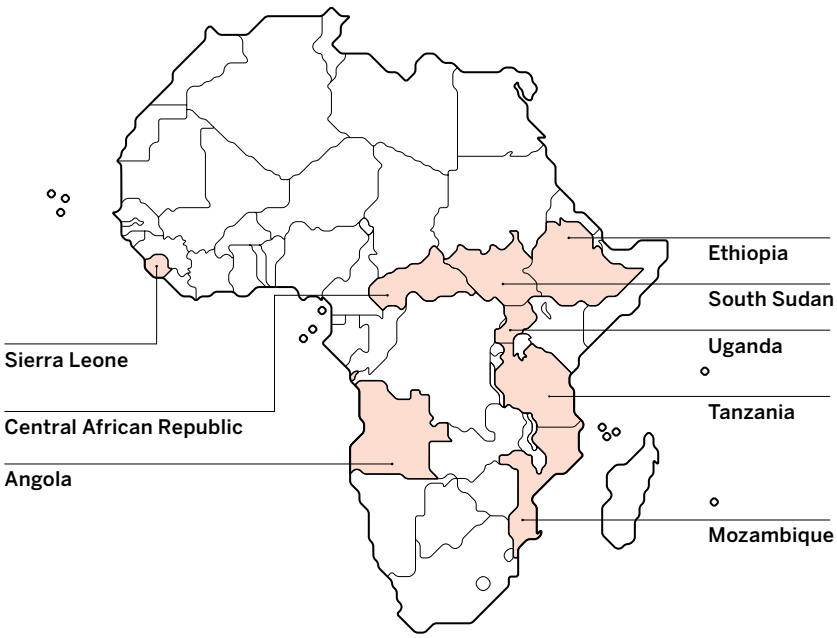
Given the deep and vital relationship between systems and quality, it seems clear that calls for the right to primary healthcare access must be accompanied by equally forceful ones for the right to quality healthcare. Doctors with Africa CUAMM has pondered this matter for years now; one need only glance at the research we conducted and published in 2018 to grasp how central the topic of quality is for our organization, and how crucial we believe it is to delve deep into the opportunities and limitations posed by each of the settings in which we work. Thus the type of research we've been developing – operational research – becomes even more valuable, thanks to its ability to dive into real-life contexts, identifying critical areas and seeking out evidence-based, quality solutions that help bring about improved systems even in the most remote parts of Africa.

In closing, let's turn once more to the words of Avedis Donabedian: *"Systems awareness and systems design are important for health professionals, but they are not enough. It is the ethical dimensions of individuals that are essential to a system's success. Ultimately, the secret of quality is love. You have to love your patient, you have to love your profession, you have to love your God".* This statement still holds as true as ever, and aligns perfectly with CUAMM's own history and vision. Enjoy your reading.

Don Dante Carraro
Director, Doctors with Africa CUAMM

Giovanni Putoto
Head of Operational Planning and Research

Doctors with Africa CUAMM



Doctors with Africa CUAMM currently operates in Angola, Central African Republic, Ethiopia, Mozambique, Sierra Leone, South Sudan, Tanzania and Uganda.

23
hospitals

64
districts (for public health activities, mother-child care, the fight against HIV/AIDS, tuberculosis and malaria, training)

3
nursing schools

1
university (Mozambique)

605
international professionals

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 8 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**.

Operational research in 2018

5 main thematic areas, **23 published studies, 7 posters** and **7 oral presentations** shared at conferences in Italy and abroad. Operational field research carried out with over 30 Italian, African and other international partners to **improve the quality of our interventions** on the ground and help **develop effective health policies** even in countries with limited resources.

- Maternal and child health
- Infectious and tropical diseases
- Universal coverage and equity
- Nutrition
- Chronic diseases

YOUTH, QUALITY, GROWTH: OUR APPROACH TO FIELD RESEARCH

"Youth", "quality" and "growth": if we were asked to describe **CUAMM's operational research in 2018** in just a few words, those are the ones we would choose.

2018 was undoubtedly the year of **youth** in terms of our research activities in Africa, with numerous young people under the age of 35, doctoral students, residents and junior doctors **serving as research team members** and authoring medical publications, applying their budding skills in the service of that continent and the vital research our organization conducts there. This brings to mind the words of the great journalist – and great friend of CUAMM – Pietro Veronese, who once used the term "**field campus**" while discussing our organization's approach to health cooperation; a place, that is, where highly qualified and committed professionals work "on the ground", studying, learning and training themselves and others to ensure that some of the world's most marginalized communities will get the health services they need. Indeed, the idea of moving out of the classroom and into the field to test one's nascent competences, undertaking **research**, **hard work** and **study** in unfamiliar and often difficult settings, has begun to appeal to growing numbers of talented young people. And this too is a form of solidarity, something that in the words of CUAMM's long-time (1955-2008) director Don Luigi Mazzucato meant "helping local communities find solutions to their problems today to make sure they will have a better tomorrow".

Quality, an aspect mentioned often in this collection, is our second keyword for 2018. A critical factor in ensuring effective **health services** both in Italy and in low and middle income countries, it is also an area in which health inequities are particularly manifest. Several pieces in this collection center on the issue of quality, including one by Cavicchiolo et al that highlights the weak link in a Mozambican hospital's process for neonatal resuscitation, i.e. the poor quality of care provided by inadequately-prepared healthcare workers, and another by Cavallin et al that investigates risk factors for mortality in children with suspected cases of malaria, and also underscores the need to invest in training human resources to ensure that they are able to handle complex risks and guarantee quality care. This leads us at CUAMM to reflect further on how we envision research, i.e. as a tool for **identifying critical aspects in the healthcare process**, as Donabedian might put it, and for taking steps to improve services in our firm belief that **medicine in poor countries should never be poor-quality medicine**.

As we review our scientific output of the last twelve months, one more keyword springs to mind: **growth**. At **23**, in fact, the total number of **publications** in 2018 once again surpassed that of previous years. Each was the result of cooperative efforts with Italian, African and other international organizations, undertaken to bring **research expertise to settings where there is a dearth of it**, assessing their critical points and identifying pathways to improvement. Alongside our published papers in 2018, CUAMM launched an important partnership with the publisher Springer whereby a chapter on our work during the recent Ebola epidemic in Sierra Leone will be included in a volume entitled *Pregnant in the Time of Ebola: Women and Their Children in the 2013-2015 West African Epidemic.* Dialoguing with others who also operate within precarious health systems, and collaborating together on an entire volume (perhaps the only one, as Springer has pointed out) to discuss the effects of the epidemic on mothers and their children marked an important step forward for us, a challenge that started from a specific case and went on to look at the functioning of **healthcare systems** in general as well as how they hold up during emergencies.

CUAMM's participation at conferences also grew In 2018, with 14 different presentations, half of which were oral and the other half poster presentations. Our thematic focus grew too: two studies dealt with **adolescent health**, exploring both the complex issue of teenage pregnancy and HIV prevention and treatment in adolescents, in a reflection of the growing international interest in this key population group and its needs, both health and otherwise (there are some 1.8 billion individuals aged 10-19 years worldwide, and it is estimated that this figure will grow by 18% by 2040). Another subject examined – one that is very dear to CUAMM, and which we intend to investigate further in the upcoming years – is **neonatal stimulation**. Indeed, **early child development**, a form of medicine that is "low-cost" yet promises valuable outcomes, is an area of critical importance especially in low-income countries. Last but not least, CUAMM has done **measles** research in partnership with the Bruno Kessler Foundation, looking into the health impact on poor communities of their **distance from healthcare facilities**.

What are we looking forward to in terms of our research activities in 2019? **Networking**, an integral part of our approach to field work from the start, will continue to be an important watchword, with CUAMM committed as always to building up a network of **healthcare experts** who believe in the power of our profession to **bring about positive change**, and engaging them, young people and universities in order to bring quality healthcare to Africa.

TABLE OF CONTENTS

Maternal and child health

POSTER PRESENTATIONS

58

01 → Mozambique
7th ICCN – International Conference on Clinical Neonatology,
Turin – Italy, May 23rd – 26th 2018
- Galeazzo B. et al., *Neonatal hyperglycemia as predictor of 4-weeks mortality in a low resource setting*

60

02 → Ethiopia
51st Italian Conference SITI – Italian Society for Hygiene,
Riva del Garda – Italy, October 17th – 20th 2018
- Dalla Zuanna T. et al., *Case-control study to assess the effectiveness of maternity waiting homes in reducing perinatal mortality at the Wolisso Hospital (South West Shoa Zone, Oromia Region, Ethiopia)*

ORAL PRESENTATIONS

01 → Sierra Leone
XVII Italian Conference of the SIMIT (National Society of Infectious and Tropical Diseases),
Turin – Italy, December 2nd – 5th 2018
- Di Gennaro F. et al., *Maternal caesarian section infection (MACSI) in Sierra Leone: a case control study. Preliminary data of the first 5 months of the study*

02 → Uganda
5th Annual National Healthcare Quality Improvement Conference,
Kampala – Uganda, December 4th – 6th 2018
- Ariko A.I. et al., *Strengthening Neonatal Intensive Care Unit to improve on the quality of care for Sick Newborns: A case of Kiryandongo Hospital, Kiryandongo District*

03 → Uganda
5th Annual National Healthcare Quality Improvement Conference,
Kampala – Uganda, December 4th – 6th 2018
- Wamboya D. et al., *Improving partograph use to reduce perinatal mortality: a case of Anyiribu Health Centre III, Arua District, Uganda*

04 → Mozambique
1st International Conference on Social Determinants of Health – Medicus Mundi International,
Maputo – Mozambique, December 5th – 7th 2018
- Fogliati P. et al., *Inequitable access to antenatal services in rural primary health care facilities in northern Mozambique. Findings from a community and health facility assessment in Cabo Delgado Province.*

63

Infectious and tropical diseases

PAPERS

Infectious and tropical diseases

POSTER PRESENTATIONS

141

Universal coverage and equity

PAPERS

142

01 → Uganda

Biggeri M. et al., **Assessing the feasibility of community health insurance in Uganda: A mixed-methods exploratory analysis**, in *Social Science & Medicine*, January 2018

POSTER PRESENTATIONS

144

01 → Italy

XV Congresso della Società Italiana di Medicina delle Migrazioni,
Catania – Italy, April 18th – 21st 2018

- Cavagna C. et al., *Doctors with camper vans (CUAMM): itinerant primary healthcare service for migrant farm workers in the Foggia (Apulia) area*

146

02 → Italy

51st Italian Conference SITI – Italian Society for Hygiene,
Riva del Garda – Italy, October 17th – 20th 2018

- Bertoncello C. et al., *Network initiatives to help build a new culture of health in Italy's Veneto Region: the "Train of Health"*

ORAL PRESENTATIONS

01 → Mozambique

X Conferência Científica UEM,
Maputo – Mozambique, September 26th – 28th 2018 Maputo

- De Meneghi G. et al., *Pattern of domestic violence from 2011 to 2015 in Beira, Mozambique*

149

Nutrition

PAPERS

150

01 → Uganda

Wanzira H. et al., **Quality of care for children with acute malnutrition at health center level in Uganda: a cross sectional study in West Nile region during the refugee crisis**, in *BMC Health Services Research*, July 2018

ORAL PRESENTATIONS

01 → Uganda

5th Annual National Healthcare Quality Improvement Conference,
Kampala – Uganda, December 4th – 6th 2018

- Wangubo A. et al., *Improving reporting on nutrition indicators into the health management information system using the continuous quality improvement approach: A case of Nakapiripirit District*

161

Chronic diseases

PAPERS

162

01 → Mozambique
Ferro J. et al., **Frequency and pattern of gynecologic cancers from 2010 to 2014 in Beira, Mozambique**, in *Current Gynecologic Oncology*, January 2018

168

02 → Mozambique
Muhelo A.R. et al., **Successful management of a parasitic ischiopagus conjoined twins in a low-income setting**, in *Clinical Case Reports*, January 2018

175

03 → Mozambique
Antunes M. et al., **Bilateral Mastectomy as Radical Treatment of Gynecomastia Secondary to Antiretroviral Therapy in a Low Income Setting: A Case Report**, in *Drug Safety - Case Reports*, May 2018

180

04 → Multi-Country
Rigato M. et al., **Characteristics, prevalence, and outcomes of diabetic foot ulcers in Africa. A systemic review and meta-analysis**, in *Diabetes Research and Clinical Practice*, August 2018

ORAL PRESENTATIONS

01 → Mozambique
X Conferência Científica UEM,
Maputo – Mozambique, September 26th – 28th 2018
• De Meneghi G. et al., *Physical injury and depression in six low-middle income countries*

Maternal and child health

Gastroschisis Spiral-like Closure with Umbilical Cord in a Limited-resource Setting: A Case Report

PAPER

Authors
Reggiani G., Pizzol D., Trevisanuto D., Antunes M.

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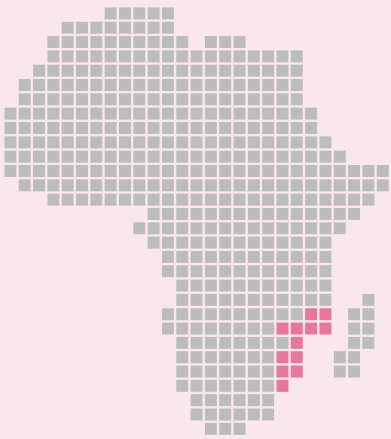
Maternal and child health

Focus country
Mozambique



Abstract

Gastroschisis is a birth defect of the abdominal wall that involves the incomplete closure of the abdominal muscles and skin. It is one of the most common surgical problems arising in infants, and its incidence is increasing worldwide. Management of the condition in limited-resource countries is often complicated, with much higher mortality rates than those found in wealthier countries.

The present case involved a newborn with a very large gastroschisis where the surgical procedure to close the abdominal wall was carried out using umbilical tissue. Although this technique has not been used before in limited-resource settings, it seems to be a viable, low-cost solution to the problem, particularly in order to reduce the risk of infection and of the main potential complication: abdominal compartment syndrome, which consists of increased intra-abdominal pressure and the consequent impairment of the functioning of the abdominal organs.

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OPEN ACCESS

CASE REPORT

Gastroschisis Spiral-like Closure with Umbilical Cord in a Limited-resource Setting: A Case Report

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ABSTRACT

Gastroschisis is one of the most frequent congenital surgical problems in fetuses and neonates, with a continuously increasing incidence worldwide. In limited-resource settings, the management of this condition is difficult, and the mortality rates are much higher than those observed in high-income countries. We report the case of a newborn with gastroschisis and viscero-abdominal disproportion, submitted to abdominal wall closure through utilization of umbilical cord tissue. This technique has not already been applied in low-resource countries, where it can show advantages such as lower risk of abdominal compartment syndrome and local infection, high availability, and low cost.

Key words: Gastroschisis; Intra-abdominal pressure; Limited-resource setting; Umbilical cord

INTRODUCTION

Abdominal wall defects, mainly represented by gastroschisis and omphalocele, are the most frequent congenital surgical problems in fetuses and neonates [1]. Gastroschisis is a full-thickness defect of the abdominal wall, typically on the right side of a normally inserted umbilical cord, resulting in protrusion of the abdominal organs into the amniotic cavity without a covering membrane [1].

During the past decades, the incidence of gastroschisis has steadily increased worldwide reaching values from 2 to 5:10000 live births [2]. The risk factors for gastroschisis can be subdivided into sociodemographic, mainly young maternal age and low socioeconomic status, and teratogenic ones, such as maternal smoking, alcohol, cocaine, aspirin, ibuprofen, and some vasoconstricting drugs.

Gastroschisis can be easily diagnosed antenatally during routine ultrasound monitoring, with a detection rate of 90% within the second trimester of pregnancy in developed countries. Prenatal diagnosis allows planning of early referral to a tertiary multidisciplinary center with maternal-fetal medicine, genetic counseling, neonatology, and pediatric surgery. No clear evidence supports elective preterm delivery or cesarean section in the absence of obstetric indications [1].

The gold standard surgery for newborns with gastroschisis is still to be identified, and the choice of the strategy usually depends on the degree of viscero-abdominal disproportion. The main options include primary closure and preformed silo placement with gradual visceral reduction before abdominal wall closure [1].

The leading complications of gastroschisis and its surgical treatment can be classified into: Gastrointestinal, related to intestinal damage and effects of prolonged parenteral nutrition; respiratory, caused by impairment of respiratory mechanics since intrauterine life and sudden increase of intra-abdominal pressure after closure of the abdominal wall defect; and infectious, due to loss of anatomical defense mechanisms, use of prosthesis, and central venous lines [3]. These complications account for gastroschisis-related mortality and long-term morbidity. In high-resource countries, the overall post-natal survival estimates of newborns with gastroschisis reach approximately 90–95%, but complex cases present worse outcomes [1].

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In limited-resource countries, although the quantity and quality data are lacking, the gastroschisis mortality rate seems to be much higher [4].

We report the case of a newborn presenting simple gastroschisis, with viscero-abdominal disproportion, who was submitted to closure of the abdominal wall defect through a new technique of utilization of the umbilical cord in a limited-resource setting.

CASE REPORT

A male term neonate, with low birthweight, home delivery, was taken to the Central Hospital of Beira for congenital malformation. The initial examination revealed gastroschisis, with protrusion of stomach, small bowel, cecum, and appendix, associated with viscero-abdominal disproportion. The viscera were wrapped in common non-sterile bandages. At presentation, newborn was in critical condition with severe hypothermia (33°C), desaturation, and dehydration. He was stabilized through heating, oxygen administration, fluid resuscitation, and first-line antibiotic therapy. About 20 h later, he was participated to surgical closure of the abdominal wall defect by means of umbilical cord (that had been left long), under general anesthesia wherein a longitudinal opening of the umbilical cord, dissection, and ligature of the umbilical vessels with reduction of the protruding viscera into the abdominal cavity was done. The suture of the umbilical tissue around the abdominal wall defect followed by spiral-like arrangement of the cord and final closure was done (Figure 1). No intraoperative complication was detected. At the end of the intervention, the intravesical pressure increased to 20 cm H_2O, while 24 h later, it decreased to 17 cm H_2O. In the early post-operative phase, the newborn succumbed to death owing to severe sepsis and hyperglycemia.

DISCUSSION

Congenital anomalies, and in particular gastroschisis, represent a significant contributor to the avertable global burden of disease profile [4]. The disparity in survival rates of neonates with gastroschisis between high-income and low-income countries is evident. In Sub-Saharan Africa, mortality rates of newborns with gastroschisis range from 35% to 100% and septicemia represents one of the most common complications and causes of death in limited-resource settings [4,5].

In low-income countries, the management of neonates with gastroschisis is difficult due to poor prenatal diagnosis, late referral to tertiary centers through unappropriate transport system, shortage of neonatal intensive care facilities, dearth of trained surgeons, support personnel and surgical equipment, and higher risk of sepsis [6].

Figure 1: The operative technique and its result. (a) Spiral-like arrangement of the umbilical cord around the abdominal wall defect. (b) Final result of the intervention. (c) Appearance of the abdominal wall 24 h after the operation

The surgical strategy plays a central role in the management of newborns with gastroschisis, but the gold standard intervention has not been identified and contrasting data have been reported. In fact, a review showed no significant difference in outcome between the use of preformed silos and other types of surgical treatment [7], while other authors suggested potential major benefit of primary closure over silo placement followed by delayed closure [8]. Considering the risk of abdominal compartment syndrome due to the presence of viscero-abdominal disproportion, the primary closure is not always possible and it represents a critical problem, especially in low-resource settings, where surgeons usually adopt custom silos [6]. Gastroschisis spiral-like closure with umbilical cord is an affordable alternative. In case of successful reepithelialization, this strategy represents a primary closure; otherwise, the infant could require a second surgical step for definitive closure of the abdominal wall defect.

Different techniques of umbilical cord utilization for closure of gastroschisis have previously been reported [9,10], but to the best of our knowledge, this is the first application in a limited-resource setting. It could represent a good practice as the collocation of the umbilical tissue around the abdominal wall defect in a spiral-like way can allow a primary closure of the defect avoiding excessive increase of intra-adominal pressure and therefore reducing the risk of abdominal compartment syndrome and respiratory complications. This aspect is particularly important in low-resource centers, where ventilatory support usually is not available.

Another advantage of this procedure is represented by the use of autologous tissue, with reduced risk of local infection, high availability, and low cost. These characteristics make this surgical strategy affordable in limited-resource settings. To apply this technique, it is essential to educate the obstetricians of primary and secondary health-care services to early send newborns with gastroschisis to the referral center and to leave the umbilical cord as long as possible.

Finally, although the surgery procedure was successfully performed, with an acceptable intra-abdominal pressure, our patient died because of sepsis, one of the most common complications of gastroschisis in limited-resource settings.

In conclusion, in patients with gastroschisis, especially in case of viscero-abdominal disproportion, the use of the umbilical cord for the repair of the abdominal wall defect is an option that is easily applicable and affordable even in limited-resource settings. To have the chance to perform this technique and to obtain an acceptable survival rate, without waste of resources, it is crucial to create an integrated and multidisciplinary approach and to train all the involved health workers, in particular obstetricians who should refer patients with gastroschisis early and leave the umbilical cord as long as possible.

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Thermal Effect of a Woolen Cap in Low Birth Weight Infants During Kangaroo Care

PAPER

Authors
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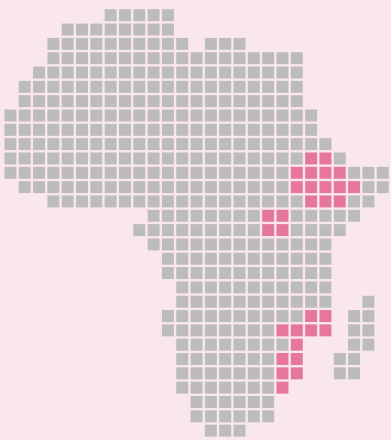

This paper is not available as open access, which is why only an abstract is posted. If you would like to read the entire paper, please go to the web page given and follow the instructions.

Abstract

The sub-Saharan African region has some of the world's highest rates of neonatal mortality, with neonatal hypothermia being one of the leading causes of death in preterm infants. The aim of this randomized controlled trial (RCT) was to assess the effectiveness of using woolen caps and booties together with the kangaroo mother care (KMC) method in order to keep the body temperature of premature newborns in the standard range.

Three hundred low-birth-weight infants about one week of age were randomly assigned to two groups, those with a woolen cap (CAP [150]) and those without (NOCAP [150]) in the hospitals of Wolisso (Ethiopia), Aber (Uganda) and Beira (Mozambique) from December 2015 to September 2016.

5,064 measurements were recorded during the study, and showed that the mean time spent in the normal thermal range was 55% for the CAP group and 56% for the NOCAP group.

The use of woolen caps does not seem, therefore, to have brought any significant advantages in terms of maintaining safe body temperatures in infants treated with the KMC method.

Thermal Effect of a Woolen Cap in Low Birth Weight Infants During Kangaroo Care

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abstract

BACKGROUND AND OBJECTIVES: World Health Organization guidelines recommend covering the head during kangaroo mother care (KMC), but the effect of a cap on neonatal thermal control during KMC remains to be defined. Our objective was to assess the effectiveness and safety of a woolen cap in maintaining low birth weight infants (LBWIs) in normal thermal range during KMC.

METHODS: Three hundred LBWI candidates for KMC in 3 African hospitals were randomly assigned to KMC with (CAP group) or without (NOCAP group) a woolen cap in a 1:1 ratio during the first week after birth. Axillary temperature was measured every 6 hours. Maternal and room temperature and adherence to skin-to-skin contact were registered at the same time points.

RESULTS: A total number of 5064 measurements were recorded (median 19 measurements per subject; interquartile range: 10–25). Mean time spent in normal temperature range was 55% (SD 24) in CAP and 56% (SD 24) in NOCAP groups. Multivariable analysis estimated a rate ratio of 0.92 (95% confidence interval: 0.84 to 1.00; $P = .06$) for the effect of the cap versus no cap on time spent in the normal temperature range.

CONCLUSIONS: In these 3 African, low-resource settings and so many days post birth, the use of a woolen cap was safe but provided no advantages in maintaining LBWI in the normal thermal range while being in a KMC ward. LBWIs spent only half of the time in the normal temperature range despite warm rooms and skin-to-skin contact. Maintaining normothermia in LBWIs remains an unfinished challenge in low-resource settings.

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Headquarters of Doctors with Africa CUAMM is located in Padua, Italy; a representative agency is located in each African country where Doctors with Africa CUAMM supports projects.

Mr Cavallin was responsible for the statistical design and analysis, drafted the manuscript, and contributed to the interpretation of the results; Miss Segafredo contributed to the design of the trial, coordinated and supervised data collection, and critically reviewed the manuscript; Dr Pizzol contributed to the design of the trial and to the submission to the ethics committee, led the study team in Beira, Mozambique, coordinated and supervised data collection, and critically reviewed the manuscript; Dr Massavon contributed to the design of the trial and to the submission to the ethics committee, led the study team in Aber, Uganda, coordinated and supervised data collection, and critically reviewed the manuscript; Dr Lusiani contributed to the design of the trial and to the submission to the ethics committee, led the study team in Wolisso, Ethiopia, coordinated

WHAT'S KNOWN ON THIS SUBJECT: Kangaroo mother care (KMC) is a low-cost intervention recommended for neonatal temperature maintenance. World Health Organization guidelines recommend covering the head during KMC, but this practice is not consistently followed. The thermal effect of a cap during KMC remains unknown.

WHAT THIS STUDY ADDS: The use of woolen caps did not provide any advantages in maintaining low birth weight infants in the normal thermal range during KMC in low-resource settings. Low birth weight infants spent only half of the time in the normal temperature range despite warm rooms and skin-to-skin contact.

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The At Risk Child Clinic (ARCC): 3 Years of Health Activities in Support of the Most Vulnerable Children in Beira, Mozambique

PAPER

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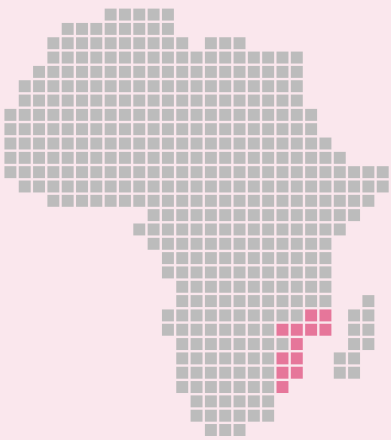

Abstract

Africa has the world's highest burden of risk factors for poor child development and health, most of which are associated with infectious diseases and the social environments in which children live.

This study analyzed the activity volumes of 15 at-risk child clinics (ARCCs) in Beira, Mozambique, in order to determine the health profiles of the children using their services from January 2015 to December 2017.

A total of 17,657 first visits were taken into consideration, 12,300 (69.7%) of which for HIV exposure, 542 (3.1%) for tuberculosis, 1,664 (9.4%) for moderate acute malnutrition (MAM), 772 (4.4%) for severe acute malnutrition (SAM) and, finally, 2,542 (14.4%) for other risk factors.

Because children represent the most vulnerable population segment, a constant focus should be kept on their health needs, especially in developing countries.

Mozambique's ARCCs could function as strategic hubs from which to better understand the health needs of young patients as well as to monitor the quality of care provided to them.

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Brief Report

The At Risk Child Clinic (ARCC): 3 Years of Health Activities in Support of the Most Vulnerable Children in Beira, Mozambique

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Abstract: The concept of "children at risk" changes worldwide according to each specific context. Africa has a large burden of overall risk factors related to childhood health and development, most of which are of an infective or social origin. The aim of this study was to report and analyze the volumes of activities of fifteen At Risk Child Clinics (ARCCs) within the Beira District (Mozambique) over a 3 year-period in order to define the health profile of children accessing such health services. We retrospectively analyzed the data from all of the children accessing one of the 15 Beira ARCCs from January 2015 to December 2017. From this, 17,657 first consultations were registered. The motivations for accessing the services were in order of relevance: HIV exposure (n. 12,300; 69.7%), other risk conditions (n. 2542; 14.4%), Moderate Acute Malnutrition (MAM) (n. 1664; 9.4%), Severe Acute Malnutrition (SAM) (n. 772; 4.4%), and TB exposure (n. 542; 3.1%). During the first consultations, 16,865 children were screened for HIV (95.5%), and 7.89% tested HIV-positive. In our three years of experience, HIV exposure was the main indication for children to access the ARCCs in Mozambique. ARCCs could represent a strategic point to better understand health demands and to monitor the quality of care provided to this vulnerable population group, however significant effort is needed to improve the quality of the data collection.

Keywords: Mozambique; children at risk; HIV-exposed infants (HEI); Mother and Child Health (MCH) services; children's health

1. Introduction

The concept of "children at risk" is dynamic worldwide, so the health risk profile of children is changing according to each specific geographic and social context. In the African continent, the greatest risks to children's health and development are mainly of infective and social origin, particularly exposure to Human Immunodeficiency Virus (HIV), malaria, TB, and malnutrition [1]. It is no coincidence that the scope for child development improvement at the regional level can be identified within three domains: nutrition, environment, and mother-child interaction [1].

In low income countries, despite the increasing investments in effective prevention strategies, HIV mother to child transmission (MTCT) remains a significant problem, especially in sub-Saharan Africa [2] where AIDS is still among the top causes of under-five morbidity and mortality [3]. In particular, in 2015, Mozambique was estimated to contain about 94,000 HIV-positive pregnant women, approximately 15% of whom transmitted HIV to their newborn infants, resulting in nearly 14,000 new pediatric HIV infections [2].

Again, tuberculosis (TB) in endemic settings is an under recognized, but potentially significant cause of morbidity and mortality in children [4,5]. In Mozambique, pediatric TB accounted for 7% of all new cases reported in 2012 [6]. Further, with 58% of all reported TB cases being HIV-positive, Mozambique also has one of the highest TB/HIV co-infection rates [7]. However, national data reported a decreasing trend in the under-5 mortality rate, with 71.3 deaths per 1000 live births in 2016, and among the top causes of post-neonatal death being Pneumonia, Malaria, and AIDS [8].

The impact of undernutrition on children's morbidity and mortality in Sub–Saharan Africa is also well known [9–13]. In Mozambique, according to the latest data from UNICEF, 43% of children suffer from moderate or severe stunting [8], and since children constitute 52% of the population in the country [14], it constitutes a very big health issue for the country.

If, on one hand, the deep impact of health determinants such as poverty and social disparities of child health are well known [15,16], then great attention should be paid to the emerging risks, such as climate change and environmental pollution, whose specific role on child health and development has only been better investigated in recent years [15,17,18].

In this epidemiological framework, with specific regard to health services, while consistent evidence is available for antenatal care [2,19,20], very little fragmented information on the postnatal care activities has been provided—especially for vulnerable children and their mothers.

The aim of this study was to report and analyze the volumes of activities of fifteen At Risk Child Clinics (ARCCs) within the Beira District over a 3 year-period in order to define the health profile of the children accessing these specific types of health services.

2. Materials and Methods

2.1. Study Setting

The Beira District is one of the 13 districts of the Sofala Province, laying on the eastern coast of Mozambique, and it is the third largest district in the country. The health system of the Sofala Province is articulated in 146 health facilities (1 per every 12,000 inhabitants) [21] and it is organized into four basic levels of care, including (1) one quaternary-level hospital in Beira, (2) four secondary-level rural hospitals, (3) 114 urban and rural health centers, including Maternal and Child Health Services specific to mothers and children, which are managed by the Ministry of Health (MoH), and (4) 27 health posts [22].

The ARCCs are configured as specific clinics within the Maternal and Child Health Services, and since 2012, most of the 15 ARCCs of the Beira district are supported by Doctors with Africa CUAMM.

Each ARCC provides free out-patient consultations dedicated to new-borns and children under five with specific health risks, such as HIV exposed infants (HEI), preterm, malnourished, TB exposed, referred to Maternal and Child Health Services from maternity, health posts, neonatology, or directly accessing the MCH services. Children that are presented in centers are taken charge of by clinical officers and nurses who provide care in an out-patient setting. The ones requiring more complex care and/or admission are addressed to the Beira referral hospital or to chronic disease out-patient services, except for HEI. In fact, since 2013, after a positive screening test with a PCR or Rapid test, a confirmation test with Western Blot [23] has been performed and, if positive again, the HEI remains in charge of ARCCS until 5 years old, together with his mother, in order to guarantee a better continuum of care [24].

2.2. Study Population and Period

We retrospectively analyzed all children accessing one of the 15 Beira ARCCs for a first consultation over a 3-year period, from January 2015 to December 2017.

2.3. Data Collection and Analysis

Routine service data were accessed. Data collection in Health Centers (HC) goes through several processes, from registration to assignment to the higher levels (Provincial and National). Firstly, data is recorded in each health section of HC during the consultation using a national format in a daily logbook. Health professionals have to ensure consistency and completeness (filling in all fields) of the registration in order to obtain high quality data. The daily logbook is filled exclusively by the health care professional who delivers the service. At the end of the activities, the daily summary is elaborated on. In this case, the person in charge of this activity verifies the agreement of the data. After the last day of the period under analysis (following the statistical calendar), a monthly summary is made, aggregating the daily summaries corresponding to the period in question. The direction of the HC is responsible for issuing and approving the summaries. Thus, the data analysis is done at the HC level and, subsequently, is reported to the district level and is then sent to higher levels.

We accessed the data at the district level, obtaining aggregate information on a number of consultations at each ARCCs. Information about the motives of the first consultation, the type and the timing of the first HIV test that was administered and it's result, and the type and duration of breastfeeding were also extracted. Motivations were grouped into 5 categories: TB exposure, Moderate Acute Malnutrition (MAM), Severe Acute Malnutrition (SAM), HIV exposure, and other risk conditions (e.g., malaria, preterm).

Moderate Acute Malnutrition and Severe Acute Malnutrition were defined according to the z-scores of weight-for-height [25,26].

A database was created on Microsoft Excel software and was analyzed using the STATA 13.0 statistics software. The frequencies for the categorical variables were calculated as descriptive statistics.

Data use for publication was approved by the District Health Authority in Beira, the Health District Direction (protocol reference: 293 /15), Mozambique.

3. Results

During the period between 2015 and 2017, an overall number of 17,657 first consultations were registered at the 15 different ARCCs serving the Beira district, representing 50.5% [27] of the 34,968 estimated new-borns in the study period.

Table 1 reports the first consultations per each one of the 15 ARCCs in the Beira District over the 3-year study period, ranging from a minimum of 92 first consultations for Marrocanhe to a maximum of 3105 for M-Nhaconjo.

The motivations for accessing the services were in order of relevance, (a) HIV exposure (n.12,300; 69.7 %), (b) other risk conditions (n. 2542; 14.4%), (c) MAM (n. 1664; 9.4%), (d) SAM (n. 772; 4.4%), and (e) TB exposure (n. 542; 3.1%) (Table 1). HIV exposure was the most frequent motive that was reported, with the exception of Mataduro where 54.9% (n. 62) of the children were referred to a MAM (Table 1).

During the first consultations that were done at the ARCCs of the Beira District, over the period between 2015 and 2017, 16,865 children were screened for HIV (95.5%) overall, regardless of their exposure status (Table 2).

Polymerase chain reaction (PCR) examination was tested in 8437 (49.5%) children before the 8th week and in 2216 (31.1%) between the 8th week and the 9th month. The remaining 6302 (37.4%) children were screened with a rapid test that was executed between the 9th and the 18th month (Table 2).

Of the 16,865 children who were screened for HIV, independent from their HIV exposure status, 1330 (7.89%) documented a sero-positivity. Overall, the prevalence of HIV sero-positivity was 13.3% (n. 295) among the patients who were tested with PCR between the 8th week and the 9th month,

8.9% (n. 561) among the patients who were tested with the Rapid Test between the 9th and 18th month, and 5.6% (n. 474) among the ones who were tested with PCR before the 8th week of life (Table 2). The percentages of the specific timing, type, and results of the first HIV test that was made at each ARCC are shown in Table 2.

Data on breastfeeding type was available for 10,100 children (82.1%) on 12,300 HIV-Exposed infants who were accessing the At Risk Children Clinics (ARCCs) over the study period. Eighty-three percent (n. 8405) of them were currently and exclusively breastfed by their mothers, while 11.3% were fed with formula, and 5.5% were fed with mixed breastfeeding. A similar distribution of breastfeeding type is reported by ARCC (Table 3).

Table 1. First consultations, by motivation and overall, at ARCCs of the Beira District, 2015–2017.

ARCCs of the Beira District	TB Exposure n. (%)	Moderate Acute Malnutrition n. (%)	Severe Acute Malnutrition n. (%)	HIV Exposure n. (%)	Other Risk Conditions n. (%)	Total First Consultations n. (%)
Chamba	9 (1.4)	54 (8.3)	18 (2.8)	466 (71.8)	102 (15.7)	649 (100)
Chingussura	73 (3.2)	94 (4.1)	68 (2.9)	1822 (78.7)	258 (11.1)	2315 (100)
Chota	2 (0.3)	76 (12.9)	21 (3.6)	395 (67.2)	94 (16.0)	588 (100)
Macurrungo	36 (2.3)	145 (9.1)	56 (3.5)	1154 (72.1)	209 (13.1)	1600 (100)
Manga-Loforte	0 (0.0)	33 (4.5)	6 (0.8)	613 (82.7)	89 (12.0)	741 (100)
Marrocanhe	1 (1.1)	18 (19.6)	8 (8.7)	64 (69.6)	1 (1.1)	92 (100)
Matadouro	1 (0.9)	62 (54.9)	2 (1.8)	22 (19.5)	26 (23.0)	113 (100)
M-Nhaconjo	84 (2.7)	358 (11.5)	217 (7.0)	1633 (52.6)	813 (26.2)	3105 (100)
Munhava	158 (4.8)	292 (8.9)	134 (4.1)	2288 (70.0)	398 (12.2)	3270 (100)
Nhagau	0 (0.0)	16 (8.0)	1 (0.5)	171 (85.1)	13 (6.5)	201 (100)
P-Militar	0 (0.0)	80 (18.1)	17 (3.9)	301 (68.3)	43 (9.8)	441 (100)
Ponta-gea	142 (4.8)	260 (8.8)	121 (4.1)	2062 (70.1)	358 (12.2)	2943 (100)
Sao-Lucas	5 (1.1)	28 (6.4)	3 (0.7)	362 (83.2)	37 (8.5)	435 (100)
US-Ceramica	0 (0.0)	28 (17.2)	9 (5.5)	95 (58.3)	31 (19.0)	163 (100)
US-M. Mascarenha	31 (2.7)	120 (10.3)	91 (7.8)	852 (73.2)	70 (6.0)	1164 (100)
Beira District	542 (3.1)	1664 (9.4)	772 (4.4)	12,300 (69.7)	2542 (14.4)	17,657 (100)

Table 2. First HIV test, by timing and type (PCR, Rapid Test), administered during the first consultations at the 15 ARCCs of the Beira District, 2015–2017.

ARCCs of the Beira District	PCR <8th week		PCR 8th week–9th month		Rapid Test 9th–18th month		Total Tests	
	Test Administered n.	Positive Results n. (%)	Test Administered n.	Positive Results n. (%)	Test Administered n.	Positive Results n. (%)	Test Administered n.	Positive Results n. (%)
Chamba	127	9 (7.1)	153	32 (20.9)	97	26 (26.8)	377	67 (17.8)
Chingussura	1302	39 (2.9)	226	20 (8.8)	565	30 (5.3)	2093	89 (4.25)
Chota	221	13 (5.9)	115	16 (13.9)	324	51 (15.7)	660	80 (12.1)
Macurrungo	821	28 (3.4)	149	19 (12.7)	32	9 (28.1)	1002	56 (5.6)
Manga-Loforte	335	32 (9.5)	267	63 (23.6)	350	24 (6.8)	952	119 (12.5)
Marrocanhe	8	1 (12.5)	36	2 (5.55)	37	6 (16.2)	81	9 (11.1)
Matadouro	8	0 (0.0)	5	1 (20.0)	8	2 (25.0)	21	3 (14.3)
Munhava	1574	101 (6.4)	230	20 (8.7)	1279	96 (7.5)	3083	217 (7.0)
Nhagau	60	5 (8.3)	67	11 (16.4)	127	11 (8.7)	254	27 (10.6)
M-Nhaconjo	1222	63 (5.1)	393	41 (10.4)	1326	144 (10.8)	2941	248 (8.43)
P-Militar	84	10 (11.9)	54	9 (16.6)	199	11 (5.5)	337	30 (8.9)
Ponta-gea	1679	95 (5.6)	227	23 (10.1)	1168	100 (8.6)	3074	218 (7.1)
Sao-Lucas	221	8 (3.6)	87	10 (11.5)	266	9 (3.4)	574	27 (4.7)
US-Ceramica	68	5 (7.3)	13	5 (38.5)	37	4 (10.8)	118	14 (11.9)
US-M. Mascarenha	617	65 (10.5)	194	23 (11.8)	487	38 (7.8)	1298	126 (9.7)
Beira District	8437	474 (5.6)	2216	295 (13.3)	6302	561 (8.9)	16,865	1330 (7.9)

Table 3. Type of breastfeeding reported for n. 10,100 HIV Exposed Infants, assisted at the 15 ARCCs of the Beira District, 2015–2017.

ARCCs of the Beira District	Breastfeeding in HIV-Exposed Infants			
	Exclusive n. (%)	Formula n. (%)	Mixed n. (%)	Total n. (%)
Chamba	78 (91.8)	0 (0.0)	7 (8.2)	85 (100)
Chingussura	1179 (89.5)	45 (3.4)	94 (7.1)	1318 (100)
Chota	96 (87.3)	2 (1.8)	12 (10.9)	110 (100)
Macurrungo	872 (92.5)	57 (6.0)	14 (1.5)	943 (100)
Manga-Loforte	260 (86.4)	20 (6.6)	21 (7.0)	301 (100)
Matadouro	33 (94.3)	0 (0.0)	2 (5.7)	35 (100)
Marrocanhe	23 (82.1)	0 (0.0)	5 (17.9)	28 (100)
M-Nhaconjo	1111 (80.1)	208 (15.0)	68 (4.9)	1387 (100)
Munhava	1193 (85.0)	202 (14.4)	9 (0.6)	1404 (100)
Nhagau	146 (84.9)	0 (0.0)	26 (15.1)	172 (100)
P-Militar	126 (69.2)	40 (22.0)	16 (8.8)	182 (100)
Ponta-gea	1288 (86.3)	191 (12.8)	14 (0.9)	1493 (100)
Sao-Lucas	596 (79.7)	118 (15.8)	34 (4.5)	748 (100)
US-Ceramica	49 (59.8)	2 (2.4)	31 (37.8)	82 (100)
US-M. Mascarenha	1355 (74.8)	256 (14.1)	201 (11.1)	1812 (100)
Beira District	8405 (83.2)	1141 (11.3)	554 (5.5)	10,100 (100.0)

4. Discussion

We reported data from three years of activity that was conducted at ARCCs in the Beira District, Mozambique, using the routinely collected data in order to provide an indirect picture of the health status of children under five who were accessing the local health facilities.

Over the three years of the study, HIV exposure represented the main reason for access to ARCC for consultation, as 7.89% of all of the children who visited were HIV-positive.

Of interest is that 83% of the HIV-Exposed Infants accessing the ARCCs over the study period were currently and exclusively breastfed by their mothers, while 10% were fed with formula, and 5% with mixed feeding. Since the HIV status of the mothers and the age of the children were unknown, it is not possible to draw consistent conclusions on adherence to what is recommended by WHO for HEI breastfeeding [28], however even from our inaccurate and rough data, it seems to be far from what was expected. Actions should be taken to improve the exclusive breastfeeding rate in this category, whereas mixed feeding increases the risk of HIV transmission [29,30] and poses the same risks of contamination and diarrhea as artificial feeding, which ultimately can affect infant survival.

The main limitation in the interpretation of the information that has been reported is related to the nature of the study. In fact, since we performed a retrospective study using only health data that was routinely collected, we were not able to access complete information about many aspects that were of interest. In particular, it could have been important to understand what is categorized under "other conditions", so as to extrapolate the Malaria cases, since Malaria is a leading cause of death among children in Mozambique and it causes important sequels in the surviving ones, including neuro-cognitive damage [31]. Also, knowing the burden of the patients who access care for more than one health problem could have been informative since most of the unfavorable conditions came together: a child with HIV has a higher risk of undernutrition and presents a higher risk of disease progression and mortality [9–12].

Furthermore, infants and young children (<3 years) and those with immunodeficiency caused by HIV or severe malnutrition are at the highest risk of developing TB [6], which is demonstrated to be the main cause of death among under-fives, accounting for 26% of AIDS-related deaths [7]. Moreover, to date, we are not able to estimate the number of children who are not born in health facilities that are supposed to be at a higher risk, which may be the ones who are not accessing the ARCC.

Despite the aforementioned limitations, ARCCs could represent a strategic point to better understand health demand and to monitor the quality of care that is provided to this vulnerable population group, however important efforts are needed to improve the quality of the data collection.

5. Conclusions

Children at risk are among the most vulnerable population group, which means that constant attention should be paid to their health needs, particularly in developing countries. Therefore, follow-up data collected at ARCC on children at risk and their clinical outcomes should be analyzed in order to monitor the quality of the care provided and to implement strategies for improvement.

To date, ARCCs represent a strategic source of information to address health policies and health programs [32].

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Successful management of giant hydrocolpos in a limited-resource setting

PAPER

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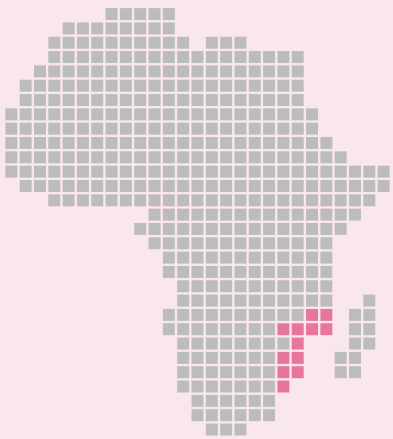

Abstract

Abdominal distension and urinary retention are rare conditions in infants. In the case of female newborns, these two conditions, particularly when concurrent, also include hydrocolpos caused by an imperforate hymen. The prognosis for the latter is generally good, and although severe nephrological, urological and infectious complications can arise they are predictable and can be treated through early diagnosis and drainage of the hydrocolpos.

In limited-resource settings, it is often difficult to make an early diagnosis of an imperforate hymen, thus greater attention and accuracy are called for during the physical examination and perineal inspection of female infants.

The case reported here involved an eight-day-old baby girl with symptoms of abdominal distension and urinary retention. The diagnosis revealed the presence of a large hydrocolpos, complicated by obstructive uropathy, sepsis and bladder perforation. Despite the gravity of the case and the lack of appropriate equipment with which to manage it, the newborn was operated on successfully and discharged in good condition.

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Case Report

CASE REPORT

Successful management of giant hydrocolpos in a limited-resource setting

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Abstract

Abdominal distention and urinary retention are rare manifestations in newborns. The differential diagnosis of a female neonate presenting these signs, especially when combined, should include hydrocolpos due to imperforate hymen. The prognosis of imperforate hymen is generally good, although it can be associated with serious nephro-urologic and infectious complications. Early diagnosis and drainage of hydrocolpos allow prevention and/or improvement of these possible complications. In limited-resource settings, diagnostic imaging is more difficult to obtain, and, therefore, increased caution and an accurate physical exam with perineal inspection are essential. We report the case of a 8-day-old female neonate showing abdominal distention and urinary retention. She had a final diagnosis of imperforate hymen with giant hydrocolpos, complicated by obstructive uropathy and following urosepsis and bladder perforation.

INTRODUCTION

Imperforate hymen is the most common congenital malformation of the female genital tract. It is defined as a genital anomaly in which a layer of the epithelialized connective tissue that forms the hymen has no opening and completely obstructs the vaginal introits. The reported incidence of imperforate hymen is 0.0014 to 0.1% per year in full term newborns and it can manifest in the neonatal period as hydro(metro)colpos or at menarche as haematocolpos [1]. Hydrometrocolpos is defined as the accumulation of secretions within the endovaginal and endometrial canal and its reported incidence is ~0.006% per year in full term newborns [1]. Although the main cause is imperforate hymen, other causes as labial adhesions, transverse vaginal septum, vaginal atresia, vaginal a-genesis and malformations of cloaca can lead to this condition [2]. If only the vagina or the uterus is distended independently, it is called hydrocolpos or hydrometra, respectively. This condition occurs when uterine and cervical glands stimulated by maternal estrogen in utero or by withdrawal of hormones after birth, secrete mucus in the presence of distal vaginal obstruction [3]. The clinical manifestations include abdominal distention and symptoms due to compression of bladder, bowel or pelvic veins. The anomalies associated with hydrometrocolpos can be isolated, such as imperforate anus or persistent urogenital sinus, or part of a

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genetic syndrome like Bardet–Biedl, McKusick–Kaufman and Pallister–Hall [4].

We report the case of a 8-day-old girl who presented abdominal swelling and urinary retention due to isolated imperforate hymen with secondary hydrocolpos.

CASE REPORT

A 8-day-old female term neonate was transferred from a peripheral health center to the Beira Central Hospital due to important abdominal distention and vomiting episodes. The neonate was born at home and before resorting to conventional treatments, traditional unspecified treatments had been carried out. Her mother referred that she had never urinated since birth, but was regularly defecating.

Upon arrival at the pediatric emergency department, the newborn was in critical conditions, febrile, with significant abdominal distention and thoraco-abdominal respiration (Fig. 1A). Perineal inspection revealed a tense bulging membrane at vaginal introits, initially misinterpreted as vaginal prolapse (Fig. 1B). The urethral orifice was not visible, while the anus was normally positioned and perforated. No other abnormalities were found by a physical examination. A plain radiograph of the abdomen highlighted a homogenous soft tissue opacity that was occupying the suprapubic and mesogastric region, causing displacement of the other abdominal structures and elevation of the diaphragm. In the light of fever and septic appearance a broad-spectrum antimicrobial therapy was started. On the ninth day of life, abdominal ultrasound revealed a septet cystic mass with fluid-debris level occupying the mesogastric and hypogastric region, with compression of both kidneys and mild dilatation of renal pelvis bilaterally. Dislocation of the liver and of the spleen without ascites was also present. Anuria was confirmed and, since it was impossible to insert a urethral catheter, on the 10th day of life the urologist performed a suprapubic aspiration in order to resolve urinary retention. Successively, the results of the initial laboratory tests showed elevated creatinine levels (230 umol/L) and moderate hypernatriemia.

On the 13th day of life, after clinical stabilization, the newborn was submitted to surgical intervention under general anesthesia. Skin was incised till peritoneum and, due to evidence of previous bladder perforation (Fig. 1C), urine was aspirated and cystorrhaphy was performed. The pelvic cyst (hydrocolpos) was then mobilized and drained by vaginal way through incision of the imperforate hymen. A urinary catheter was placed and the abdominal wall synthesis was performed. No intraoperative complication occurred.

Since the second post-operative day the newborn restarted regular breastfeeding with appropriate weight gain. On the fourth post-operative day she had fever associated to leucocytosis and we started the second line antibiotics, with good clinical response.

The following post-operative course was regular. The neonate presented adequate diuresis and normalization of creatinine levels. Ten days after the surgical intervention an abdominal ultrasound control showed a remaining moderate right pyelectasis without other pathological findings. The urinary catheter was removed after 2 weeks. On the 17th post-operative day the infant was discharged at 1 month of age.

DISCUSSION

We described a case of imperforate hymen presenting as neonatal giant hydrocolpos, complicated by obstructive uropathy due to mass effect and subsequent urosepsis and bladder perforation.

Hydro(metro)colpos is a rare cause of neonatal abdominal distension. In case of a newborn presenting abdominal swelling with identification of a cystic mass the differential diagnosis includes ovarian cyst, cystic renal masses, enteric duplication cyst, mesenteric cyst, meconium pseudocyst, choledochal cyst, adrenal cyst, splenic cyst, urachal cyst, anterior sacral meningocele, intra-abdominal cystic variety of sacrococcygeal teratoma and chylous ascites [2].

Urinary retention is rare in children, especially in newborns [5]; its association with abdominal distention in a female neonate should raise the suspect of hydrocolpos, whose most frequent cause is represented by imperforate hymen. Perineal inspection reveals the presence of a cystic mass at the vaginal introits and suggests the diagnosis, that can be confirmed trough abdominal ultrasound and magnetic resonance imaging, if needed to rule out complex genitourinary malformations [6]. The diagnosis of congenital hydrocolpos is also possible prenatally by means of ultrasonography and eventual fetal MRI [7]. In our case, the diagnosis was made at a late stage due to the lack of prenatal screening and the consultation of traditional healers as first choice. This delay led to the development of complications and, thus, to more difficult management and lower chance of good outcome.

The management of imperforate hymen depends on the age of presentation and on the severity of the condition. In

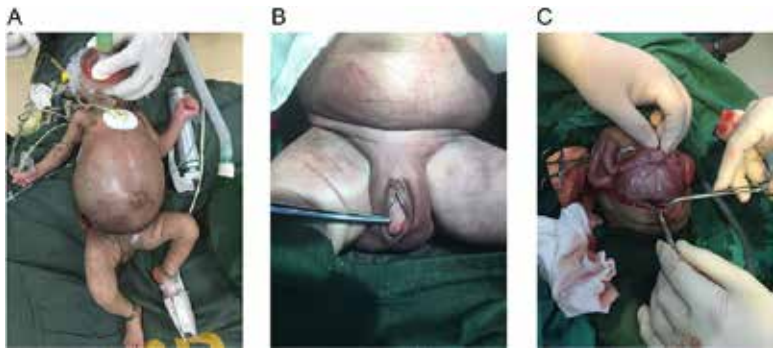

Figure 1: (**A**) Important abdominal distention in a female newborn. (**B**) Tense bulging membrane at vaginal introitus. (**C**) Intraoperatory image showing giant hydrocolpos and bladder perforation.

asymptomatic cases a conservative approach can be considered, but symptomatic patients require drainage of the secondary hydrocolpos. The drainage can solve obstructive acute kidney injury, avoiding chronic renal damage, and improve hydronephrosis, as was seen in our case and reported in the literature [8]. The surgical treatment can be made by simple hymenotomy or hymenectomy, while laparotomy is indicated for the treatment of abdominal complications [2]. In this case a laparotomy was necessary due to the bladder breakage and in order to exclude other complications. It is not clear when and how the bladder broke; this could have happened during the puncture procedure. If this hypothesis were true, we should take into account the resulting urine leak into the abdominal cavity and its consequences.

The prognosis of isolated imperforate hymen is generally good, but its presentation in the neonatal period with hydrocolpos can lead to complications associated with high morbidity and mortality [2, 9]. Despite the critical presentation, the lack of appropriate equipment and the occurrence of complications, thanks to appropriate management and accurate follow-up, the newborn was finally discharged in good conditions.

In conclusion, dealing with congenital hydrocolpos, early diagnosis, ideally in the prenatal period, and timely treatment should be the standard. However, in limited-resource settings, and considering the lack of prenatal screening, the paucity of experienced specialists and the strong belief in traditional healers, it is very difficult to achieve a prompt recognition of this condition [10]. In such a context, training of the involved health personnel towards a high index of caution could be a first step in order to prevent complications as urinary tract obstruction, renal failure, repeated urinary tract infections or hydrocolpos rupture with peritonitis. Afterwards it is obviously mandatory to strengthen the health system in terms of health workers ability and equipment and to reduce the gap between traditional and conventional medicine.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

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ETHICAL APPROVAL

No approval required.

CONSENT

The patient's mother gave informated consent for publication of the case report.

GUARANTOR

Giulia Reggiani.

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Effect of a Low-Dose/High-Frequency Training on Real-Life Neonatal Resuscitation in a Low-Resource Setting

PAPER

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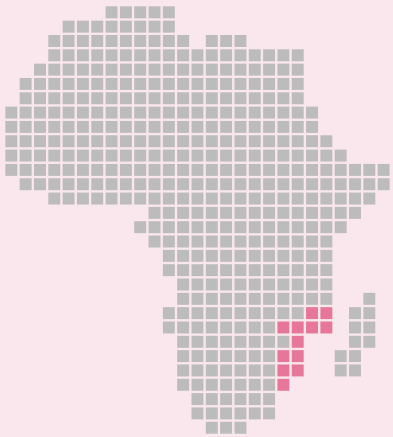

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Abstract

Every year more than 2.5 million newborns die worldwide, often due to delivery-related causes. Most of these deaths take place in limited-resource countries with poor or inadequate access to health care.

In such settings, the Neonatal Resuscitation Program (NRP) is of fundamental importance, training staff so that they can acquire the skills needed to reduce newborn mortality rates.

This study was aimed at evaluating the effectiveness of such programs in improving the performance of healthcare personnel in resuscitating newborns. Training was provided to 16 midwives in charge of postnatal management at Mozambique's Beira Hospital, with an average seven years of work experience. In order to identify possible improvements in the way the midwives handled newborns in need of resuscitation, their performances were evaluated both prior to and following the training course.

After the course ended, improvements were found in the midwives' use of masks for ventilation and chest compression performance, with a drop in the amount of time required to carry out the full procedure.

In limited-resource settings such as Mozambique, despite numerous aspects that still need to be improved, newborn treatment and care can be made more effective by providing staff with neonatal resuscitation training.

Neonatology

Effect of a Low-Dose/High-Frequency Training on Real-Life Neonatal Resuscitation in a Low-Resource Setting

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Keywords
Education · Low-resource setting · Neonatal resuscitation · Training · Video recording

Abstract
Background: As intrapartum-related events represent a quarter of all neonatal deaths, education on neonatal resuscitation is a critical priority. ***Objective:*** To assess the impact of a low-dose/high-frequency neonatal resuscitation training on clinical practice of midwives in a low-resource setting. ***Methods:*** Eight months after a modified Neonatal Resuscitation Program (NRP) course, we implemented a low-dose/high-frequency training for midwives at Beira Central Hospital, Mozambique. The training lasted 6 months and included weekly practice sessions. Fifty consecutive resuscitations after the low-dose/high-frequency training were compared with those registered before (n = 50) and after (n = 50) participation in the adapted NRP course using video recording. ***Results:*** All 150 neonates received the initial steps; 103 required bag-mask ventilation and 41 required chest compressions. The scores for initial steps, bag-mask ventilation and chest compressions improved after the course ($p < 0.0001$, $p = 0.005$ and $p = 0.03$) and did not change after the low-dose/high-frequency training ($p = 0.34$, $p = 0.99$ and $p = 0.30$). The low-dose/high-frequency training decreased the total time of the procedure ($p < 0.0001$) and anticipated start time of airway suctioning and tactile stimulation ($p = 0.003$ and $p < 0.0001$), but had no effect on the time of initiation of bag-mask ventilation ($p = 0.30$). ***Conclusions:*** In a low-income setting, a low-dose/high-frequency training after participation in an adapted NRP course contributed to improving the initiation and times of some procedures. However, many aspects of neonatal resuscitation remained poor. Low-dose/high-frequency training should focus on improving the prevention of thermal loss, face mask ventilation and heart rate assessment.

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Risk Factors for Mortality in Children Admitted for Suspected Malaria to a Pediatric Emergency Ward in a Low-Resource Setting: A Case-Control Study

PAPER

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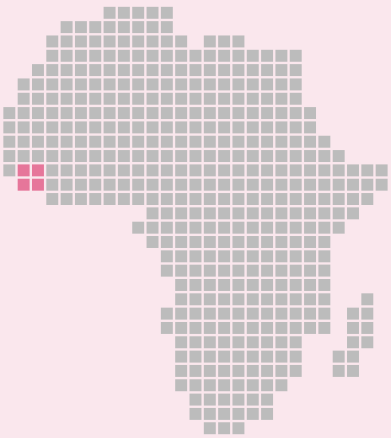

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Abstract

Malaria is a serious public health problem, with some 212 million new cases and nearly half a million malaria deaths worldwide in 2015 alone. Despite recent progress in control and treatment of the disease, the African region continues to bear the brunt of the global malaria burden. Most of the population there continues to lack access to the appropriate tools and care for its prevention and treatment. Under-5 children, whose immune systems are not yet fully developed, are the most at risk for and vulnerable to the disease.

The aim of this study was to investigate the main risk factors for mortality in children hospitalized for suspected malaria infection in the pediatric ward of the Pujehun Hospital in Sierra Leone. It looked at 320 children from 1 January 2015 to 31 May 2016, 232 (72.2%) of whom were found to be infected. Nearly all of the children were given antibiotics and anti-malarial drugs upon admission to the hospital.

An analysis of the data collected confirmed that impaired neurological status at the time of admission was one of the top mortality risk factors for the children. Respiratory arrest, malnutrition and dehydration were identified as additional health risk factors. The study's findings point to a need to intensify malaria prevention and treatment interventions and to expand equipment and personnel levels.

Risk Factors for Mortality in Children Admitted for Suspected Malaria to a Pediatric Emergency Ward in a Low-Resource Setting: A Case-Control Study

Francesco Cavallin, MS[1]; Luigi Pisani, MD[2]; Lorenzo Stancari, MD[3]; Vandi Massaquoi, BS[4]; Allieu Sharif, BS[5]; Enzo Pisani, MD[5]; Giovanni Putoto, MD[3]; Daniele Trevisanuto, MD[6]

Objectives: To identify the risk factors for mortality after admission for suspected malaria in a pediatric emergency ward in Sierra Leone.

Design: Retrospective case-control.

Setting: Pujehun Hospital Pediatric Ward in Pujehun, Sierra Leone.

Patients: All cases were pediatric deaths after admission for suspected malaria at the Pujehun Hospital Pediatric Ward between January 1, 2015, and May 31, 2016. The case-control ratio was 1:1. The controls were infants admitted at Pujehun Hospital Pediatric Ward for malaria and discharged alive during the same period. Controls were selected as the next noncase infant admitted for malaria and discharged alive, as recorded in local medical records.

Interventions: None.

Measurements and Main Results: Children characteristics, vital variables on hospital access, comorbidity status at admission, antibiotic and antimalarial therapy at admission; presence of hematemesis, respiratory arrest or bradypnea, abrupt worsening, and emergency interventions during hospital stay; final diagnosis before discharge or death. In total, 320 subjects (160 cases and 160 controls) were included in the study. Multivariable analysis identified being referred from peripheral health units (odds ratio, 4.00; 95% CI, 1.98–8.43), cerebral malaria (odds ratio, 6.28; 95% CI, 2.19–21.47), malnutrition (odds ratio, 3.14; 95% CI, 1.45–7.15), dehydration (odds ratio, 3.94; 95% CI, 1.50–11.35), being unresponsive or responsive to pain (odds ratio, 2.17; 95% CI, 1.15–4.13), and hepatosplenomegaly (odds ratio, 3.20; 95% CI, 1.74–6.03) as independent risk factors for mortality.

Conclusions: Risk factors for mortality in children with suspected malaria include cerebral malaria and severe clinical conditions at admission. Being referred from peripheral health units, as proxy of logistics issue, was also associated with increased risk of mortality. These findings suggest that appropriate interventions should focus on training and resources, including the increase of dedicated personnel and available equipment. (*Pediatr Crit Care Med* 2018; XX:00–00)

Key Words: cerebral malaria; low-resource settings; malaria; mortality; pediatric emergency; sub-Saharan Africa

Malaria is one of the most severe public health problems worldwide, with around 3 billion people (half the world's population) living in areas at risk of malaria transmission. According to the World Health Organization (WHO), there were 212 million new cases of malaria worldwide and more than 0.4 million malaria deaths in 2015 (1).

The WHO African Region accounted for 90% of malaria cases and 92% of malaria deaths in 2015. In the last 5 years, progress in vector control measures and preventive treatment strategies has reduced malaria case frequency by 21% and malaria death rate by 31% in this area (1, 2). However, malaria still represents a heavy burden because many people in endemic countries lack access to the tools that prevent, diagnose, and treat the disease (2).

Children under 5 years old are one of most vulnerable groups affected by malaria, accounting for 70% of all malaria deaths (1). In fact, children between 6 months and 5 years old have lost maternal immunity and have not yet developed specific immunity to infection (3). Malaria is actually one of the leading cause of child mortality (7.3% of total deaths), following pneumonia and diarrhea. The burden is extremely

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Neonatal tactile stimulation at birth in a low-resource setting

PAPER

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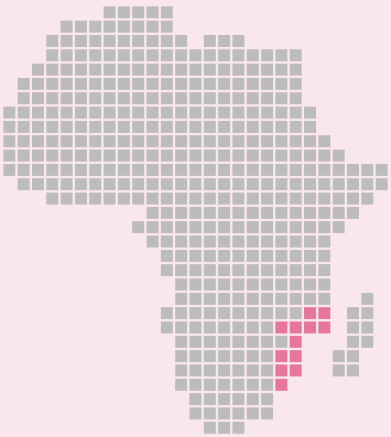

Abstract

Our study reviewed and evaluated the neonatal stimulation of 150 newborns at the Beira Central Hospital in Beira, Mozambique. In low-resource settings, such manual stimulation can be of critical importance in the resuscitation of infants who are having difficulty breathing.

Monitoring the stimulations performed on the 150 newborns, for a total of 546 separate episodes (an average of four stimulations per newborn), we observed that the timeliness with which the technique was implemented was inadequate, with an average time of 134 seconds before stimulation was begun. There was also poor adherence to the techniques recommended in international guidelines, i.e. stimulation of the feet, back and abdomen.

Only 9 of the 150 newborns responded positively to stimulation.

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Neonatal tactile stimulation at birth in a low-resource setting

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Abstract

Background: Stimulation is the most common intervention during neonatal resuscitation at birth, but scarce information is available on the actual methods, timing and efficacy of this basic step. To evaluate the occurrence, patterns and response to tactile stimulation at birth in a low-resource setting.

Methods: We reviewed 150 video recordings of neonatal resuscitation at Beira Central Hospital (Beira, Mozambique). Timing, method, duration and response to tactile stimulation were evaluated.

Results: One hundred two out of 150 neonates (68.0%) received stimulation, while the remaining 48 (32.0%) received positive pressure ventilation and/or chest compressions directly. Overall, 546 stimulation episodes (median 4 episodes per subject, IQR 2–7) were performed. Median time to the first stimulation episode was 134 s (IQR 53–251); 29 neonates (28.4%) received stimulation within the first minute after birth. Multiple techniques of stimulation were administered in 66 neonates (64.7%), while recommended techniques (rubbing the back or flicking the soles of the feet) only in 9 (8.8%). Median duration of stimulation was 17 s (IQR 9–33). Only 9 neonates (8.8%) responded to stimulation.

Conclusions: In a low-resource setting, stimulation of newly born infants at birth is underperformed. Adherence to international guidelines is low, resulting in delayed initiation, inadequate technique, prolonged duration and low response to stimulation. Back rubs may provide some benefits, but large prospective studies comparing different methods of stimulation are required.

Keywords: Delivery room, Low-resource setting, Neonatal resuscitation, Newborn, Stimulation

Background

Initiation of breathing is critical in the physiologic transition from intra-uterine to extra-uterine life [1]. In high-resource settings, approximately 85% of babies born at term initiate spontaneous respirations within 10 to 30 s after birth, 5–10% respond to simple stimulation, 3–6% start breathing after basic resuscitation (positive-pressure ventilation, PPV) and less than 1% require advanced resuscitation (intubation, chest compressions and drugs) [2]. Resuscitation includes different interventions based on progressive steps (Table 1). In low-resource settings, a large observational study in a rural hospital in Tanzania suggested that 85% of infants would require only simple newborn care, whereas 15% would need stimulation, including 7% requiring bag-mask ventilation and less than 1% requiring advanced care [3].

The need for neonatal resuscitation is most urgent in low-resource settings, where access to intrapartum obstetric care is poor and long-term impairments from intrapartum-related events represent a heavy burden [4]. While babies requiring advanced resuscitation may not survive without ongoing ventilation and neonatal intensive care, neonatal mortality from intrapartum-related events in low- and middle-resource settings can be reduced by 30% with basic training in neonatal resuscitation [5]. Expert consensus estimates a 10% reduction in intrapartum-related deaths with immediate newborn assessment and stimulation alone [6].

Although stimulation is the most common intervention during neonatal resuscitation/stabilization at birth

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Table 1 Steps of neonatal resuscitation and interventions

Initial steps	Ventilation	Chest compressions	Medications
Warming Suctioning Stimulation Evaluation	Face-mask ventilation Laryngeal-mask ventilation[a] Intubation[a]	Chest compressions with two-thumb techniques	Adrenaline[a] Volume expanders[a]

[a] interventions not available in the study setting

and is also recommended by all neonatal resuscitation guidelines, [7–9] scarce information is available on the actual methods, timing and efficacy of this basic step. A limited number of retrospective observational studies in high-resource settings have investigated this topic so far. Dekker et al. reviewed 164 neonatal stimulations at birth of infants with a gestational age of < 32 weeks and reported large variability in the use of tactile stimulation without a clearly demonstrable effect on infants [10]. Gaertner et al. evaluated video recordings of 75 stimulated infants, including very preterm infants, and suggested that truncal stimulation (drying, chest rubs and back rubs) might be more effective than foot flicks [11]. All authors indicated the need for further studies in order to confirm such preliminary findings. It is noteworthy that these results might underestimate the number of stimulations received by healthy near-term and at term newborns. Moreover, the number and types of stimulation may vary in different settings or with less experienced staff.

The aim of this study was to evaluate the occurrence, patterns and response to tactile stimulation at birth in newly born infants in a low-resource setting.

Methods

Setting

This study was performed at Beira Central Hospital (Beira, Mozambique) where about 4500 deliveries occur every year. Beira Central Hospital is the referral hospital for a geographical area that covers about 7 million people, with large referral services for maternal and neonatal care in the province [12].

Study design

This study presents a secondary analysis of data collected during a prospective study on education in neonatal resuscitation using videorecording. The main study was designed to assess the impact of a Neonatal Resuscitation Program course followed by a continuous refresher training on clinical practice of midwives at Beira Central Hospital [13]. The research protocol was approved by the National Committee of Bioethics (Ref. 315/CNBS/13; November, 1, 2013) and by the Minister of Health of the Republic of Mozambique (Ref. 08/GMS/002/2014; January, 7, 2014). Parental consent to record neonatal delivery room management and to use the data was obtained before every delivery. Written informed consent was given by parents and caregivers for clinical records to be used in this study. All information, including informed consent and all the material used in the study was written in Portuguese in a clearly understandable form.

Patients

All 150 neonates who were enrolled in the original study were considered for inclusion in the present analysis. All of them needed resuscitation of some form at birth. Neonates who required stimulation were included in the analysis. Resuscitation was defined as any intervention performed by healthcare providers: initial steps (drying and stimulation), bag mask ventilation, and/or chest compressions. Lack of parental consent was the only exclusion criterion.

Procedures

Neonatal resuscitation was performed routinely under radiant warmers in the delivery room or in the obstetric operating room and was based on an adapted algorithm of 2010 American Heart Association Guidelines, with the exclusion of intubation and medication administration [13, 14].

Stimulation was defined as any intervention provided to the baby under the infant warmer, [6, 11, 15] including back rub (any rub to the back), foot flick (any stimulation targeting the sole, i.e. flicking or rubbing), chest rub (any rub to the front or side of the thorax) and abdomen rub (any rub to the front or side of the abdomen). A stimulation was recorded as a separate episode if there was a gap of at least 2 s between two stimulations or if the nature of the stimulation changed. Concurrent stimulations (i.e. flicking the foot while rubbing the chest) were recorded as separate stimulations [11]. Only the stimulations that led to a complete newborn recovery, without need for further resuscitation, were considered effective.

All interventions at birth were video-recorded with a camera installed above the radiant warmers and data were collected until the end of resuscitation maneuvers or until the video was stopped because the infant transitioned well and was brought to the mother. Two researchers (DT and AP) drafted a categorical scheme based on Gaertner et al. [11] to identify the patterns of stimulation objectively. Two researchers (AP and AO) reviewed and evaluated all 150 videos of neonatal resuscitation, with a third researcher (SM) resolving any

conflicts. Time of birth was defined as the time the Apgar clock was started or birth was announced [11].

Video recording

Interventions were recorded using a webcam for video monitoring (ENXDVR-4C, Encore Electronics. www.encore-usa.com), consisting of 1 fixed camera installed above the radiant warmers both in the delivery room and in the operating room. The cameras provided a 24-h video recording without audio. The image was zoomed to show only the neonate and the hands of the resuscitation team. Parents, obstetric procedures and faces of the caregivers were not visible [16]. The video camera displayed a continuous time readout at the bottom of the recorded image allowing timing of performed procedures to the nearest second. All videos were stored on a hard disk and sent to the coordinating center (University of Padua). In order to protect the identities of the subjects and the data, all data about resuscitation date and location were removed, and shipment was insured. All 150 recordings were complete and of good quality.

Outcomes

The main variable of interest was the response to stimulation defined as the complete newborn recovery, i.e. spontaneous breathing without need for PPV. The initiation time, the duration and the technique of stimulation were also evaluated.

Statistical analysis

This study presents a secondary analysis of data collected during a prospective study on education in neonatal resuscitation using videorecording. Thus, a convenience sample consisting of all 150 videos of the original study was analyzed. Continuous data were summarized using median and interquartile range (IQR), and categorical data as number and percentage. Data were compared between two groups using Mann-Whitney test (continuous data) or Fisher's exact test (categorical data). Correlation between continuous variables were evaluated using Spearman rank correlation coefficient. All test were 2-sided and a p-value less than 0.05 was considered statistically significant. Statistical analysis was performed using R 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria) [17].

Results

Of the 150 video recordings, 102 neonates (68.0%) received stimulation because of apnea (4 neonates), hypotonia (12 neonates) or both (86 neonates). The remaining 48 neonates went directly.

to PPV and/or chest compressions and were excluded from the analysis (Fig. 1). Characteristics of included neonates are shown in Table 2. Median gestational age was 38 weeks (IQR 37–40) and median birth weight was 2875 g (IQR 2200–3280).

Overall, 546 stimulation episodes (median 4 episodes per subject, IQR 2–7) were performed. Description of stimulations is reported in Table 3. Median time elapsed from birth to the first stimulation was 134 s (IQR 53–251); 29 neonates (28.4%) received stimulation within the first minute after birth. Figure 2 shows the total time of stimulation comparing when a specific procedure was performed or not. Rubbing the thorax (upper left) was not associated with total time of stimulation ($p = 0.35$). Instead, rubbing the abdomen (upper right, $p = 0.0009$), rubbing the back (lower left, $p = 0.0002$) and flicking the soles of the feet (lower right, $p < 0.0001$) were associated with longer total time of stimulation compared to not performing the corresponding procedure (Fig. 2). The number of different techniques included in the stimulation was associated with longer total time of stimulation (Spearman rho 0.57, $p < 0.0001$), but not with time to first stimulation episode (Spearman rho 0.05, $p = 0.62$). Nine neonates (8.8%) responded to stimulation. The low number of responding neonates prevented any meaningful analyses, but data suggested that rubbing the back might increase the efficacy of the stimulation (Fig. 3).

Discussion

The present study evaluated the methods, timing and response to tactile stimulation in late preterm and full-term infants in low-resource settings. To our knowledge, only two retrospective studies conducted in preterm infants in high-resource settings, investigated such aspects [10, 11]. In these studies, the effect of stimulation was assessed as recovery of heart rate > 100 bpm and/or regaining breathing/increased breathing effort, [10] or as changes in crying, movement and grimace. [11] In the present study, the stimulation was considered as effective when it provided a complete newborn recovery, avoiding the need for PPV.

Our main result was the very low number of infants (9%) who responded to stimulation. A previous study in Tanzania suggested that around 50% of newly born infants might respond to stimulation thus avoiding the need for PPV [3]. This difference could be related to some study features such as the different definition of response to stimulation, the inclusion of infants needing resuscitation under the infant warmer in our series and the resulting longer delay of initiation of stimulation. Face-mask ventilation is a crucial step in neonatal resuscitation but it is a difficult skill to teach and maintain in low-resource settings [18]. Therefore, effective stimulation during the first steps of resuscitation may reduce the need for additional neonatal resuscitation procedures such as face-mask ventilation or intubation. Expert consensus indicates that

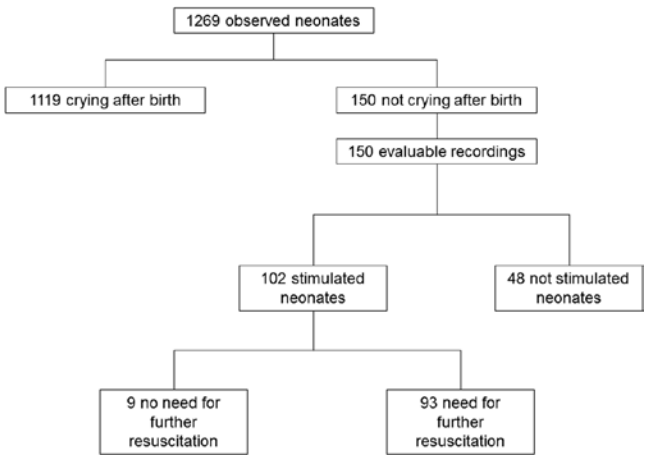

Fig. 1 Flowchart of included neonates

immediate newborn assessment and stimulation alone may avoid 1 out of 10 intrapartum-related deaths [6].

In our series, the recommended stimulation techniques (i.e. rubbing the back or flicking the soles of the feet [19]) were rarely performed alone and were usually associated with others techniques (i.e. rubbing the abdomen or the thorax), thus preventing any meaningful conclusions on efficacy. However, stimulations including rubbing the back seemed to be promising in terms of response rate, but the low number of responding infants suggested caution in interpreting the observed results. Low response rate and large variation in the use of tactile stimulation were also reported in the two studies in high-resource settings. Dekker et al. observed that 80% of their study cohort received recommended stimulation technique and 18% of stimulation episodes were effective, while the overall effect per infant remained unclear. [10] Gaertner et al. suggested that truncal stimulation (i.e. drying, chest rubs and back rubs) might increase the response to stimulation, but the low sample size prevented definitive conclusions [11].

It is noteworthy that 1 out of 3 infants did not receive stimulation in our series, thus confirming

Table 2 Demographics

No. of stimulated neonates	102
Reason for stimulation	
Apnea	4 (3.9)
Hypotonia	12 (11.8)
Apnea and hypotonia	86 (84.3)
Mode of delivery	
Vaginal	53 (52.0)
Caesarean	49 (48.0)
Sex	
Male	66 (64.7)
Female	36 (35.3)
Birth weight, grams	2875 (2200–3280)
Gestational age, weeks	38 (37–40)
Apgar score at 1 min	5 (3–6)
Apgar score at 5 min	6 (4–7)

Data expressed as No. (%) or median (IQR)

Table 3 Stimulations

Timing and number of stimulations	Time elapsed from birth to stimulation, seconds	134 (53–251)
	Duration of the first stimulation episode, seconds	4 (2–7)
	Number of stimulations/neonate	4 (2–7)
	Total time of stimulation, seconds	17 (9–33)
Technique of stimulation	The stimulation involved rubbing the thorax	81 (79.4)
	The stimulation involved rubbing the abdomen	40 (39.2)
	The stimulation involved rubbing the back	55 (53.9)
	The stimulation involved flicking the soles of the feet	40 (39.2)
	Truncal stimulation (rubbing the thorax and/or the back)	98 (96.1)
	Technique of stimulation	
	Single technique	36 (35.3)
	Two techniques	31 (30.4)
	Three techniques	22 (21.6)
	Four techniques	13 (12.7)

Data expressed as No. (%) or median (IQR)
Single technique: 26 only thorax, 1 only abdomen, 6 only back, 3 only feet

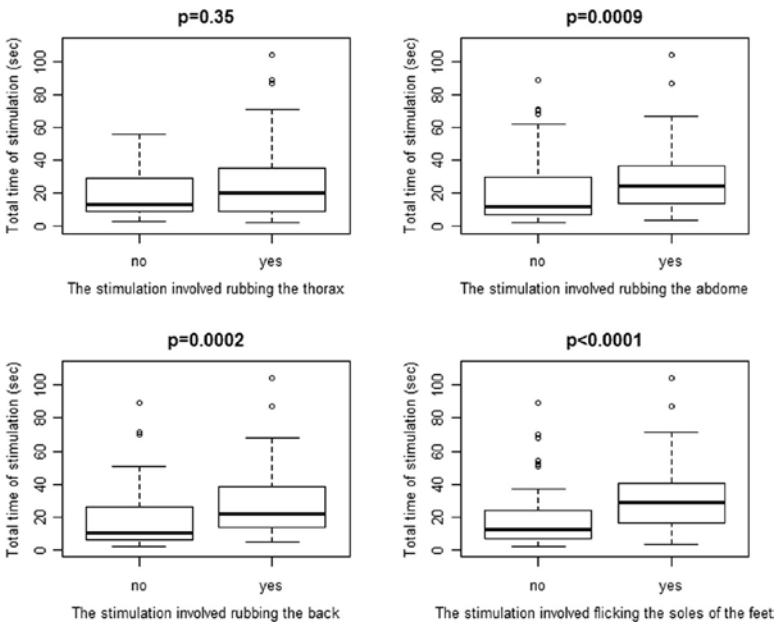

Fig. 2 Total time of stimulation

available data in high-resource settings [10, 11]. While the number of immature infants and medical team's focus on respiratory support might have been the reasons for skipping stimulation in other studies, [10, 11] we believe that low-resource setting and less-experienced staff were more likely to be associated with skipping stimulation in our series. In fact, a previous study showed limited ability of the staff to adhere to the resuscitation algorithm [18].

Overall, our data showed low adherence to the international guidelines in term of initiation, duration and method of stimulation [7–10]. The initiation of stimulation was frequently delayed, with only 28.4% of infants receiving stimulation within the first minute after birth. In high-resource settings, Dekker et al. also reported delayed initiation of stimulation (less than 25% of infants receiving stimulation within the first minute after birth), [10] while Gaertner et al. reported prompt initiation

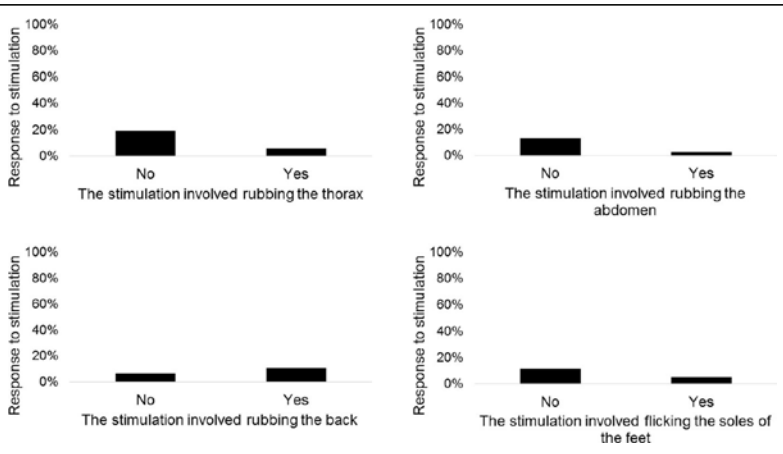

Fig. 3 Response to stimulation

(median time to first stimulation of 19 s) [11]. The method of stimulation was mostly inadequate, with 35% of infants stimulated using a single technique and only 9% as recommended (i.e. rubbing the back or flicking the soles of the feet). The majority of infants were stimulated using multiple techniques, in agreement with findings in high-resource settings [10, 11]. As consequence, the duration of stimulation was longer than recommended, as reported also by Dekker et al. [10] The prolonged duration of stimulation represents an additional hazard for infants, because it delays the initiation of PPV thus compromising the efficacy of the overall resuscitation process. Therefore, the low adherence to the international guidelines might have contributed to the low response to stimulation in our series.

The strengths of the present study include the evaluation of the response to stimulation as complete newborn recovery preventing the need for PPV, the objective evaluation of resuscitation procedure by using video-recording and the detailed review of stimulation maneuvers.

This study has also some limitations. First, it is a secondary analysis of data collected during a previous prospective study [13]. The original study was designed to video record only the resuscitation maneuvers applied when the newborns were moved under the infant warmer, thus the analysis might not include some depressed newborns who recovered after stimulation administered immediately after birth. Second, the low number of responding neonates and the heterogeneity of combinations of stimulation techniques did not provide strong indications on efficacy of single stimulation approaches.

Conclusions

In low-resource settings, stimulation of newly born infants needing resuscitation is underperformed. Adherence to international guidelines is low, resulting in delayed initiation, inadequate technique, prolonged duration and low response to stimulation. Back rubs may provide some benefits, but large prospective studies comparing different methods of stimulation are required.

Abbreviations

IQR: Interquartile range; PPV: Positive-pressure ventilation

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available to protect participant confidentiality, but are available from the corresponding author (DT) on reasonable request.

Authors' contributions

AP watched the videos, contributed to interpret the results and wrote the first version of the manuscript. FC analyzed the data and contributed to result interpretation and writing the manuscript. AO watched the videos and contributed to result interpretation. MEC, DP and GP were involved in planning, conducting and reporting of the work. DT conceived and designed the study and was involved in data interpretation as well as manuscript writing and supervised the project. All the Authors approved the final manuscript as submitted and are responsible for the accuracy and the integrity of the data.

Ethics approval and consent to participate

The research protocol was approved by the National Committee of Bioethics (Ref. 315/CNBS/13; November, 1, 2013) and by the Minister of Health of the Republic of Mozambique (Ref. 08/GMS/002/2014; January, 7, 2014). Parental consent to record neonatal delivery room management and to use the data was obtained before every delivery. Written informed consent was given by parents and caregivers for clinical records to be used in this study.

Consent for publication

Consent from parents of participants was obtained for this study, which included consent for publication without any identifying participant information.

Competing interests

The authors declare that they have no conflict of interest.

Publisher's Note

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Decision Making and Situational Awareness in Neonatal Resuscitation in Low Resource Settings

PAPER

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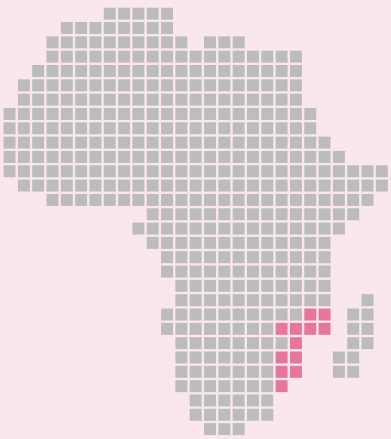

Abstract

The aim of this study was to assess the non-technical skills of the midwifery staff at Mozambique's Beira Central Hospital to manage complex health situations. Indicators assessed included staff members' management of their own tasks (e.g., the ability to understand priorities and to use available resources), team work (e.g., the ability to coordinate and to exchange information with colleagues), situational awareness (e.g. the ability to anticipate situations of risk) and decision-making (e.g., the ability to balance risks).

We found no substantial changes or improvements when assessing the performance of the midwifery staff before and after their participation in a neonatal resuscitation (NR) training course. One hundred and fifty videos of NR situations were recorded: 50 prior to the course, 50 following the course and 50 after the midwifery staff took part in another low-dose/high-frequency training course. The neonatologists who viewed the videos (both with expertise in high-fidelity simulation) found that staff performance was inadequate in terms of most of the indicators under consideration both prior to and following the courses, pointing up the need to implement a different training approach.

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Simulation and education

Decision making and situational awareness in neonatal resuscitation in low resource settings

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Abstract

Introduction: Data on non-technical skills (i.e. task management, team working, situation awareness and decision-making) of healthcare providers during real-life newborn resuscitation in low-resource settings are lacking. We aimed to assess non-technical skills of trained midwives during real-life newborn resuscitation in a low-resource setting before and after participation in a modified NRP course, and after a low-dose/high-frequency training.

Methods: One-hundred and fifty video-recorded resuscitations (50 before and 50 after participation in a modified NRP course, and 50 after a low-dose/high-frequency training) collected at the Beira Central Hospital (Mozambique) were independently viewed and rated by two neonatologists with expertise in high fidelity simulation. Non-technical skills regarding task management, situation awareness and decision-making were evaluated using the modified Anesthetists' Non-Technical Skills tool.

Results: Overall, most non-technical skills were scored as poor or marginal. Small improvements were observed in task management (planning and preparing $p = 0.02$; providing/maintaining standards $p = 0.03$) after the course. Limited improvements were observed in task management (prioritizing $p = 0.03$; providing/maintaining standards $p = 0.04$; identifying and utilizing resources $p = 0.02$) and decision-making (identifying options $p = 0.04$; balancing risk/selecting options $p = 0.02$) after the low-dose/high-frequency training. No differences were observed in situation awareness, apart from a small improvement in recognizing/understanding ($p = 0.04$) after the low-dose/high-frequency training.

Conclusion: An educational intervention including a modified NRP course and a low-dose/high-frequency training on neonatal resuscitation had a limited impact on non-technical skills of participants. All items remained significantly under the recommended standards. Behavioral skills should be considered in training programs in order to improve the quality of neonatal resuscitation in low resource settings.

Keywords: Education, Low-resource setting, Neonatal resuscitation, Non-technical skills

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Introduction

Neonatal deaths account for a significant proportion of mortality in children less than 5 years.[1] Neonates are at the highest risk of dying around the time of birth, due to intrapartum-related complications that contribute to approximately one-quarter of neonatal deaths.[2] The vast majority of these deaths (98%) occur in low- and middle-resource countries and can be prevented by simple resuscitation and newborn care interventions.[2,3]

Education in neonatal resuscitation is crucial in the prevention of neonatal morbidity and mortality.[4] Appropriate translation of the science of resuscitation into a training programme aims to transfer the knowledge and the skills of resuscitation into improved clinical practice.[5] Educational programs to reduce neonatal deaths include the WHO Essential Newborn Care (ENC), the American Academy of Pediatrics Neonatal Resuscitation Program (NRP) and Helping Babies Breathe (HBB), specifically designed to teach neonatal resuscitation in a low-resource setting.[6–8]

There is a growing literature suggesting that teaching neonatal resuscitation through training based on low-dose, high frequency simulation practices has a positive effect on long-term knowledge and skills of healthcare providers and significantly decreases perinatal mortality rate.[9–13] Although these results seem promising, research aimed on determining and refining components that improve retention of neonatal resuscitation skills and clinical performance is warranted.[14–16]

Video analysis of real-life newborn resuscitations showed limited adherence to NRP and HBB guidelines in both, high and low-resource settings.[17–21] Such findings confirm that further research in educational methods is needed in order to improve acquisition and retention of knowledge and skills related to newborn resuscitation.

Several educational aspects may play an important role in translating the knowledge and skills acquired during a standardized formal neonatal resuscitation training into clinical practice.[5,14] In fact, staff performance depends on individual skills but also on the ability to manage other relevant aspects such as planning and preparing the field, recognizing priorities, providing and maintaining standards, identifying and utilizing resources.[22,23] Crisis resource management (CRM) refers to a set of abilities (so-called “non-technical skills”) that are not strictly included in medical knowledge and manual skills, but are required to effectively manage emergency situations.[24] However, neonatal resuscitation programs such as NRP and HBB dedicate no attention on non-technical skills.[7,8] Previous studies evaluated technical skills of healthcare providers during real-life newborn resuscitation in low-resource settings,[9–13,19–21] but very little is known about behavioural and non-technical skills.

The aim of the present study was to assess non-technical skills of trained midwives during real-life newborn resuscitation in a low-resource setting before and after participation in a modified NRP course, and after a low-dose/high-frequency training.

Methods

Study design

This study evaluated the non-technical skills of trained midwives during an educational intervention at Beira Central Hospital (Mozambique). Three time points of assessment were defined: before the course (BC), after the course (AC) and after a low-dose/high-frequency training (LDHFT). This study is part of a research assessing the impact of an educational intervention in neonatal resuscitation.[19,21] The study protocol was approved by the National Committee of Bioethics (Ref. 315/CNBS/13; November, 1, 2013) and by the Minister of Health of the Republic of Mozambique (Ref. 08/GMS/002/2014; January, 7, 2014). Before delivery, parents gave their consent to obtain video recordings of neonatal delivery room management and to use the data for scientific purpose. In addition, written informed consent to use clinical records in the study was also given by parents and caregivers. All information including informed consent and the material used in the study was written in Portuguese in a clearly understandable form.

Setting

The study was performed at Beira Central Hospital, in the province of Sofala, Mozambique where about 4500 deliveries occur every year. Beira Central Hospital is the referral hospital for a geographical area that covers about 7 million people.[24] At this hospital, midwives are responsible for immediate postnatal care of all neonates, including resuscitation. Available equipment includes gloves, clean towels, wall suction device, suction catheters, bulb suction, a self-inflating bag with two available facemasks (size 0 and 1) and an oxygen source. Neonatal resuscitation program was based on the NRP algorithm (6th edition) apart from use of pulse oximetry, intubation and medications.[25]

Patients

All neonates needing resuscitation at birth were included in the study. Resuscitation was defined as any intervention provided by healthcare providers: initial steps in order to initiate spontaneous breathing, bag mask ventilation, and/or chest compressions. Lack of parental consent was the only exclusion criterion.

Intervention

This study is part of a research assessing the impact of an educational intervention and details of the intervention have already been described elsewhere.[20] On January 31, 2014, all midwives (median age 30 years; median experience in delivery room 7 years) responsible for immediate postnatal management of the newborns at Beira Central Hospital participated in an adapted NRP course held by expatriate instructors in local language. We decided to teach the modified NRP course because the NRP algorithm was already in use and known by midwives involved in neonatal resuscitation at the Beira Central Hospital. About 8 months after the adapted NRP course, we implemented a LDHFT focused on maintaining and improving the skills that were acquired during the course.[20] The LDHFT lasted 6 months and consisted of weekly 3-hour practical sessions on resuscitation held by a local instructor using a manikin (Neonatal Resuscitation Baby, Laerdal, Stavanger, Norway). Each midwife of the unit attended 4–5 sessions during the 6-month training. The content of the sessions consisted of continuous repetition of manual skill stations (initial steps including equipment preparation, prevention of heat loss, airway, stimulation and assessment; bag-mask ventilation; chest compressions) and scenarios guided and supervised by the same expert midwife, who was trained in NRP.[20] During the session, participant performance was not scored, but incorrect procedures and inadequate techniques were appropriately discussed

with and corrected by the instructor. However, the sessions did not include structured debriefing or review of the videos by the learners to underline mistakes. The same group of midwifes participated in the study during all three phases.

Data collection

One-hundred and fifty resuscitations (50 before the modified NRP course, 50 after the modified NRP course and 50 after the LDHFT) were video recorded and analysed by using a predefined composite score.[26] As described in a previous study,[19] video recording was performed by using a webcam for video monitoring (ENXDVR-4C, Encore Electronics. www.encore-usa.com), consisting of one fixed camera installed above the radiant warmers both in the delivery room and in the operating room. The image was zoomed to show only the newborn and the hands of the resuscitation team. Parents, obstetric procedures and faces of the caregivers were not visible. The videos did not include audio-recording. All videos were stored on a hard disk and sent to the coordinator centre (University of Padua). Maternal and neonatal data were also collected. In order to protect the identities of the subjects and the data, all data about resuscitation date and location were removed, and shipment was insured.

Assessment of non-technical skills

Non-technical skills were evaluated using the Anesthetists' Non-Technical Skills (ANTS) tool.[26] This tool is based on four categories (task management, team working, situation awareness and decision-making) that include individual items representing important actions or behaviors (Table 1). Each item was scored using a Likert scale from 1 (poor performance) to 4 (good performance). All video-recordings were viewed and evaluated by two neonatologists (MEC and DT) who were high fidelity simulation instructors. Additional expertise was also received from a CRM expert neonatologist (AS) in case of doubts or disagreement between the two assessors. A descriptive anchor was provided for each item, in order to reduce personal bias in interpreting performance (Table 1).

Statistical analysis

Continuous data were expressed as median and interquartile range (IQR), categorical data as number and percentages. Non-technical skills (scored as poor, marginal, acceptable, good) were compared among the three groups (before the course - BC, after the course - AC and LDHFT) using Fisher's test, followed by pairwise comparisons as appropriate. Pairwise comparisons were performed between BC and AC groups (to evaluate the improvement due to the course), and between AC and LDHFT groups (to evaluate the outcome of the low-dose/high-frequency training). All p-values were adjusted according to Benjamini-Hochberg method for multiple endpoints.[27] A p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using R 3.3.2 software (R Foundation for Statistical Computing, Vienna, Austria).[28]

Table 1 – Descriptive anchor for each item of Anesthetists' Non-Technical Skills tool, in order to reduce personal bias in interpreting performance. (modified from Fletcher et al. [26]).

Category	Individual items	Descriptive anchor
Task management	-planning and preparing	*1: no equipment available/ 2: very limited equipment available (i.e. suction system) / 3: acceptable equipment available (at least SIB & oxygen) / 4: all equipment available (pre-warmed linen, suction system, SIB, oxygen)*
	-prioritizing	*understand the problem and act 1: only prolonged stimulation and/or suction / 2: PPV after prolonged stimulation and/or suction / 3: PPV within 1 minute after birth/ 4: effective PPV and re-evaluation*
	-providing and maintaining standards	*follow the steps of resuscitation: 1: without order / 2: with order / 3: correct order and timing / 4: correct order and timing and re-evaluation*
	-identifying and utilizing resources	*use the available equipment/material (suction system, SIB, oxygen, etc.): 1: do not use material / 2: wrong use/ 3: use discreetly / 4: adequate use*
Team working	-coordinating activities with team members	*confirm roles and responsibilities of team members; consider requirements of others before acting*
	-exchanging information	*discuss maternal history with team members; mutual feedback during resuscitation among team members*
	-using authorities and assertiveness	*adequate coordination by the team leader and cooperation by team members*
	-assessing capabilities	*adequate assignment of roles among team members (according to individual experience and capabilities)*
	-supporting others	*mutual motivation and cooperation among team members (helping each other when necessary)*
Situation awareness	-gathering information	*collect and interpret the information correctly*
	-recognizing and understanding	*choose correct interventions based on patient's clinical response*
	-anticipating	*anticipate clinical deterioration starting adequate interventions and avoiding wasting time*
Decision-making	-identifying options	*choose the best option when available (i.e. PPV rather than prolonged stimulation and/or suction or oxygen)*
	-balancing risks and selecting options	*avoid prolonged suction and/or stimulation / start PPV immediately and choose corrective options / start CC after effective PPV has been established*
	-re-evaluating	*patient's re-evaluation: HR assessment: 1: never / 2: at least 1 time during resuscitation; 3: before starting and after PPV; 4: at every step of resuscitation (before starting and after PPV, and before and after CC)*

Results

Participants

The resuscitations were performed on 150 newborn (99 males and 51 females) with a median gestational age of 38 weeks (IQR 36–40) and a median birth weight of 2575 g (IQR 2200–3220 g). Median Apgar score was 5 (IQR 2–6) at 1 minute and 6 (IQR 4–7) at 5 minutes. Seventy-two (48%) subjects were born through cesarean section. Mothers had a median age of 23 years (IQR 19–29) and 62 of them were primiparous (41%).

All 150 neonates received the initial steps of resuscitation; 103 of them received bag-mask ventilation, and 41 also required chest compressions. The midwives had a median age of 30 years (IQR 28–36) with a median experience in delivery room of 7 years (IQR 4–10).

Non-technical skills

The specific skills of team working (i.e. coordinating activities with team members; exchanging information; using authorities and assertiveness; assessing capabilities; supporting others) were unobserved in most resuscitations (by group: 47 in BC, 47 in AC and 42 in LDHFT) because only one health caregiver was present at birth, and could therefore not be evaluated.

All non-technical skills were scored as poor/marginal in BC and in AC, except from one item in "planning and preparation" in AC (Figs. 1–3). Fourteen resuscitations had at least one item scored as acceptable/good in LDHFT. Numeric results are reported in Supplementary Table 1.

All aspects of task management significantly changed across the three groups (Fig. 1). Planning and preparing improved from BC to AC ($p = 0.02$) but was similar in AC and LDHFT ($p = 0.10$). Prioritizing was similar in BC and AC ($p = 0.99$) but improved from AC to LDHFT ($p = 0.02$). Providing/maintaining standards improved from BC to AC ($p = 0.03$) and from AC to LDHFT ($p = 0.04$). Identifying and utilizing resources was similar in BC and AC ($p = 0.99$) but different between AC and LDHFT ($p = 0.02$).

Regarding situation awareness, no statistically significant differences were observed among the three groups about gathering information and anticipating ($p = 0.61$ and $p = 0.14$, respectively; Fig. 2). Most participants received a poor score about gathering information (88% in BC, 90% in AC and 82% in LDHFT) and anticipating (92% in BC, 90% in AC and 78% in LDHFT). Recognizing/understanding was similar in BC and AC ($p = 0.20$) but improved from AC to LDHFT ($p = 0.04$).

Small improvements were observed in decision-making (Fig. 3). Identifying options and balancing risk / selecting options were similar in BC and AC ($p = 0.45$ and $p = 0.85$, respectively) but improved from AC to LDHFT ($p = 0.04$ and $p = 0.02$, respectively). Re-evaluating was not significantly different among the three groups ($p = 0.06$).

Discussion

The present study evaluated the non-technical skills of trained midwives during an educational intervention including a modified NRP course and a low-dose/high-frequency training. Our findings showed a limited impact of this educational intervention on non-technical skills during real-life newborn resuscitation in a low-resource setting. In addition, all items indicated unsatisfactory performance regarding several aspects, thus suggesting the need for a different educational approach.

Recent studies showed encouraging results of the HBB program in improving the quality of delivery room interventions and perinatal mortality rate in low-resource settings,[9–13] but the transfer of theoretical knowledge and skills into the delivery room remains an important barrier to the success of neonatal resuscitation training programs.[14,15] To better understand this phenomenon, we chose to evaluate the performance of midwives providing neonatal

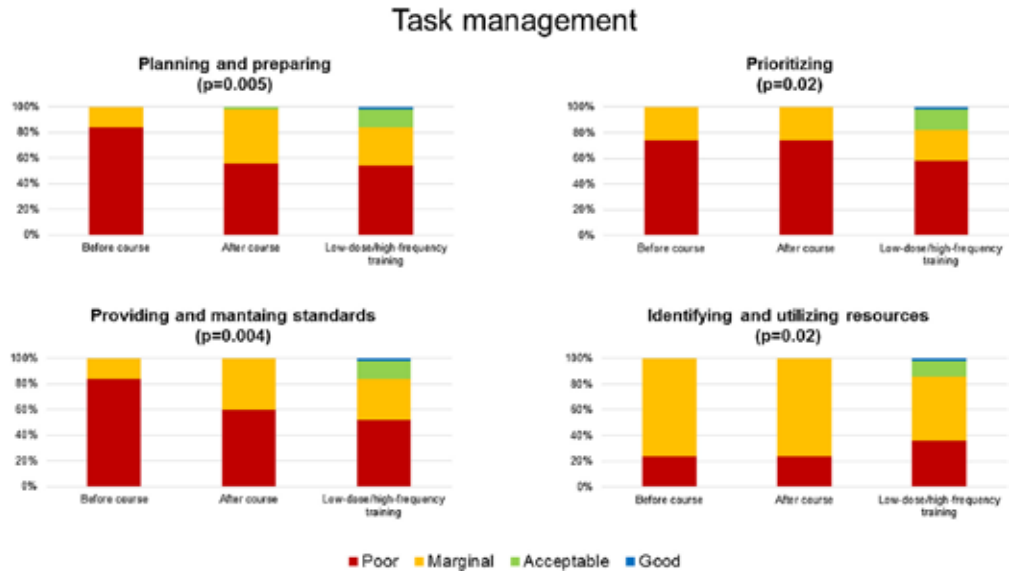

Fig. 1 – Task management.

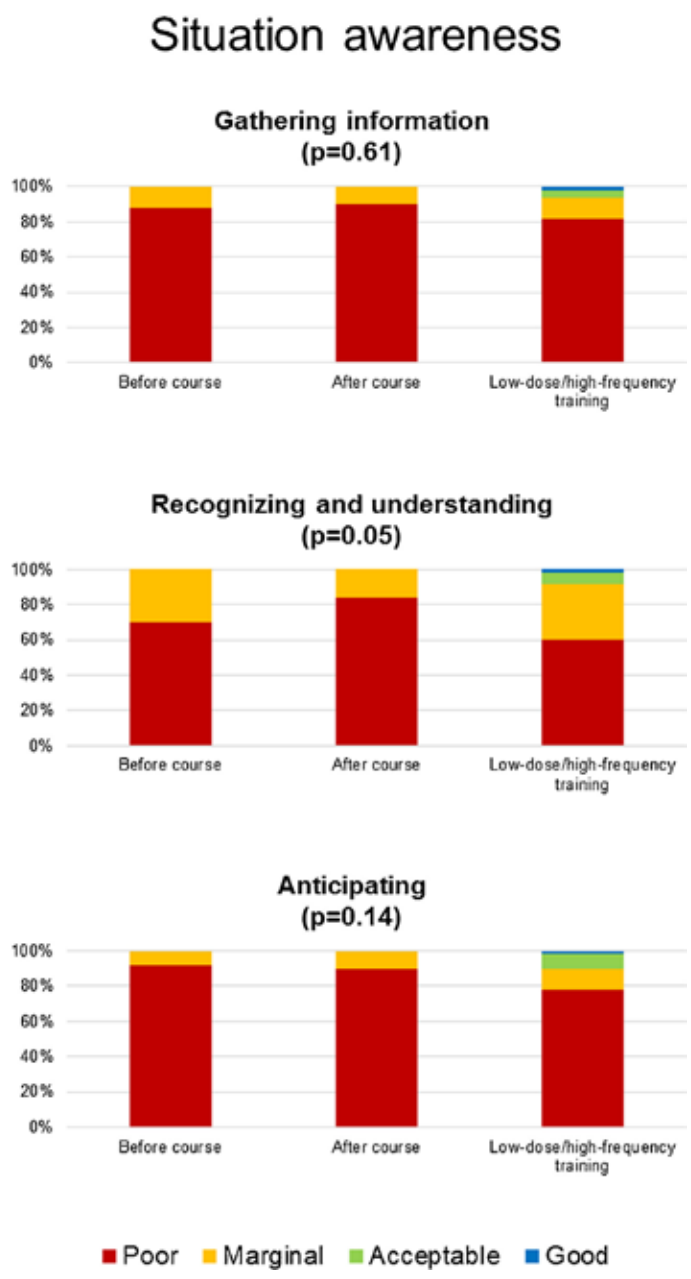

Fig. 2 – Situation awareness.

resuscitation in a low-resource setting from a different point of view. As previous studies in high-resource settings clearly showed that non-technical skills had the most relevant role in effectively managing emergency situations,[22,23] we evaluated the behavioral skills of healthcare providers during real-life neonatal resuscitation in a low-resource context.

Non-technical skills related to task management showed some improvements during the training. These results could be explained by the aspects included in the task management category (i.e. planning and preparing, prioritizing, providing/maintaining standards and identifying/utilizing resources), which mostly reflected the knowledge and the skills taught during the NRP course and the

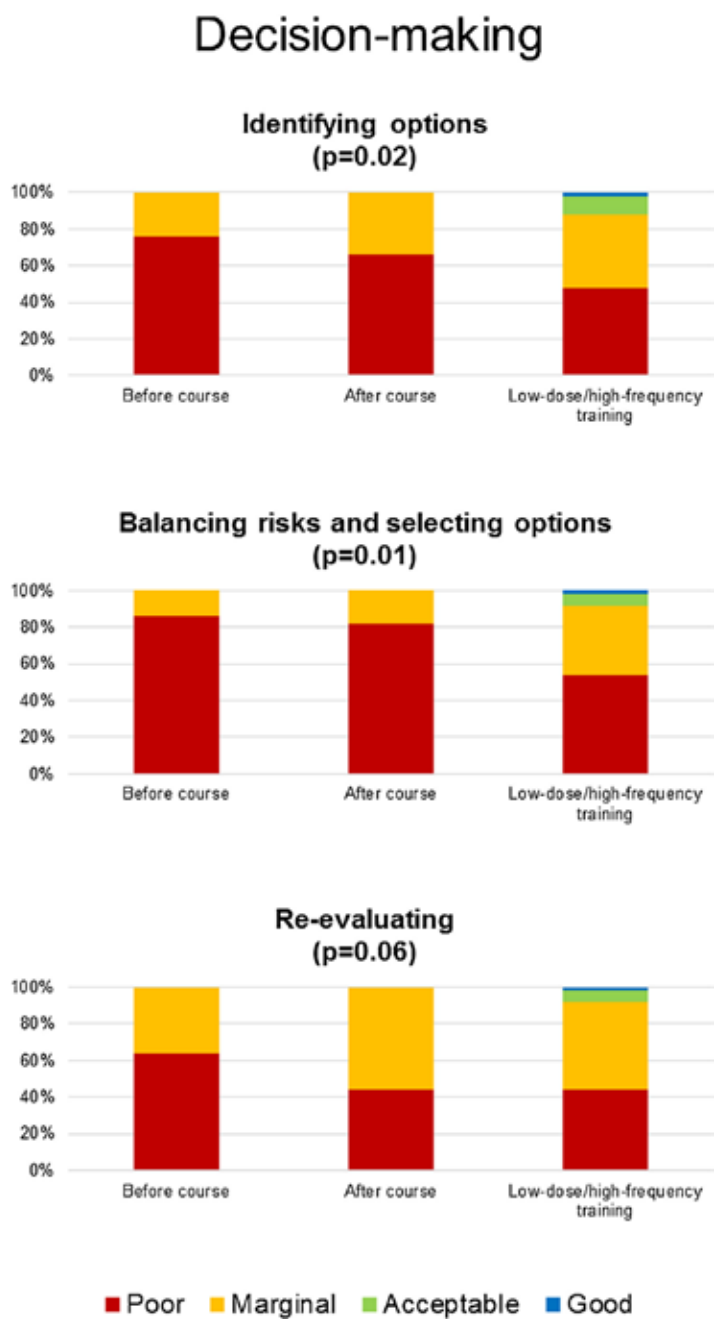

Fig. 3 – Decision-making.

LDHFT. However, the improvement was heterogeneous, with some items improving after the course while other skills were developed only after the LDHFT. These findings were in broad agreement with previous studies that evaluated the impact of newborn resuscitation training on technical skills of healthcare providers in resource-limited settings.[15,16,19–21]

Overall, the non-technical skills related to situation awareness were poor, with no relevant effect of the educational intervention. It is noteworthy that items in this category mostly mirror "cultural" approach to the problem, thus limiting the effect of a resuscitation training. In fact, a previous survey showed that "the fate of the baby is independent from my intervention" was one of the most common

opinions to interpret the scarce application in real life of knowledge and skills acquired during a modified NRP course.[29] In our study, only recognizing/understanding showed a little improvement after the LDHFT, thus suggesting that such training could help in overcoming some cultural fatalistic behavior.[9,13–15] These findings clearly indicate that further initiatives on this field should take into account additional aspects such as the lack of motivation and/or the fatalist approach of healthcare providers involved in the care of the newborns at birth.[30] An approach focused on the evidence-based clinical practice and Quality Improvement initiatives at facility level could also contribute to ameliorate this gap.[14,15,31]

The LDHFT led to small improvements in two aspects of decision-making (i.e. identifying options and balancing risk/selecting options), which overall remained unsatisfactory. These results could be explained by the educational training (modified NRP course) that was adopted. A different educational program, such as HBB that focuses on ventilation and omits chest compressions, could help participants in identifying and selecting the right options in a resource-limited setting.[8–15]

A further explanation for the limited scores obtained by the midwives in this study could be the lack of a simulation training based on CRM principles.[22,23,29] In high-resource settings, simulation training in an immersive environment replicating a real clinical scenario could facilitate the training in behavioral and communication skills.[25,26] Simulation has been used as an educational methodology to teach cognitive, technical, and behavioral skills also in neonatal resuscitation, but its superiority on "traditional" training in improving delivery of care remains to be confirmed.[32–35] Additional educational challenges in low-resource settings include lack of dedicated education time, sustainability challenges of LDHF practices and lack of focus on critical thinking skills (opposed to text book learning).

It is noteworthy that the majority of our deliveries (91%) only had one single provider, thus we could not focus on teamwork or use other assessment tools (such as TEAM scale[36]). This situation represents a common challenge of neonatal resuscitation in low-resource settings, where usually there is only one provider for caring mother and baby.

Teamwork represent an urgent need in order to improve neonatal and maternal morbidity/mortality in low-resource settings. At least one health-care worker focused on the mother postpartum and one on the newborn asphyxiated baby should be available in each delivery setting.

The strengths of the study include the evaluation of staff performance based on video-recording, the recording of actual resuscitations rather than a video of a skill and the evaluation of staff performance based on video-recording by two high fidelity simulation experts using a predefined tool.

The present study has also some limitations. First, the evaluation of non-technical skills was based on the modified Anesthetists' Non-Technical Skills tool,[26] thus some aspects regarding behavioral skills could not be taken into account. Using high-resource assessment measures represents a challenge in low-resource settings. However, the assessment was performed by two neonatologists with expertise in high fidelity simulation and a descriptive anchor (Table 1) was provided for each item, in order to reduce personal bias. Second, inter-rater variability was not assessed since the two neonatologists viewed and evaluated the video-recordings simultaneously, then achieved a shared decision on the score. Third, the training was based on a modified NRP course because the NRP algorithm was already in use and known by participants at the Beira Central Hospital. Further studies may investigate the effect of different training programs, such as the HBB package,[8] on behavioral skills of health care providers.

Conclusion

An educational intervention including a modified NRP course and a low-dose/high-frequency training had a limited impact on the non-technical skills of trained midwives during real-life newborn resuscitation in a low-resource setting. All items remained significantly under the recommended standards. Behavioral skills should be considered in training programs to improve the quality of neonatal resuscitation in low-resource settings. Challenges of this topic include educational disparities in low-resource settings (i.e. focus on textbook opposed to hands-on learning, lack of previous exposure to simulation, cultural differences) and the lack of a validated tool to evaluate non-technical skills in neonatal resuscitation. Further studies should evaluate the impact of training including non-technical skills on relevant clinical outcomes.

Contributors' Statement

Dr Cavicchiolo wrote the initial draft of the manuscript, contributed to data collection, assessed the videos and made a substantial contribution to the interpretation of the data.

Dr Cavallin participated in the conception of the study, performed the data analysis, redrafted the manuscript, and gave a substantial contribution to the design and interpretation of the data.

Dr. Staffler assessed the videos, participated in the conception and design of the study and made a substantial contribution to the analysis and interpretation of the data.

Drs Pizzol, Matediana and Wingi Manzungu contributed to data collection, strictly followed all the local phases of the study and made a substantial contribution to the interpretation of the data.

Dr. Da Dalt supervised all the phases of study and made a substantial contribution to the interpretation of the data.

Dr. Putoto participated in the conception and design of the study and made a substantial contribution to the analysis and interpretation of the data.

Dr. Trevisanuto conceived and designed the study; made substantial contribution to the analysis and interpretation of the data; redrafted the manuscript and revised it for important intellectual content.

All authors critically revised the manuscript for important intellectual content; and approved this version of the manuscript.

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Conflict of interest

The authors have no potential conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2018.10.034.

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Neonatal hyperglycemia as predictor of 4-weeks mortality in a low resource setting

POSTER PRESENTATION

Conference
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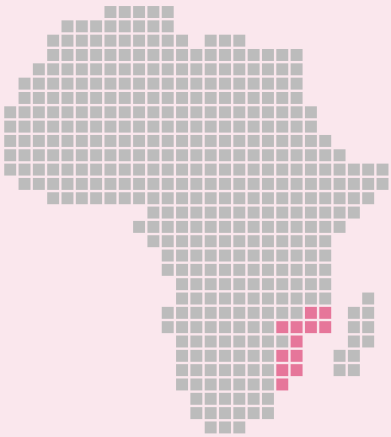
May 23rd – 26th 2018

Authors
Galeazzo B., Galderisi A., Pizzol D., Putoto G., Baraldi E., Da Dalt L., Trevisanuto D.

Focus country
Mozambique



Neonatal hypoglycemia is associated with acute neurologic dysfunction and long-term neurodevelopmental impairment. Glycemic test during the first hours of life is still a challenging procedure in low-resource settings.

We assessed the prevalence and the determinants of neonatal glucose impairment during the first 12 hours of life in a low-resource setting in order to optimize the neonatal glucose screening recommendations.

The study was conducted at Beira Central Hospital in Mozambique. We tested glucose level by heel prick in the first 12 hours of life according to the hospital's protocol. Hypoglycemia was defined as a blood glucose reading <2.8mmol/L (50mg/dl), while hyperglycemia was >8mmol/L (144mg/dl). A multivariate regression model was adopted to individuate the main predictors of hypo and hyperglycemia among the following neonatal variables: birthweight, gestational age, need for resuscitation in delivery room. A logistic regression analysis was conducted to assess the predictors of mortality at 28 days of life.

In a low resource setting, hyperglycemia affects about ten percent of neonates admitted to the special care unit and is a significant predictor of mortality at four weeks of life. Glucose test could be considered as one of the tools for risk-definition of neonates in low-resource settings.

Neonatal hyperglycemia as predictor of 4-weeks mortality in a low resource setting

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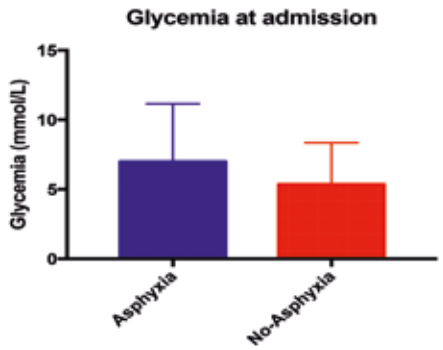
Background: Neonatal hypoglycemia is associated with acute neurologic dysfunction and long-term neurodevelopmental impairment. Hyperglycemia is associated with adverse outcomes in premature infants and critically ill children. Glycemic test during the first hours of life is still a challenging procedure in low-resource settings.
We assessed the prevalence and the determinants of neonatal glucose impairment during the first 12 hours of life in a low-resource setting in order to optimize the neonatal glucose screening recommendations.

Methods: The study was conducted at Beira Central Hospital in Mozambique. We tested glucose level by heel prick in the first 12 hours of life according to the hospital's protocol. Hypoglycemia was defined as a blood glucose reading <2.8mmol/L (50mg/dl), while hyperglycemia was >8mmol/L (144mg/dl). A multivariate regression model was adopted to individuate the main predictors of hypo and hyperglycemia among the following neonatal variables: birthweight, gestational age, need for resuscitation in delivery room. A logistic regression analysis was conducted to assess the predictors of mortality at 28 days of life.

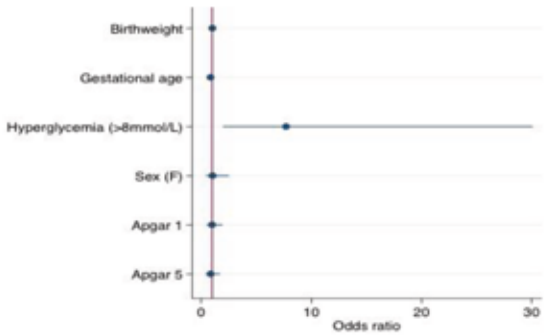
Results: We enrolled 152 neonates, GA 36.3±4.2 weeks' gestation, birthweight 2432±906 g from November 1, 2016 to December 24, 2016 at Beira Central Hospital. 18% of neonates had a gestational age <32 weeks' gestation with a mean BW of 1190±312g; 63,2% were male.
Principal diagnosis were sepsis (61,2%), prematurity (< 36 weeks'gestation 36,8%); asphyxia (34,2%). Death at 28 days occurred in 34,8% of cases.
We detected 7 hypoglycemic events and 18 hyperglycemic events; most of the hypo and hyperglycemic events occurred during the first 120 minutes of life.

Figure 1. Glycemia and need for resuscitation



Subjects requiring neonatal resuscitation exhibited higher values of glucose (6.99±0.58 mmol/L vs 5.37±0.29 mmol/L, p0.0064) than their peers

Figure 2. Mortality at 28 days of life



The occurrence of an hyperglycemic event was the single predictor of mortality at 28 days of life, when assessed by a logistic regression model accounting for with an odds ratio for death of 7.6±5.3 (p0.003)

Conclusion: In a low resource setting, hyperglycemia affects about ten percent of neonates admitted to the special care unit and is a significant predictor of mortality at four weeks of life. Glucose test could be considered as one of the tools for risk-definition of neonates in low-resource settings.

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7th ICCN - International Conference on Clinical Neonatology - Turin, May 23rd-26th, 2018

Case-control study to assess the effectiveness of maternity waiting homes in reducing perinatal mortality at the Wolisso Hospital (South West Shoa Zone, Oromia Region, Ethiopia)

POSTER PRESENTATION

Original title
Studio caso controllo per valutare l'efficacia delle case d'attesa materne nella riduzione della mortalità perinatale nell'ospedale di Wolisso, South West Shoa Zone, Regione Oromia – Etiopia

Conferenza
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October 17th – 20th 2018

Authors
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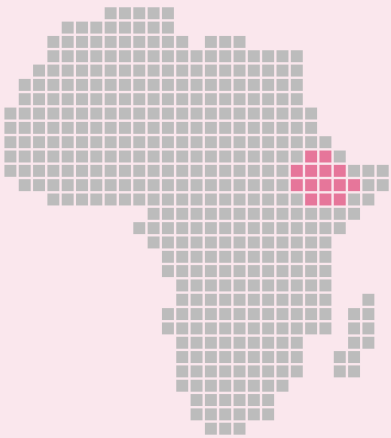
Focus country
Ethiopia



The aim of this study was to assess the effectiveness in reducing perinatal mortality of maternity waiting homes (MWHs), residences close to health facilities where women with high-risk pregnancies can stay as they approach their expected date of delivery, being monitored and receiving access to emergency care should complications arise.

We analyzed data from 1,207 cases and 2,414 controls. Preliminary results suggested that MWHs are effective in reducing perinatal mortality through hospital care, particularly given the greater risk of adverse outcome in the women admitted to them.

51 CONGRESSO NAZIONALE SItI RIVA DEL GARDA 17-20 OTTOBRE 2018

POSTER

Argomenti Vari

Studio caso controllo per valutare l'efficacia delle case d'attesa materne nella riduzione della mortalità perinatale nell'ospedale di Wolisso, South West Shoa Zone, Regione Oromia - Etiopia

T. Dalla Zuanna [1], M. Fonzo [1], C. Resti [2], A. Tsegaye [2], G. Azzimonti [2], F. Manenti [2], G. Putoto [2], C. Bertoncello [1]

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INTRODUZIONE

La casa d'attesa materna (Maternity Waiting Home-MWH) è una struttura residenziale situata in prossimità di una struttura sanitaria, dove le donne con gravidanza a rischio possono alloggiare a ridosso del travaglio, con monitoraggio sanitario, ed essere trasferite alla struttura sanitaria all'insorgere di complicazioni. Nonostante le MWH siano diffuse nei paesi a risorse limitate, l'evidenza circa la loro efficacia è scarsa. Lo scopo dello studio è valutare se la MWH sia utile a ridurre la mortalità perinatale nel contesto dell'ospedale di Wolisso, in Etiopia, dove l'ONG Italiana Medici con l'Africa CUAMM opera dal 2000.

MATERIALI E METODI

Con uno studio caso-controllo è stata confrontata la frequenza di decessi perinatali tra donne ricoverate nella MWH situata dentro l'ospedale di Wolisso e donne entrate direttamente in ospedale. "Casi" erano le donne con almeno un figlio nato morto o deceduto prima della dimissione tra l'1/1/2014 e il 31/12/2017. Sono stati selezionati come controlli le prime due mamme con gravidanza con esito positivo dopo ciascun caso. Per ciascuna donna si è valutata l'esposizione alla MWH, e dai registri e dalle cartelle cliniche sono state raccolte variabili materne, neonatali, e condizioni legate al parto. Con il programma SPSS v23 è stata condotta un'analisi descrittiva, con test $\chi 2$ e t-test con $p<0,05$ laddove appropriati, ed è stato calcolato l'Odds Ratio (OR) con IC al 95% fra casi e controlli esposti/non esposti alla MWH.

RISULTATI

Nello studio sono stati inclusi 1207 casi e 2414 controlli, 53 casi e 145 controlli erano stati in MWH. I risultati statisticamente significativi ($p<0,05$) hanno evidenziato che le donne accolte in MWH erano in media più vecchie (28,4 vs 26,3 anni), avevano già avuto più parti (22% con almeno 5 parti, vs 11%), avevano più frequentemente parto gemellare (14% vs 5,4%), e avevano effettuato visite prenatali (46% vs 24%). I nati da madri ricoverate in MWH avevano un peso medio maggiore (3,04kg; DS:0,69 vs 2,85kg; DS:0,73) e un APGAR score più elevato. Per le madri non ricoverate in MWH la probabilità di mortalità perinatale era del 40% più alta rispetto alle madri in MWH (OR:1,40; IC95%:1,01-1,92).

CONCLUSIONI

I risultati preliminari dello studio sembrerebbero dimostrare l'efficacia della MWH a livello ospedaliero nella riduzione della mortalità perinatale, soprattutto considerando la presenza maggiore di fattori di rischio nelle donne ricoverate in MWH. Il ricorso a un'analisi multivariata potrà fornire ulteriori evidenze circa l'efficacia delle MWH, e valutare quali categorie siano maggiormente protette da tale strumento.

Infectious and tropical diseases

Predictors of therapy failure in newly diagnosed pulmonary tuberculosis cases in Beira, Mozambique

PAPER

Authors
Pizzol D., Veronese N., Marotta C., Di Gennaro F., Moiane J., Chhaganlal K., Monno L., Putoto G., Mazzucco W., Saracino A.

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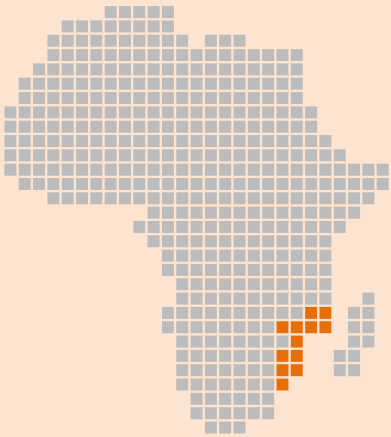

Abstract

Tuberculosis (TB) is one of the top ten causes of death worldwide. Mozambique is one of the countries worst affected by the disease, with a significant failure rate in the treatment of TB patients.

In order to develop effective TB treatment regimens even for the most vulnerable groups within a population, it is necessary to identify the risk factors associated with treatment failure. In this study we evaluated the treatment of 300 TB patients (32% of whom were female, and an average age of 31) in the city of Beira and analyzed those factors.

The standard six-month treatment regimen failed in 62 of the patients (20.6%). Our multivariate analysis associated this failure with their low levels of education and income: almost half of them, in fact, had received no education at all and almost 70% had a monthly income of less than 50 Euros. These determinants lead to both a lack of knowledge about and attention to health issues and limited access to health care and services. As a result, the drugs used to treat the disease are sometimes administered inappropriately, with either inadequate or excessive dosages. Thus a multi-sectoral approach is called for in the treatment of TB, one that takes into account not only pharmacological aspects but also the socio-economic predictors linked to treatment failure.

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BMC Research Notes

RESEARCH NOTE Open Access

Predictors of therapy failure in newly diagnosed pulmonary tuberculosis cases in Beira, Mozambique

Damiano Pizzol[1], Nicola Veronese[2], Claudia Marotta[3], Francesco Di Gennaro[4,5*], Jorge Moiane[6], Kajal Chhaganlal[6], Laura Monno[4], Giovanni Putoto[7], Walter Mazzucco[3] and Annalisa Saracino[4]

Abstract

Objective: Tuberculosis (TB) remains a major global health issue, ranking in the top ten causes of death worldwide. A deep understanding of factors influencing poor treatment outcomes may allow the development of additional treatment strategies, focused on the most vulnerable groups. Aims of the study were: (i) to evaluate the treatment outcome among TB subjects followed in an outpatient setting and (ii) to analyze factors associated with treatment failure in newly diagnosed patients with pulmonary TB in Beira, the second largest city of Mozambique.

Results: A total of 301 TB adult patients (32.6% females) were enrolled. Among them, 62 (20.6%) experienced a treatment failure over a 6 months follow-up. On multivariate model, being males (O.R. = 1.73; 95% CI 1.28–2.15), absence of education (O.R. = 1.85; 95% CI 1.02–2.95), monthly income under 50 dollars (O.R. = 1.74; 95% CI 1.24–2.21) and being employed (O.R. = 1.57; 95% CI 1.21–1.70), low body mass index values (O.R. = 1.42; 95% CI 1.18–1.72) and HIV status (O.R. = 1.42; 95% CI 1.10–1.78) increased the likelihood of therapy failure over 6 months of follow-up. In this study, patients who need more medical attention were young males, malnourished, with low income and low educational degree and HIV positive. These subjects were more likely to fail therapy.

Keywords: Tuberculosis, Mozambique, Therapy failure

Introduction

Tuberculosis (TB) remains a major global health issue, ranking in the top ten causes of death worldwide [1]. In 2015, 10.4 million people were estimated as newly diagnosed with TB and 1.8 million deaths were registered worldwide [1], not equally distributed all over the world. Particularly, over 90% of global TB cases and deaths occurs in low and middle income countries, and especially in fragile states [2]. Moreover, despite effective anti-tuberculosis chemotherapy, case-fatality rates of up to 25% are described in both industrialized and resource-poor settings [3].

Mozambique is ranked 19th among the 22 TB High Burden Countries in the world, with an estimated TB incidence rate of 551/100.000 population in 2015 [4]. However, TB treatment covers only 38% of the population, and an increasing rate of TB–HIV co-infection is usually documented (49% of TB patients were HIV-positive) [4]. In Mozambique, the treatment success rate among new sputum smear-positive cases has increased from 76% in 2003–79% in 2007 and 87% in 2015 [4].

In this African Country, among the many challenges dealing with TB control, both ensuring proper TB diagnosis and treatment as well as implementing the one-stop model for TB care have been regarded as national priorities [5] Worryingly, recent data from Manhiça, a district located in southern Mozambique, show an alarming mortality rate among TB adult cases co-infected with HIV [6]. The potential threat of increasing multi-drug resistance (MDR) cases in the country—the latest national survey documented a MDR incidence of about 3.5% among new TB cases—could jeopardize the achievement of the

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treatment success targets set in the strategic plan 2014–2018 of the National TB Control Programme (NCTP) [5, 7].

A deep comprehension of factors influencing poor treatment outcome may allow the development of additional treatment strategies, focusing on the most vulnerable groups. Unfortunately, very few data are available addressing this issue, particularly in Mozambique. In general, predictors for unsuccessful treatment are considered socio-demographic, behavioral, disease-related and treatment-related factors [8]. In Mozambique, only one study conducted in the country highlighted factors associated with a higher risk of death during the TB treatment: HIV status, being male and lack of laboratory confirmation [6]. For these reasons, the aims of our study were (i) to evaluate the treatment outcomes among TB subjects followed in an outpatient setting and (ii) to analyze factors associated with treatment failure in newly diagnosed cases with pulmonary TB in Beira, the second largest city of Mozambique.

Main text

Study population and design

An observational study was implemented.

All cases of pulmonary TB diagnosed between January and August 2016 were recruited in this observational study from three urban outpatient health-care centers of Beira district, namely Ponta-Gea, Munhava and Macurungo, the largest in Sofala's Province, involved in the National Tuberculosis Control Programme (NCTP).

Inclusion criteria were to be a subject aged $\geq$ 18 years, having a confirmed TB diagnosis (positive sputum smear result, GeneXpert positive result, culture positive result or Positive chest X-ray) [1] and able to undergo anti-TB treatment, not having any anti-TB treatment or TB treatment started within the previous 2 months.

Anti-TB treatment was prescribed according to the Mozambique National Tuberculosis and Leprosy Control Programme guidelines [5]. So, when GeneXpert was negative for resistances, patients underwent an initial phase of therapy with Isoniazid, Rifampin, Pyrazinamide and Ethambutol lasting the first 2 months and then a continuation phase with Isoniazid and Rifampin for the next fourth months. While, when GeneXpert documented a resistance to Rifampin a second line therapy was implemented.

At the end of therapy every patient underwent a general visit, X-rays and/or sputum smear, and diabetes diagnosis test.

A face-to-face interview conducted by a trained nurse encompassed questions about demographic characteristics (age, residence, education, occupation, marital status, monthly income), pregnancy, behaviours (sexual behaviour, concurrent sex partners, condom use, smoke and alcohol abuse, etc.) and medical history, including TB and diabetes symptoms. A basic physical examination (vital signs, weight, height, waist circumference, blood pressure and general appearance) was performed. The body mass index (BMI) was calculated. Moreover, subjects with unknown HIV status received a pre-HIV test or a rapid HIV test, if not done before.

Each participant, during two consecutive clinic visits, underwent two fasting blood glucose tests to investigate on diabetes: according to WHO guidelines, patients were considered as non-diabetic if both measurements were $\leq$ 110 mg/dl, and as diabetic if both measurement were above 126 mg/dl. If at least one value was between 110 and 126 mg/dl, the Oral Glucose Tolerance Test (OGTT) was further performed: patients were considered diabetic when plasma glucose at 2 h was $\geq$ 200 mg/dl [9]. All TB-diabetic patients underwent assessment of diabetic complications.

Treatment outcomes were defined according to WHO criteria [10]. Successful treatment outcome was defined as a clinical and radiological improvement in a patient with a baseline smear positivity and evidence of at least two negative sputum smears, the first during the maintenance period, and the second as the treatment was completed. Treatment failure was defined as the detection of positive sputum smear in a patient at month 5 or later of treatment.

Statistical analysis

Data were reported as mean and standard deviations for continuous variables. Absolute and relative frequencies (percentages) were used for categorical variables.

Independent T-test was used to compare groups for continuous variables, whilst a Chi square test (with the Fisher's correction if less than 5 cases were present in a cell) was applied for categorical variables.

A logistic regression model was implemented as follows. Treatment failure was considered as dependent variable and each one of the available factors at the baseline evaluation as independent variables (univariate analysis). In the multivariate analysis all the factors with a p-value < 0.10 at the univariate analyses were included. Multicollinearity among covariates was assessed through the variance inflation factor (VIF), taking a value of 2 for excluding a covariate. However, no variable was excluded according to the previous criterion.

Odds Ratios (ORs) as adjusted Odds Ratios (Adj–ORs) with their 95% confidence intervals (CIs) were used to measure the association between factors at the baseline (exposure) and treatment failure (outcome).

All statistical tests were two-tailed and statistical significance was assumed for a p-value < 0.05. Analyses were

performed by using the SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois).

Results

A total of 301 TB adult patients (32.6% females) were enrolled in the study (Table 1), distributed among the three outpatient health-care centers as follow: 132 (43.8%) Ponta-Gea, 63 (20.9%) Munhava and 106 (35.2%) Macurungo. The whole sample had a mean age of 31 years (S.D.: 12.5). Nearly half of the participants (48.2%) reported to have no education, 187 (62.0%) participants were employed and only 83 (27.6%) had a monthly income higher than 50 dollars.

With regard to participants' lifestyle and behaviour information, 25 participants (8.3%) reported to be current smokers and 38 (12.6%) daily drinkers. The majority of the participants reported to have one sexual partner, whereas only 7 (4.7%) reported to have more than one, and the remaining part (36.5%) had no partner.

According to medical history and examination, 56.0% of participants presented a BMI (< 18.5) below the healthy range, whereas arterial hypertension was found just in only 1 patient (0.3%).

The HIV status was known to be positive in 131 patients (43.5%) and 93 (70.9%) of them were receiving antiretroviral treatment (ART). Furthermore, diabetes or impaired glucose tolerance (IGT) was diagnosed in 9 patients (3%).

TB was diagnosed by a positive chest X-ray examination in 148 patients (49.2%); 246 patients (81.7%) had a positive sputum examination and 56 patients (18.6%) a positive GeneXpert sputum test.

The most reported symptoms before the initiation of treatment were cough (98.3%), loss of weight (86.7%), asthenia (71.4%), night sweats (67.1%) and fever (57.8%).

A total of 62 patients (20.6%) experienced a treatment failure over a 6-month follow-up.

No difference was documented between patients experiencing treatment failure or success as regards age (p-value: 0.84) and gender (p-value: 0.25). On the contrary, employed subjects (93.1%; p-value < 0.0001), with no education (71.7%; p-value < 0.0001) and with a

Table 1 Characteristics of the 301 recruited TB patients and differences in treatment outcomes

Characteristics	Study population n. 301	Treatment		p-value
		Failure n. 62	Success n. 239	
Average age (years)	31 (12.5)	33.3 (12.8)	30.4 (12.1)	0.84
Female n. (%)	98 (32.6)	24 (24.5)	74 (75.5)	< 0.0001
No education	145 (48.2)	41 (28.3)	104 (71.7)	< 0.0001
Employed	187 (62.0)	13 (6.9)	174 (93.1)	< 0.0001
Monthly income ≤ 50 dollars	218 (72.4)	49 (22.5)	169 (77.5)	< 0.0001
Lifestyles and behaviours				
Current smoking	25 (8.3)	17 (68.0)	8 (32.0)	< 0.0001
Alcohol use	38 (12.6)	21 (55.3)	17 (7.1)	<0.0001
Sexual partner/s				< 0.0001
No	110 (36.5)	24 (21.8)	86 (78.2)	< 0.0001
Yes	184 (61.1)	35 (56.4)	149 (62.3)	
Medical history and examination				
Low BMI (< 18)	169 (56.0)	45 (26.6)	124 (73.4)	< 0.0001
HIV positive	131 (43.5)	39 (37.4)	92 (62.6)	< 0.0001
Antiretroviral treatment (ART)	93 (30.9)	18 (19.3)	75 (80.7)	< 0.0001
Diabetes or IGT	9 (3.0)	6 (66.7)	3 (33.3)	< 0.0001
Positive chest X-ray	148 (49.2)	9 (6.0)	139 (94.0)	< 0.0001
Positive sputum examination	246 (81.7)	40 (16.3)	206 (83.7)	< 0.0001
Positive GeneXpert	56 (18.6)	35 (62.5)	21 (37.5)	< 0.0001
Symptoms before treatment				
Cough	296 (98.3)	59 (20.4)	237 (79.6)	<0.0001
Loss of weight	261 (86.7)	33 (12.6)	228 (87.4)	< 0.0001
Astenia	215 (71.4)	25 (11.6)	190 (88.4)	< 0.0001
Fever	174 (57.8)	24 (13.8)	150 (86.2)	< 0.0001
Night sweat	202 (67.1)	26 (12.8)	176 (87.2)	< 0.0001

monthly income < 50 dollars (77.5%; p-value < 0.0001) were more frequent in the success group, whereas daily alcohol users (55.3%; p-value < 0.0001) and current smokers (77.5%; p-value < 0.0001) exceeded in failure one.

The multivariate model considered the effects of gender, BMI, education, alcohol use, being employed, monthly income, smoking habits, HIV status, being on ART, sputum examination and GeneXpert positivity. Significant predictors of therapy failure over 6 months of follow-up are reported in Table 2: male sex (O.R. = 1.73; 95% CI 1.28–2.15), absence of education (O.R. = 1.85; 95% CI 1.02–2.95), monthly income under 50 dollars (O.R. = 1.74; 95% CI 1.24–2.21) and being employed (O.R. = 1.57; 95% CI 1.21–1.70), low BMI values (O.R. = 1.42; 95% CI 1.18–1.72) and HIV status (O.R. = 1.42; 95% CI 1.10–1.78).

Table 2 Predictors of treatment failure over 6 months of follow-up

Characteristics	Univariate analysis O.R.	Multivariate analysis Adj–O.R.
Age (years)	1.02 (0.98–1.04)	–
Female	0.28 (0.16–0.40)	0.58 (0.47–0.78)*
Low BMI (< 18)	1.80 (1.42–2.02)	1.42 (1.18–1.72)*
No education	1.50 (1.28–1.74)	1.85 (1.02–2.95)*
Alcohol use	0.04 (0.00–0.10)	0.45 (0.08–1.03)
Employed	0.51 (0.43–0.70)	0.64 (0.59–0.83)*
Monthly income ≤ 50 dollars	1.85 (1.35–2.45)	1.74 (1.24–2.21)*
Actual smoking	2.02 (1.27–2.53)	1.33 (0.85–178)
Sexual partner/s	0.10 (0.04–0.85)	0.39 (0.08–1.28)
Positive chest X-ray	–	–
HIV positive	1.80 (1.50–2.00)	1.42 (1.10–1.78)*
Antiretroviral treatment (ART)	0.64 (0.38–0.78)	0.74 (0.50–1.03)
Diabetes or IGT	–	–
Positive sputum examination	0.25 (0.10–0.40)	0.71 (0.28–1.23)
Positive GeneXpert	2.00 (1.45–2.55)	1.28 (0.74–2.79)

* $p < 0.05$

Limitations

Very few data are available about the outcome of TB treatment in high burden countries, leaving a lack of important evidences for the implementation of future public health and clinical strategies. In our sample of patients referring to the three urban health centers of the Beira District, a percentage of 20% of patients experiencing a treatment failure over a 6 months follow-up was found.

In the present study these unsuccessful treatment outcomes were found to be associated with a low education level, low income and low BMI (< 18.5), resulting as the most relevant predictors of therapy failure from the multivariate analysis.

In fact, in our sample nearly half of patients had no educational degree and almost 70% had a monthly income lower than 50 dollars, defining a low socioeconomic status. This patients' profile, according to the literature [11, 12], is more likely to have less awareness of health issues, reduced access to health services, low self-care attention, resulting in delays in the TB diagnosis and treatment. Also, patients with low education level will be more likely to misuse and discontinue drug use during treatment [13, 14].

Similarly more then half of our patients presented a BMI below the healthy range, and it is well known that malnutrition is associated with an increased risk of mortality and relapse of active TB, whereas the use of macronutrient supplementation during treatment with weight gain at 2 months may result in improvement in physical function, sputum conversion and treatment completion [15].

In agreement with current literature, in our study, an association of poor TB treatment outcome with HIV infection was found [16, 17]. HIV co-infection is the most important risk factor for developing active TB, which increases susceptibility to primary infection, re-infection and/or reactivation of latent TB. TB also has a negative impact on the immune response to HIV, increasing the progression from HIV infection to acquired immunodeficiency syndrome (AIDS) [18].

The risk of poor treatment outcome in that particular subpopulation is higher. Hence, a particular attention should be destined for HIV/TB-co-infected patients whose TB treatment is burdened by frequency of drug administration, pill burden, drug interactions, drug toxicity and worse general health conditions, [19, 20].

Instead, we did not find additional risk factors for TB treatment default such as smoking and alcohol use [21], probably because our data could be underreported because they were not verified and were based on personal interview.

This study has some limitations. First, no sufficient data on MDR or XDR, no data on check at 2 month from start therapy and delay in diagnosis. This points, together with a deeper exploration of the role of comorbidities, such as diabetes [22] should influence future research on this field. On the contrary strengths are the high number of patients and the data from country where there are few notice about treatment outcome.

We describe the phenotype of patients that need more medical attention: young, male, malnourished, with low income and low educational degree, HIV positive. They

have more possibility to failure therapy and they need close follow up. Counseling and education on TB is always recommended in this more vulnerable patients [23, 24].

These considerations suggest that a drug approach is not enough to treat tuberculosis and further policies will have to take into account a multidisciplinary approach including education and social equity. Moreover, it is crucial to create a simple and effectiveness monitoring system, allowing a national overview also on multi-drug resistance and delay in diagnosis, in order to obtain complete and quality data to guide public health actions.

In conclusion, this study underlines that only pharmacological approach isn't longer sufficient to guarantee a reduction of TB burden. Social determinants of health have a crucial role, and more work, more instruction, in other words less poverty, HIV educational associated with pharmacological approach and early diagnosis can real improve TB patients outcomes and global TB burden. We believe that this is the way forward.

Abbreviations
TB: tuberculosis; WHO: World Health Organization; OR: odds ratio; BMI: body mass index; HIV: human immunodeficiency virus; MDR: multi-drug resistance; NCTP: National Tuberculosis Control Programme; OGTT: Oral Glucose Tolerance Test; VIF: variance inflaction factor; Adj–ORs: adjusted odds ratios; ART: antiretroviral treatment; IGT: impaired glucose tolerance; SDH: social determinants of health.

Authors' contributions
All individuals listed as authors have contributed substantially to designing, performing or reporting the study and every specific contribution is indicated as follows. Conception and design of the study: DP FDG KC JM GP AS LM. Data collection: KC FDG DP. Statistical analysis: NV JM. Interpretation of data: DP NV CM FDG WM. Manuscript writing and drafting: DP FDG CM NV. Revision of the manuscript: DP, NV, CM, FDG, CG, GP, LM, WM, AS. Approval of the final version of the manuscript: DP, NV, CM, FDG, CG, KG, JM, GP, LM, WM, AS. The document has been reviewed and corrected by a native English speaker with extensive scientific editorial experience to ensure a high level of spelling, grammar and punctuation. All authors read and approved the final manuscript.

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Competing interests
The authors declare that they have no competing interests.

Availability of data and materials
The data that supports the findings of this study are available on demand from the authors upon reasonable request and with permission of Doctors with Africa CUAMM.

Consent to publish
No individual consent for publication was required as all the analyses were made on aggregated data.

Ethics approval and consent to participate
The study was approved by the Comité Nacional de Bioetica para a Saúde—National Bioethics Committee for Health (protocol reference: 168/CNBS/15), Mozambique. An informed consent was administered to all the enrolled patients. Confidentiality was maintained keeping all the data in anonymity.

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Teenage pregnancies in Mozambique: the experience of Servicios Amigos dos Adolescentes clinics in Beira

PAPER

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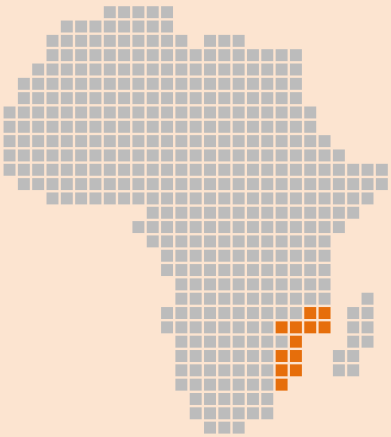
Infectious and tropical diseases + Maternal and child health

Focus country
Mozambique



This paper is not available as open access, which is why only an abstract is posted. If you would like to read the entire paper, please go to the web page given and follow the instructions.

Abstract

Since 2014, Doctors with Africa CUAMM has supported a network of clinics in Beira, Mozambique, aimed specifically at young people aged 10 to 24 – the *Servicios Amigos dos Adolescentes* (SAAJ) – which offer counseling, diagnostic tests and treatment to help adolescents learn more about sexual and reproductive health.

The present study involved an analysis of the data collected on the 8,290 girls and young women who had had outpatient visits at one of the SAAJs in 2014. It revealed that 3,021 of them (36%) were either currently or had recently been pregnant; the majority (59%) were aged from 15 to 19 and had dropped out of school.

Sixty percent of the 8,290 girls and young women agreed to take an HIV test, and HIV prevalence was found in 4-5% of the adolescents and 25% of the women aged 25 or older. The situation vis-à-vis pregnant girls and women was alarming, with very high HIV prevalence rates: 2% in girls aged 10-14, 8% in those aged 15-19, 10% in those aged 20-24, and 28% in those aged 24-25.

Based on our analysis, there seems to be a clear need to expand both health services and awareness-raising activities for Mozambican adolescents in order to improve their access to HIV treatment.

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Teenage pregnancies in Mozambique: the experience of Servicios Amigos dos Adolescentes clinics in Beira

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The purpose of this article is to provide insights into the demand for pregnancy-related health services by adolescent girls and young women in Mozambique. We analysed the patient registers for the first year of operation (2014) of the Servicios Amigos dos Adolescentes (SAAJ) [Friendly Services for Adolescents] clinics in Beira, Mozambique. These registers provide details of the service demands of, and services provided to the 8 290 adolescent girls and young women who accessed the 6 SAAJ clinics in 2014. Analysis of that record, with disaggregation of the patients according to age (9 years or less; 10–14; 15–19; 20–24; 25 and older), show that 3 021 (36%) were pregnant or had previously been pregnant; most being girls in the 15–19 age band (59%). Being pregnant or having been pregnant previously was associated with dropping out of school. Of all the girls and women, 60% agreed to HIV testing and counselling; the HIV prevalence rate amongst this group was 4–5% amongst adolescents and 25% amongst women 25 years and older. A minority of the girls and women who were pregnant or had been pregnant previously agreed to HIV testing and counselling. Notwithstanding the limitations for analysis, the results were alarming: substantially high HIV prevalence rates were indicated (2% amongst 10–14 year old girls; 8% amongst 15–19 year olds; 10% amongst 20–24 year olds; and 28% amongst >24 year olds). The data from the SAAJ clinics and results pertain only to conditions in Beira. However, as the first empirical assessment of pregnancy-related service demand amongst adolescent girls and young women in the country and involving a relatively large sample, we contend that this study affirms the need for expansion of sexual and reproductive health (SRH) services, including HIV services, for adolescent girls and young women in Mozambique.

Keywords: adolescent health, Doctors with Africa, Friendly Services for Adolescents, HIV, SAAJ, teenage pregnancy

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Breast tuberculosis in men: A systematic review

PAPER

Authors
Quaglio G., Pizzol D., Bortolani A., Manenti F., Isaakidis P., Putoto G., Olliaro P.L.

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Abstract

Breast tuberculosis in men is a rarely reported and poorly described condition. The aim of this systematic review of the available literature was to quantify its incidence and describe its clinical features and the procedures used to diagnose and treat it.

The average age of the men in the 26 cases analyzed was 56.5. In most of the cases (89%) the patients presented an isolated lump, associated in 27.8% of the cases with axillary lymphadenitis and in 33.3% with topical inflammation. The most commonly reported symptoms were pain (64.7%) and fever (35.3%).

Breast tuberculosis is not easy to diagnose in either men or women, and no specific treatment guidelines are currently available. Even though men are not at high risk for the condition, diagnosis often takes a very long time and involves inappropriate empirical treatments, thereby negatively impacting the health conditions of those affected by it as well as their ability to receive effective treatment.

PLOS ONE

RESEARCH ARTICLE

Breast tuberculosis in men: A systematic review

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Competing interests: The authors have declared that no competing interests exist.

Abstract

Setting

Breast tuberculosis in male is a rarely reported and poorly described condition.

Objective

To quantify the number of breast tuberculosis in men, to describe clinical presentation and to present the diagnostic and therapeutic procedures applied.

Design

A systematic review of the literature including reports published in English, Spanish and French until December 2017.

Results

The search yielded 26 cases of male breast tuberculosis, median age 56.5 years. Most presented with an isolated breast lump (89%), associated with axillary lymphadenitis (27.8%) and skin inflammation (33.3%). The most common constitutional symptoms were pain (64.7%) and fever (35.3%). Fine-needle aspiration cytology and culture were the most common diagnostic modality (61.5%). Standard anti-tuberculosis regimen was the main treatment, alone or accompanied or preceded by incision and drainage.

Conclusions

The risk of breast tuberculosis in men appears to be low, but the condition can be difficult to diagnose and the diagnostic delays can be long. Overall prognosis is good following standard anti-tuberculosis regimen with or without incision/drainage.

Introduction

Tuberculosis (TB) is a chronic granulomatous inflammation usually involving the lung parenchyma and hilar lymph nodes. Extra-pulmonary involvement is seen in ~20% of all TB cases [1]. TB of the breast is an uncommon disease, particularly in men [2,3]. The first case of breast TB was reported in a woman in 1829 [4], but the first detailed description of the disease was only made by the end of the 19th Century [5, 6]. The first case of breast TB in a man was reported about a century later in 1927[7], and by 1945 there were only 21 known cases of breast TB in men [7–10]. It is generally believed that the infection of the breast is usually secondary to tuberculous foci elsewhere in the body, which may or may not be clinically apparent [11, 12]. There are no well-defined clinical features of male breast TB, which may be confused with other clinical conditions, such as gynecomastia and breast carcinoma [13]. Therefore, TB of the breast can be difficult to diagnose and the diagnostic delay can amount to several months. To our knowledge, one systematic review has been published to-date on breast TB in man [3]. The review identified 24 cases, which presented mostly with an isolated breast lump; constitutional symptoms were rare; fine needle aspiration cytology (FNAC) was the most common diagnostic modality. However the review had limitations: it covered only the English literature, 16 of these cases were from mixed female and male series (where information on the male cases were challenging to extrapolate), and only 8 described as single case report. Therefore, we aimed to update and expand the existing evidence-base by systematically reviewing the English, Spanish and French literature for single-case reports and case-series about risk factors, clinical appearance of lesion and clinical presentations, constitutional symptoms, diagnostic procedures; and anti-tubercular and surgical treatments. of breast TB in men.

Methods

Search strategy

Searches were undertaken in PubMed, Embase and Web of Science. A search strategy was developed using a combination of free text and controlled vocabulary terms and adapted for each database. We used the following search strategy: (tuberculosis OR TB) AND (breast OR mammary OR mastitis) AND (men OR male). We included reports of studies published in English, Spanish and French until December 2017. Additional studies were identified by contacting the authors and by searching the reference lists of primary studies. The process of study selection is summarized in Fig 1. Titles and abstracts identified through the searches were reviewed independently by two reviewers (GQ and DP). In case of duplicate publications, the most recent publication which reported full data was included. Full text copies of the selected studies were retrieved and independently reviewed against the inclusion criteria by two reviewers from a team of three (DP, GP, GQ). Outcome measures included: i) risk factors for breast TB; ii) clinical appearance of lesion and clinical presentations; iii) constitutional symptoms; iv) diagnostic procedures; and v) anti-tubercular and surgical treatments.

Data extractions and analysis

Each of the included studies was coded with a pre-formulated rating sheet with relevant data extracted and recorded by two reviewers. The data extracted included: name of the first author, year of publication, country where the study was conducted, general participant characteristics (age and gender) risk factors (HIV+, previous history of TB), breast affected (right, left), type of lesion (lump, abscess, disseminated), clinical presentations (sinus or fistula, skin ulceration, nipple retraction, discharging sinus), constitutional symptoms (fever, decreased appetite, decreased weight, pain), duration of symptoms, previous empirical antibiotic treatment,

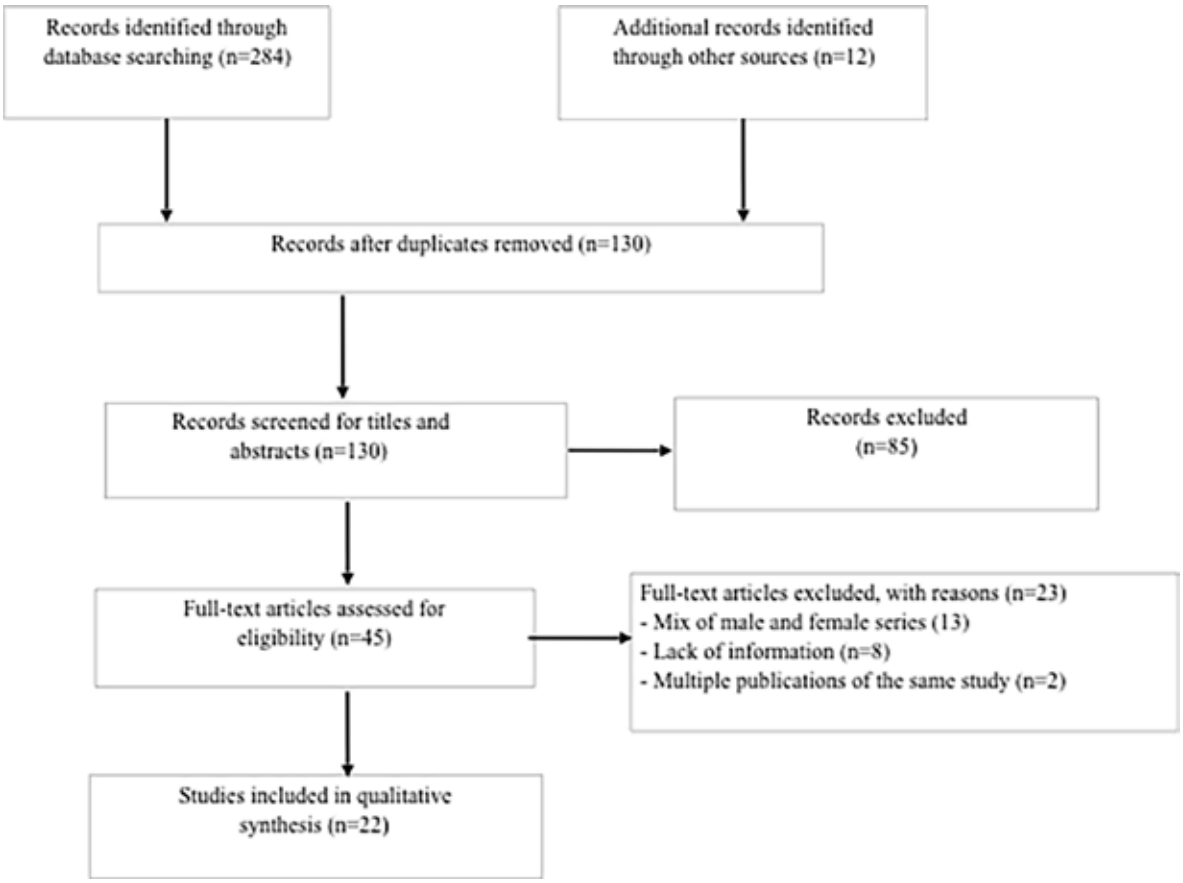

Fig 1. Study selection flowchart.

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previous steroids treatment, previous chemotherapy, chest X-ray results, diagnostic procedure (biopsy, FNAC, Ziehl-Neelsen, culture, polymerase chain reaction (PCR), surgical procedure and type and duration of anti-tubercular treatment. Since this review identified mainly case-reports and a limited number of small case-series, a meta-analysis was not considered relevant.

Publication bias

This is a systematic review of non-analytical studies i.e. case-series and cases-reports and the assessment of publication bias might not be practically applicable [14].

Quality evaluation of studies

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) and the approach by the Agency for Healthcare Research and Quality (AHRQ), are not suitable to be used for our systematic review of non-analytical studies. For this reason we have not performed a formal evaluation of the quality of the included studies [14].

Results

Study selection and characteristic of included studies

We identified 284 potentially eligible studies from the database searches, and 12 studies screening of bibliographies and by contacting the authors. We removed duplicates and screened the titles and abstracts of the remaining 130 records: 45 publications were selected for full-text screening, from which 22 articles were included in the final analysis (Fig 1). Thirteen articles reported mixed males and females cases, from which it was not possible to obtain specific information on individual male cases, and therefore could not be included in the analysis [15–27] (Table 1).

Other studies were excluded for lack of information or multiple publications of the same study (Fig 1). These 22 articles reported on 26 cases of male breast TB [3, 28–48]; one article included 3 cases [37], two reported 2 cases [28, 39] and 19 are single case reports [3, 29–36, 38, 40–48] (Table 2). The information collected on different variables differ from study to study as the data were not fully available in the case reports collected.

Geographic distribution and clinical characteristics

Cases were from Asia (n = 8 (30.8%), of which 6 from India and 2 from China), the USA (n = 7, 26.9%), Europe (n = 5 (19.2%) one each in Spain, Italy, Germany, UK and France), Africa (n = 4 (15.4%) from Morocco and Madagascar) and the Middle East (n = 2 (7.7%) from Jordan and Turkey). The median age was 56.5 years (range 17–92).

Location was reported as unilateral in all 26 cases, 14 of which in the right breast, 10 in the left breast and 2 not reported. Clinical presentation as a lump was described in 23 cases (89%), of which one case was accompanied by an abscess; the others were one case of isolated breast abscess and two cases of disseminated lesions. Associated findings were skin inflammation (alone or associated with discharge and/or lymphadenopathy) in 6 cases (33.3%), axillary lymphadenopathy (either alone or associated with discharge and/or skin inflammation), in 5 cases (27.8%), skin ulceration (along with discharge and/or lymphadenopathy) in 3 (16.7%); there was one case of nipple retraction and sinus or fistula (5.5%); no associated findings were reported in 8 cases. General symptoms were unknown in 9 cases (34.6%). Three patients did not report any accompanying symptoms. In the remaining 14 cases, pain (alone or with fever and/or weight loss), was reported by 11 subjects (64.7%) fever by 6, weight loss by 5 and cough by 3, all with other symptoms.

Table 1. Articles reported mixed males and females cases.

Author	Reference	Year	Country	No. of male cases
Shinde	15	1995	India	3/100
Kakkar	16	2000	India	6/160
Khanna	17	2002	India	2/52
Puneet	18	2005	India	1/42
Bani-Hani	19	2005	Jordan	1/9
Harris	20	2006	India	1/38
Metha	21	2010	India	1/63
Lin	22	2010	Taiwan	1/26
Meerkotter	23	2011	South Africa	1/21
Chandanwale	24	2012	India	1/11
Ramaema	25	2015	South Africa	1/65
Raza	26	2016	India	1/9
Darré	27	2017	Togo	2/28

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Prior history and diagnosis

The duration of symptoms before seeking medical care was reported for 13 cases, as was highly variable, ranging from 3 to 260 weeks (median 18 weeks). Earlier history of TB was reported for 13 subjects, 5 of them (38.5%) had previous history of the disease. HIV status was reported for three cases, all negative. Information relating to previous antibiotic treatment was reported for 14 subjects, of whom three had received empirical antibiotic treatment before the final diagnosis of breast TB. In the clinical history of the 26 cases described, there was no information related to previous steroid treatments. One patient received chemotherapy for a lymphoma 5 years before developing breast TB [46].

The diagnostic procedure was documented in all 26 cases. Different diagnostic methods were combined. A chest X-ray was performed in 16 cases: it was negative in 12 (75%), showed signs of active TB in 2 and previous TB in another 2. FNAC was carried out in 16 cases all negative except 3 positive. Ziehl-Neelsen acid-fast bacilli (AFB) staining was performed in 16 patients, of which 11 were positive. Culture was performed in 16 cases, all but 2 positive. Biopsy was positive in 8 out 9 cases. PCR was performed in 4 cases, all of which positive. Using culture or PCR as the gold standard, the sensitivity of AFB was 66.7% (8/12 culture- and/or PCR positive cases; the specificity could not be determined as there were no concomitant culture-negative cases tested with AFB); all six cases tested with FNAC and culture were positive on both. The only negative culture was positive by PCR.

Medical treatment and surgical treatment

Twenty patients (76.9%) received surgical treatment (10 drainage, 9 excision, one both drainage and excision). Eight subjects (30.8%) received surgical treatment without systemic medication. Six patients (23.1%) received systemic medication without surgical treatment. Twelve subjects (46.1%) received a combination of surgical and medical treatment. The standard antituberculosis regimen (four-drug intensive phase with isoniazid, rifampicin, pyrazinamide and ethambutol, followed by a two-drug continuation phase with isoniazid and rifampicin) was the main treatment, used in 18 (76%) patients. Twenty-four subjects reported complete remission, and no cases of recurrences were described. Information on the follow up was missing for two cases. The follow up period (reported for ten cases) was 49.8 + 50.3 months.

Discussion

This systematic review identified 26 cases of breast TB in men reported in the literature. It provides an up-to-date description of the clinical presentation, diagnostic and therapeutic procedures of breast TB in men, though it cannot conclude whether this condition is actually rare or under-diagnosed. Previous studies of breast TB (see Table 1) have identified low numbers of cases altogether, with women being at much higher risk with ratios of 8 women to 1 man reported in Tunisia (1980–2001) [19]; 65:1 in South Africa (2000–2013) [25]; 63:1 (1992–2008) [21] and 52:2 in India (1986–2000) [17]; 30:0 in Pakistan (1999–2007) [49]; 29:0 in Peru (2002–2011) [50]. In addition, in some series of male breast lesions, TB was not represented: in a series of 113 men with breast lesions over 15 years, 93% had gynecomastia, 2 patients had primary breast cancer and one had metastatic lymphoma [13]. In another series of 241 males over 8.5 years no case of breast TB was reported [51].

There is no known risk factor for male breast TB. It is generally though that in pregnant and lactating women the increased vascularity of the breast with dilated ducts can predispose to tubercular infection. Pregnancy suppresses the T-helper 1 pro-inflammatory response, which may increase susceptibility to new infection [52]. HIV coinfection exposes people to an increased risk for primary or reactivation TB and for second episodes of TB from exogenous

Table 2. Table summary of 26 reported cases of breast TB in men.

Author, year and ref.	Country	Age	Duration of symptoms (weeks)	Type of lesion (localization)	Signs	Symptoms	Diagnosis	Medical therapy (months)	Surgery
Wilson, 1990 [28]	USA	83	130	Disseminated lesion (L)	Discharge, lymphadenopathy	Pain	X-ray-, culture+, AFB-	OATT (24)	Drainage
Wilson, 1990 [28]	USA	66	3	Lump (L)	None	None	X-ray*, biopsy-, culture+, AFB-	OATT (18)	Excision
Jaideep, 1997 [29]	India	43	12	Lump (R)	Nipple retraction	Pain	X-ray-, FNAC+	ATT (6)	Excision
Thompson, 1997 [30]	USA	58	4	Lump (R)	Skin inflammation	Weight loss, fever, cough	X-ray-, FNAC+, culture+, AFB+	U	Excision and drainage
Reyes, 1999 [31]	USA	68	4	Lump (R)	Skin inflammation	Weight loss, fever, cough	X-ray-, FNAC+, culture+, AFB+	U	Drainage
Luna, 2000 [32]	Spain	17	8	Lump (L)	U	U	Biopsy+, culture+, AFB-	OATT (6)	Drainage
Gupta, 2002 [33]	India	25	U	Lump (R)	U	Pain, fever	FNAC+	ATT (6)	None
Bani-Hani, 2005 [34]	Jordan	68	U	Lump (L)	U	U	X-ray*, biopsy+	ATT (6)	Excision
Winzer, 2005 [35]	Germany	53	U	Lump (R)	U	U	X-ray-, culture-, PCR+	U	Excision
Marie, 2007 [36]	France	63	12	Lump (R)	U	U	Biopsy+,Culture+, AFB+, PCR+	OATT (U)	Drainage
Reyes, 2007 [37]	USA	68	U	Disseminated lesion (R)	Skin inflammation	Fever, chills, poor appetite, nonproductive cough	FNAC+, AFB +culture+	U	Drainage
Reyes, 2007 [37]	USA	59	U	Lump (U)	Skin ulceration, discharge	U	FNAC+, AFB+	U	Drainage
Reyes, 2007 [37]	USA	29	U	Lump (U)	Skin ulceration, discharge	U	FNAC+, AFB+	U	Drainage
Ursavas, 2007 [38]	Turkey	41	8	Lump (R)	None	Pain	X-ray-, FNAC+, culture+, AFB+	ATT (9)	None
Luh, 2007 [39]	China	92	8	Lump (R)	Skin inflammation, discharge	Pain, anorexia, body weight loss	X-ray-, culture-, FNAC-, biopsy+	U (6)	Excision
Luh, 2007 [39]	China	80	U	Lump (L)	Skin inflammation, discharge	U	FNAC-, biopsy+	U (6)	Excision
Rajagopala, 2008 [3]	India	25	U	Lump (R)	None	Pain	X-ray+, FNAC+, AFB+	ATT (6)	None
Moujahid, 2011 [40]	Morocco	50	U	Lump and abscess (L)	Skin ulceration, discharge, lymphadenopathy	Pain, weight loss, fever	X-ray-, biopsy+, culture+	ATT (9)	Drainage
Cantisani, 2013 [41]	Italy	28	U	Lump (R)	U	Pain	X-ray-, FNAC+, culture+, AFB+	ATT (5)	None
Ssen, 2013 [42]	Madagascar	23	20	Lump (R)	Lymphadenopathy	None	X-ray-, biopsy+	ATT (8)	Excision
Mahajan, 2014 [43]	India	20	12	Lump (L)	Lymphadenopathy	Pain	X-ray-, FNAC+, culture+, AFB+	ATT (6)	None
El Hammoumi, 2014 [44]	Morocco	55	U	Lump (L)	Skin inflammation, lymphadenopathy	U	X-ray-, FNAC+, biopsy+, culture+	ATT (6)	Drainage
Prakash, 2015 [45]	India	60	260	Lump (R)	U	U	FNAC+, biopsy+, AFB-	ATT (U)	Excision
Khaparde, 2015 [46]	India	60	8	Lump (R)	None	Pain	FNAC-, culture+, AFB+, biopsy+	ATT (6)	Excision
Brown, 2016 [47]	UK	44	U	Abscess (L)	U	None	X-ray+, culture+, AFB-, PCR+	ATT (6)	Drainage
Orerah, 2016 [48]	Kenya	70	24	Lump (L)	None	Pain, weight loss, fever, night sweats, loss of appetite	PCR+	ATT	None

L = Left; R = Right; ATT = Antitubercular Therapy; OATT = Others Antitubercular Therapy; FNAC = Fine-Needle Aspiration Cytology; AFB = Acid-Fast Bacilli; PCR = Polymerase Chain Reaction; U = Unknown; X-ray* = Previous TB.

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reinfection [53, 54]. HIV has been considered as potential risk factor for breast TB, in both genders, however, this is not supported by evidence: no case of breast TB in women was found to be HIV-positive in a prospective series carried out in Peru of 28 female cases [55] or in a

retrospective series of 20 female cases [56]. Breast TB as a presenting manifestation of HIV is extremely rare [57]; although in the present study HIV status was described in only 3 males, none was positive.

The clinical presentation of breast TB in men is poorly described in the literature, and important elements are not uniformly reported, or not reported at all. The combination of a-specific signs and symptoms, the challenges of diagnosing breast TB especially in resource-constrained settings, and lack of awareness of the condition, both by the patient and the health provider, leads to significant diagnostic delay: the median delay in diagnosis was 18 weeks in this review. The main differential diagnosis to be considered are, among others, gynecomastia [13], breast cancer [58], non-tubercular granulomatous mastitis [59, 60], atypical mycobacterial mastitis [61], plasma cell mastitis [62], ethionamide and isoniazid associated gynecomastia [63, 64].

Breast TB is often difficult to diagnose in both genders. Computer tomography scan, magnetic resonance, mammography and ultrasound can provide useful information, particularly on the extent of the disease. However, none of these image findings are specific for breast TB. Coexistent pulmonary TB may be suggestive of breast TB, but active disease is often absent; in this review, chest X-ray was reported in 16 cases, with only two cases positive for active TB. FNAC, culture, and biopsies have been used for diagnosis [3, 43, 44]. Culture might be seen as the gold standard, though its complexity, time-lag between sampling and obtaining a result, and possibility of false-negative results in paucibacillary specimens makes it unsuited to large-scale use [47]. However, culture performed well in the present review, with all but one of the cultures done testing positive. The yield of FNAC, which detects the presence of epithelioid cell granulomas and necrosis, is variable. In the present and past reviews [3], it was the most common diagnostic modality for breast TB. Here, it proved highly sensitive, as all specimens tested for both FNAC and culture were positive. The ongoing roll-out of PCR closer to the point of care may increase the utility of this method [65]. Here, it was used in only four cases, too few to draw any conclusion, except that PCR was positive in the single culture-negative case. This review suggests that diagnosing breast TB requires a combination of clinical, history and radiological findings complemented with when possible two diagnostic techniques, including FNAC with AFB staining, PCR or culture, whenever possible.

Breast TB overall appears to have a good prognosis, though no specific guidelines are available for the treatment of breast TB, whether in men or women. The optimum duration of therapy is unclear, and objective criteria for assessing response are lacking [3]. A standard anti-TB regimen (four-drug two-month intensive phase followed by a two-drug four-month continuation phase), often accompanied (or preceded) by incision and drainage or lump excision appears to achieve satisfactory responses. Twelve subjects received surgical treatment. However, it is not possible to determine to which extent these procedures were performed as an initial step towards establishing a diagnosis, rather than being part of the treatment plan.

In conclusion, breast TB in men is a rarely reported entity, even in high TB burden countries. Since the clinical features are not well defined, TB of the breast can be difficult to diagnose and the diagnostic delays can be long. The most common presentation is a lump with skin inflammation, pain and the involvement of axillary lymph nodes. FNAC, culture, and biopsies have been used for diagnosis. No specific treatment guidelines are available. Standard anti-TB drugs appear to achieve satisfactory responses and overall prognosis is good.

Supporting information

S1 PRISMA Checklist.
(PDF)

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Health-care services for young people with HIV in Mozambique

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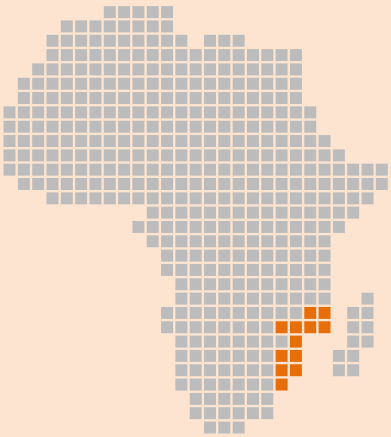

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Abstract

Adolescence is a delicate phase vis-à-vis adherence to antiretroviral therapy (ART) by young HIV-positive patients, who often drop out of treatment due to personal reasons or the transfer of their therapy management from pediatric to adult services.

Mozambique has the eighth-highest HIV prevalence in the world, particularly among adolescents aged 15-19. To help protect youth from sexually-transmitted diseases (STDs) and treat those who are affected by them, in 1999 Mozambique launched the "Geração Biz" program. Its centerpiece was the setting-up of clinics (SAAJs) that provide advice to young people aged 10-24 to help them learn more about HIV prevention.

Aided by volunteer health activists, Doctors with Africa CUAMM has worked in support of five of these clinics in Beira since 2004, helping to promote reproductive health and STD prevention education. ART is immediately initiated in patients who test positive for HIV.

The improved adherence to therapy now being seen among these young people underscores the importance of tailoring specific programs for this population segment aimed at lowering treatment dropout rates.

Correspondence

Health-care services for young people with HIV in Mozambique

Adolescence is a crucial phase for adherence to antiretroviral therapy (ART). In this period, many children who receive ART from birth experience difficulties, which put them at risk of abandoning therapy. Non-adherence to therapy happens not only because of personal problems related to this dynamic phase of life, but also because of the transition of care management from paediatric to adult services, as Diane Straub and Amanda E Tanner highlighted in their Review in *The Lancet Child & Adolescent Health*.[1] Tailored health services for adolescents could help reduce the risks.

Mozambique has a high prevalence of HIV, especially in the adolescent population aged between 15 and 19 years; the prevalence is around 2·5% in boys and 6·2% in girls.[2] Moreover, HIV infection is a major cause of death for those aged between 15 and 24 years.[3] To respond to the specific needs of aid for this vulnerable population, in 1999 Mozambique started the Geração Biz programme,[4,5] the main aim of which is the prevention of sexually transmitted infections and promotion of sexual and reproductive health in adolescents and young people aged between 10 and 24 years. A milestone of the programme was the creation of specific health services for adolescents aged between 10 and 24 years: Serviço amigo do adolescente e jovem (SAAJ).

The SAAJ offers a package of sexual and reproductive health services such as counselling; contraception; prevention and treatment of sexually transmitted infections; prenatal, postnatal, and post-abortion care; HIV testing; and antiretroviral treatment. The SAAJ was developed with the aim of not only addressing the health problems related to adolescence, but to also specifically follow adolescents on antiretroviral treatment. SAAJ provides services for adolescents and young adults until age 24 years through the transition from adolescent to adult care. After 24 years, they are referred to adult services in the same health-care unit maintaining the same medical record. Moreover, because of the scarce health professional resources, the same health workers often attend both SAAJ and adult HIV services. On one hand, this is a weakness that increases work load and thus might lower the quality of the service. On the other hand, it represents continuity of care for an adolescent with HIV to adulthood.

Our organisation Doctors with Africa CUAMM supports the Geração BIZ programme in the city of Beira (Mozambique) with SAAJs in five of the 15 health-care centres. At school level, our intervention is based on the promotion of reproductive health and education on the prevention of HIV and sexually transmitted diseases by activists and trained teachers. At community level and in the SAAJs, activists and dedicated health-care workers undertake free counselling and HIV testing. HIV-positive adolescents identified during community screenings are referred to SAAJs to start ART. Another important milestone of the CUAMM intervention is the follow-up of HIV-positive patients who start ART, to enable better adherence and long-term retention. Finally, to address the issue of therapy abandonment, activists actively find HIV-positive adolescents who default treatment. Indeed, the number of adolescents who drop-out of ART in Beira is high; after a few months of treatment almost 60% default, mostly for cultural, social, and educational reasons. Adherence is about 65%, an increase of 20% compared with adherence before CUAMM support. This outcome confirms the importance of having a specific tailored programme that targets adolescents to minimise abandonment of treatment, even if further work is needed.

In the coming years, we plan to build other specific SAAJs to assist adolescents in other health centres in Beira and to strengthen those already active. The SAAJ is only a model of structure and organisation to individualise assistance to adolescents, but it could be reproduced and adapted to other settings where young people are among the most vulnerable populations.

We declare no competing interests.

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Pathways of care for HIV infected children in Beira, Mozambique: pre-post intervention study to assess impact of task shifting

PAPER

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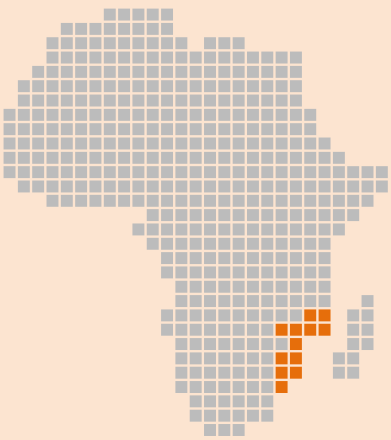

Abstract

Mozambique has the eighth highest HIV prevalence in the world. In June 2013 the country launched a task-shifting (TS) initiative for the administration of antiretroviral therapy (ART) to under-5 HIV-positive children, to be carried out not only by doctors working in HIV outpatient services but also nurses trained in mother and child care.

This study, which involved 588 HIV-infected children, 330 of whom were part of the post-intervention phase, sought to evaluate the effectiveness or lack thereof of the TS.

While we found an increase in regular nutritional visits and preventive therapy with isoniazid for children following the shift of activities to mother and child care-focused centers, no clear benefits were seen in terms of ART initiation and maintenance in the young HIV-infected patients.

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Pathways of care for HIV infected children in Beira, Mozambique: pre-post intervention study to assess impact of task shifting

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Abstract

Background: In 2013, Mozambique implemented task-shifting (TS) from clinical officers to maternal and child nurses to improve care for HIV positive children < 5 years old. A retrospective, pre-post intervention study was designed to evaluate effectiveness of a new pathway of care in a sample of Beira District Local Health Facilities (LHFs), the primary, local, community healthcare services.

Methods: The study was conducted by accessing registries of At Risk Children Clinics (ARCCs) and HIV Health Services. Two time periods, pre- and post-intervention, were compared using a set of endpoints. Variables distribution was explored using descriptive statistics. T-student, Mann Whitney and Chi-square tests were used for comparisons.

Results: Overall, 588 HIV infected children (F = 51.4%) were recruited, 330 belonging to the post intervention period. The mean time from referral to ARCC until initiation of ART decreased from 2.3 (± 4.4) to 1.1 (± 5.0) months after the intervention implementation (*p*-value: 0.000). A significant increase of Isoniazid prophylaxis (O.R.: 2.69; 95%CI: 1.7–4.15) and a decrease of both regular nutritional assessment (O.R. = 0.45; 95%CI: 0.31–0.64) and CD4 count at the beginning of ART (O.R. = 0.46; 95%CI: 0.32–0.65) were documented after the intervention.

Conclusions: Despite several limitations and controversial results on nutrition assessment and CD4 count at the initiation of ART reported after the intervention, it could be assumed that TS alone may play a role in the improvement of the global effectiveness of care for HIV infected children only if integrated into a wider range of public health measures.

Keywords: Human immunodeficiency virus, HIV exposed infants, HIV infected children, Task-shifting, Pathways of care, Paediatric HIV care and treatment

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Background

In past years, massive effort has been made globally in order to improve maternal and child mortality with regard to Human Immunodeficiency Virus (HIV) care and treatment in countries documenting highest prevalence [1].

Since 2001, according to the Prevention of Mother to Child Transmission (PMCT) Programs promoted by the World Health Organization (WHO) [2], the proportion of HIV infected pregnant women with access to the antiretroviral drugs has constantly increased, achieving 77% (69–86%) coverage worldwide in 2016 [3]. This improvement resulted in an indirect reduction of the number of HIV infected children (0–14), estimated at 150,000 (110,000–190,000) new infections in 2016, globally [3]. However, in 2016, the paediatric antiretroviral treatment (ART) coverage was still at 49% (42–55%) [3].

Mozambique, an east African country, has documented the world's 6th highest HIV prevalence, with an estimated 12.3% (10.6–13.9%) of adults aged 15–49 and 13,000 (7000–120,000) children under 15 years old "living with" HIV in 2016 [4]. Although the number of new HIV infections has decreased from 160,000 in 2001 to 83,000 in 2016, there are still 13,000 newly infected children every year [4]. Access to ART significantly increased in the country after 2010 due to the decentralization of HIV care from urban hospitals to the spread of local health facilities (LHFs) [3], the healthcare services nearest to the communities. Notwithstanding the documented advances, only 38% (25–48%) of the HIV positive children eligible for ART were estimated to receive the treatment in 2016 [4].

In June 2013, Mozambique aligned its PMCT policies to those recommended by WHO [5], implying the implementation of "Option B+" consisting of lifelong ART for all HIV infected and breastfeeding women regardless of their CD4 count and/or clinical status as well as ART being administered to all HIV infected children < 5 years old, independently from CD4 cell count and/or clinical status. In order to guarantee the sustainability of Option B+, Mozambican health authorities implemented a task-shifting (TS) from clinicians to Maternal and Child Health (MCH) nurses within a one stop model (OSM) of care delivered by the same provider in the same consultation. Indeed, until June 2013, in Mozambique, after the identification of the HIV status of the infected child within At Risk Children Clinics (ARCC), the HIV infected mother and her child were referred to an HIV health service (HHS) integrated within the outpatients department (OPD) for a further follow up, where a clinical officer took care of the child and a nurse of the mother.

Beira is the capital of Sofala province, one of the 5 Mozambican provinces in the country with the highest HIV prevalence (15.5%) [6]. In 2013, the coverage of paediatric ART in Sofala was at 32%, so below the national average, and ART initiation for children only reached 70% of the expected provincial target for that same year [6]. In June 2013, in an effort to improve ART initiation and retention of HIV infected children, Beira District Directorate of Health decided to provide the continuum of care for newly HIV positive children < 5 years old and their mothers within the ARCC, postponing their transfer to the HHS integrated by the OPD after the fifth year of age.

The aim of the study was to evaluate a sample of LHFs from the Beira District and determine the impact of the implementation of a different approach to the organization of human health resources based on TS from the clinical officers to nurses in regard to the effectiveness of the new pathway of care on i) the taking charge of HIV infected children, and ii) the administering of paediatric ART therapy.

Methods

Study setting, design and population

A retrospective pre-post intervention study was conducted [7].

The LHFs' inclusion criteria defined by the study protocol included: 1) to have implemented HHS since June 2012; 2) shifting to Option B+ and OSM in June 2013, including ART administered to children within the ARCC.

Of the 15 LHFs of the Beira District, 5 (33.3%) met the previous criteria and were enrolled in the study: Ponta Gêa, Munhava, Macurungo, Nhaconjo, Mascarenha.

All the HIV infected children < 5 years old accessing the ARCC of one of the 5 LHFs between June 2012 to May 2014 were identified through the Antiretroviral (ARV) registries and were recruited in the study. In particular, HIV Exposed Infants (HEI) were identified as HIV infected according to WHO guidelines: through a polymerase chain reaction using a dried blood spots test (PCR-DBS) if less than 18 months old, or through a HIV rapid test if older than 18 months.

Since health data of all children accessing the ARCC of the LHFs who met the study inclusion criteria were available, no sample size calculation was performed.

Intervention

The health district-level intervention of interest, introduced in Beira by the Local Health Authorities in June 2013, consisted in the TS of the care and treatment of HIV infected children from clinical officers to MCH nurses to ensure a continuum of care within the ARCC.

As the intervention was introduced in June 2013, two time periods lasting 365 days each were compared: one pre-intervention, from June 2012 to May 2013 (T1), and

one post-intervention, from June 2013 to May 2014 (T2).

Figure 1 shows the pathways of care provided in pre- and post- intervention time periods.

In the pre-intervention pathway of care (pre-TS), all HEIs were followed at the ARCC from the first month of life to the definition of their HIV status. Any child identified as HIV positive was then referred to a HHS integrated within the OPD of the same LHF receiving HIV care and treatment from a clinical officer, occasionally present in the structure, while mothers were under the responsibility of a nurse. In the post-intervention pathway of care (post-TS) all HEIs were monitored at the ARCC until the definitive diagnosis of their HIV status was determined, while any child identified as being infected was hosted in the ARCC until they turned 5 years old. Therefore, HIV infected children and their mothers were monitored and treated by the MCH nurses according to TS. Only after 5 years old could the children, together with the mothers, be referred to the OPD-HHS.

Endpoints

We compared the post intervention group (post-TS) with the pre intervention group (pre-TS) by using the following set of endpoints as a proxy to assess the impact of the new pathway of care, including TS implementation, on the effectiveness of taking charge of patients:

a) ART initiation according to the national guidelines:

1. initiation of ART before/after 9 months; 2. the mean time from the referral to initiation of ART; 3. the mean time from the HIV results to initiation of ART; 4. the mean age at initiation of ART;

b) Cotrimoxazole (CTZ) prophylaxis against HIV-related infection, Isoniazid (INH) prophylaxis

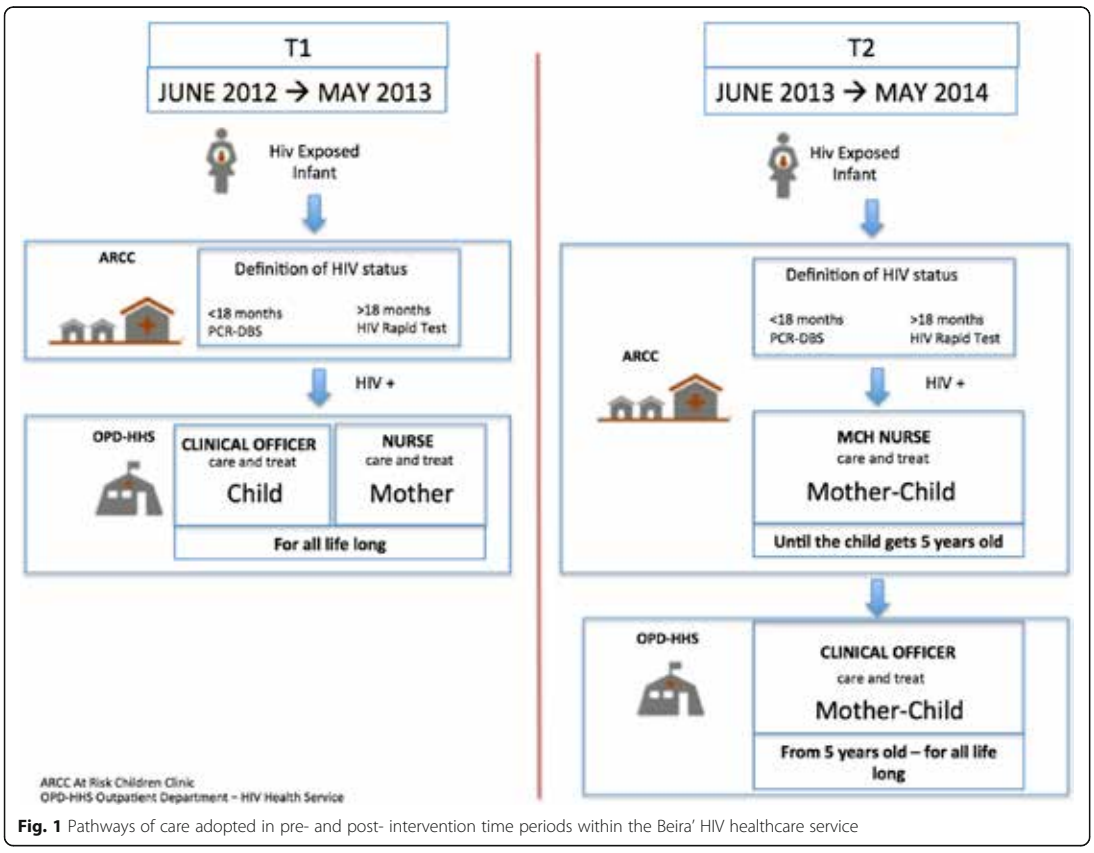

Fig. 1 Pathways of care adopted in pre- and post- intervention time periods within the Beira' HIV healthcare service

against tuberculosis (TB) both were implemented according to the national guidelines;
c) Assessment of nutritional status at each consultation.

Further, we considered CD4 count at the beginning of ART as an indicator of the process of taking charge of patients' care.

Data collection and analysis

Individual-level, routinely collected data were extracted from ARCC registries and HHS patients' files. Patients' information were further enriched with pharmacy files.

Record linkage was possible through a unique code assigned to the patient. Data extraction was performed between January and March 2016 by trained personnel of "Doctors with Africa" and the research Centre of Infectious Disease (CIDI) of the Catholic University of Mozambique (UCM). Data entry and management was in charge of CIDI research and was performed by using Microsoft Access 2013.

The variables distribution was explored by frequency tables and descriptive statistics such as mean and median. Comparison of the means of the two groups was done by using the t-student test, when data presented a normal distribution, while comparison of medians was performed using the nonparametric Mann Whitney test. The Chi-square test was used to compare the two groups by categorical variables, while Fisher's exact test was applied when the expected values were below or equal to 5.

Crude Odds Ratios (ORs) were calculated to measure the association between endpoints and intervention (independent variable), being ORs values > 1 predictive of a more effective care.

Data were analyzed by IBM SPSS Software 23 version (IBM Corp., Armonk, NY, USA). All *p*-values were two-sided and p-value < 0.05 was considered statistically significant.

Ethical approval of the protocol was achieved and (as this study used secondary data) informed patient consent was not required.

Results

Overall, 588 HIV infected children (F = 51.4%) were recruited in the study. Two-hundred fifty eight children (mean age = 15.9 months; range = 14.1–17.7) belonged to the pre-intervention group and 330 (mean age = 16.8 months; range = 15.4–18.3) to the post-intervention group.

Comparisons of the characteristics between the two groups are shown in Table 1. No differences were observed in HIV infected children's gender, age, weight, height, breastfeeding (breastfeeding or not, duration of breastfeeding) and nutritional status (normal nutrition or level of malnutrition). Also, no significant differences were documented in the two groups with regard to general information concerning HIV infected parents (age of mother/father, mother/father alive at consultation and HIV positive father). A significant statistical difference (*p*-value: 0.007) was highlighted for PMCT implementation to the mother at the first prenatal visit, being that ART was more frequently administered to mothers in the post-intervention group (31.5% versus 23.9%).

Table 2 summarizes the results of the further comparison between the pre- and post-intervention groups by clinical and laboratory information of the 588 HIV infected children obtained by the LHF registries.

Significant statistical differences between the two groups were observed with regard to ART prophylaxis at birth (*p*-value: 0.026), being more frequent in the post-intervention group (80.7% versus 70.9%), to tuberculosis (TB) treatment (p-value: 0.002), resulted less frequently in the post-intervention group (5.6% versus 13.8%), and to Haemoglobin test at the initiation of ART (*p*-value: 0.027), less practiced in the post-intervention group (32.6% versus 51.8%). Furthermore, no difference was documented for Acid Bacilli Fast (AFB) test (*p*-value: 0.31) used to detect positivity to TB.

Table 3 reports the comparison between the post and pre intervention groups by the explored endpoints of taking charge of the 588 HIV infected children afferent to the 5 Beira's LHFs. The initiation of ART after the 9th month of life was documented with a frequency of 54.5% (n.180) in the intervention group and 56.9% (n.147) pre-intervention group, respectively, but no statistical difference was highlighted (*p*-value: 0.703). The mean age in months of HIV infected children at the beginning of ART was 17.2 (± 14.1) for the intervention group and 18.1 (± 15.6) for the pre-intervention group, but no statistical difference was documented (*p*-value: 0.835).

The mean time from referral to ARCC until the initiation of ART decreased from 2.3 (± 4.4) to 1.1 (± 5.0) months after the implementation of the new pathway of care including TS (*p*-value: 0.000), while the mean time from HIV test results to the initiation of the therapy was lower before the intervention (1.7 ± 3.8 versus 2.1 ± 4.8 months) but no statistical significance was found.

No difference was observed in the CTZ prophylaxis administration, while a significant statistical difference was registered for INH prophylaxis against TB in the post-intervention group, with a documented improvement from 13.2% (n. 34) to 28.5% (n. 94) after the intervention (p-value: 0.000).

After the new pathway implementation, 48.2% (n.159) of HIV infected children underwent regular nutritional assessment as compared to the 29.8% (n.77) of the

Table 1 Characteristics of the 588 HIV infected children afferent to in the 5 Beira's Local Health Facilities and comparison between pre- and post-intervention groups

Characteristics		All N 588	Post-intervention group (postTS) n (%)	Pre-intervention group (preTS) n (%)	*p*-value
Gender	Female	302 (100.0)	163 (49.4%)	139 (53.9%)	0.281
	Male	286 (100.0)	167 (50.6%)	119 (46.1%)	
Mean Age (months)		588 (100.0)	16.8 ± 13.6	15.9 ± 14.6	0.4
Weight at birth	< 2.5 Kg	62 (100.0)	28 (19.7%)	34 (24.8%)	0.306
	> 2.5 Kg	217 (100.0)	114 (80.3%)	103 (75.2%)	
Breastfeeding	Yes	304 (100.0)	153 (77.3%)	151 (84.4%)	0.082
	No	73 (100.0)	45 (22.7%)	28 (15.6%)	
Duration of breastfeeding (months)		100 (100.0)	10.1 ± 4.6	12.4 ± 6.4	0.053
Weight (Kg)		578 (100.0)	8.1 ± 3.1	7.8 ± 3	
Height (cm)		538 (100.0)	69.6 ± 16.2	67.7 ± 16	
Nutritional status (Weight/ Height)					
Normal		309 (100.0)	163 (55.6%)	146 (63.5%)	0.236
Slight malnutrition		83 (100.0)	47 (16%)	36 (15.7%)	
Moderate malnutrition		56 (100.0)	35 (11.9%)	21 (9.1%)	
Severe malnutrition		75 (100.0)	48 (16.5%)	27 (11.7%)	
PMCT implementation for mother at first prenatal visit					
None		106 (100.0)	64 (32.4%)	42 (23.9%)	0.007
HIV Mono prophylaxis		72 (100.0)	36 (18.3%)	36 (20.5%)	
HIV Bi-prophylaxis		91 (100.0)	35 (17.8%)	56 (31.7%)	
HIV ART prophylaxis		104 (100.0)	62 (31.5%)	42 (23.9%)	
Age of mother		512 (100.0)	26 ± 5.7	26.7 ± 6.1	0.226
Mother alive at consultation	Yes	465 (100.0)	263 (93.3%)	202 (92.7%)	0.7494
	No	35 (100.0)	19 (6.7%)	16 (7.3%)	
Age of father		344 (100.0)	32.6 ± 7.4	32.3 ± 9	0.275
Father alive at consultation	Yes	387 (100.0)	222 (90.2%)	165 (91.2%)	0.748
	No	40 (100.0)	24 (9.8%)	16 (8.8%)	
HIV positive father	Yes	101 (100.0)	61 (71.8%)	40 (65.6%)	0.722
	No	45 (100.0)	24 (28.2%)	21 (34.4%)	

Table 2 Clinical and laboratory information provided for the 588 HIV infected children afferent to the 5 Beira's Local Health Facilities: comparison between the pre- and post-intervention groups

Clinical and laboratory information		All N 588	Post-intervention group postTS n (%)	Pre-intervention group preTS n (%)	p-value
ART prophylaxis at birth	Yes	292	146 (80.7%)	146 (70.9%)	0.026
	No	95	35 (19.3%)	60 (29.1%)	
AFB test	Positive	21	7 (4.4%)	14 (7%)	0.31
	Negative	338	151 (95.6%)	187 (93%)	
TB treatment	Yes	51	13 (5.6%)	38 (13.8%)	0.002
	No	457	220 (94.4%)	237 (86.2%)	
Haemoglobin test at initiation of ART	Yes	236	77 (32.6%)	159 (51.8%)	0.027
	No	307	159 (67.4%)	148 (48.2%)	

Table 3 Endpoints explored in the taking charge of the 588 HIV infected children afferent to the 5 Beira's local health facilities: comparison between the pre- and post-intervention groups

Endpoints	All N 588	Post-intervention group (postTS)	Pre-intervention group (preTS)	Crude-OR	95% CI	*p*-value
Initiation of ART						
< 9 months	167	95 (28.8)	72 (27.9)	1.08	0.74–1.57	0.703
≥ 9 months	327	180 (54.5)	147 (56.9)			
Missing	94	55 (16.7)	39 (15.2)			
Mean time from referral to initiation of ART						
	494	1.1 (± 5.0)	2.3 (± 4.4)	–	–	0.000
Missing	94					
Mean time from HIV results to initiation of ART						
	359	2.1 (± 4.8)	1.7 (±3.8)	–	–	0.028
Missing	229					
Mean age at initiation of ART						
	494	17.2 (± 14.1)	18.1 (± 15.6)	–	–	0.835
Missing	94					
CTZ prophylaxis						
Yes	528	296 (89.7)	232 (89.9)	1.04	0.54–1.99	0.896
No	40	22 (6.7)	18 (7.0)			
Missing	20	12 (3.6)	8 (3.1)			
INH prophylaxis						
Yes	128	94 (28.5)	34 (13.2)	2.69	1.7–4.15	0.000
No	420	213 (64.5)	207 (80.2)			
Missing	40	23 (7.0)	17 (6.6)			
Regular nutritional visits						
Yes	236	159 (48.2)	77 (29.8)	2.21	1.56–3.15	0.000
No	307	148 (44.9)	159 (61.7)			
Missing	45	23 (6.9)	22 (8.5)			
CD4 count at beginning of ART						
Yes	326	158 (48.0)	168 (65.1)	0.46	0.32–0.65	0.000
No	231	155 (47.0)	76 (29.5)			
Missing	31	17 (5.0)	14 (5.4)			

pre-intervention group (*p*-value: 0.000). On the contrary, the CD4 count at the beginning of ART was performed more frequently in the pre-intervention group with 65.1% (n. 168) versus 48.0% (158) of the post-intervention group (p-value: 0.000).

The most relevant changes highlighted by comparing the pre-post intervention groups (Table 3) resulted in a significant association between the new pathway of care and INH prophylaxis administration against TB (O.R.: 2,69; 95% CI: 1.7–4.15) and regular nutritional assessment during the visits provided in the ARCC (O.R. = 2.21; 95% CI: 1.56–3.15). Again, a significant statistical association was documented between the TS implementation and a decreasing of the CD4 count monitoring at the beginning of ART (O.R. = 0.46; 95% CI: 0.32–0.65).

Discussion

This pre-post interventional study aimed to retrospectively evaluate the impact on the effectiveness of a new pathway of care for HIV infected children in Mozambique introducing the implementation of TS from clinical officers to MCH nurses.

TS was defined in the First Global Conference as Task Shifting, as a way for the public health communities and national governments to address one of the major constraints to tackling both the HIV/AIDS pandemic and global access to essential health care services [8]. TS

refers to transferring tasks to healthcare workers who have not conventionally performed these tasks as part of their practice, (generally, they are more readily available) have completed shorter training and have fewer qualifications [9]. Four levels of TS have been identified based on the extension of the scope of practice of non-physician officers, nurses and midwives, lay health workers or community workers and people living with HIV to self-managed aspects of their care [10].

Particularly, two different pathways of taking charge of HIV infected children and their mothers were compared after the implementation of a second level of TS in 5 LHFs of the Beira district, according to an OSM approach consisting in patients' care delivered by the same provider in the same consultation in order to guarantee a continuum of care. In fact, the old pathway of care, characterized by the transfer to a different level of health service together with the changing of providers, was assumed to be responsible for a possible delay in taking charge and initiating ART as well as in the retention of care of the newly identified HIV infected children. Such a second level of TS for HIV health care from physicians to nurses has already been demonstrated to be effective, or, no different to the quality of care in Mozambique [11] and in African countries [12–15]. Moreover, a recent review documented no significant difference in the effectiveness of care provided by doctors as compared to nurses on paediatric HIV care [16], but evidence supporting TS of HIV paediatric care is still limited.

Comparing pre and post intervention pathways, we observed some relevant statistical differences. In particular, ART prophylaxis at birth resulted as being practiced at a higher frequency in the post-intervention group, documenting values higher than the expected provincial target for 2013 [6]. Moreover, according to the explored endpoints, an improvement after the TS implementation was highlighted in terms of decreasing in mean time from referral to ARCC until the initiation of ART. Anyway, these results should be re-interpreted in light of the evidence of a more frequent distribution of mothers of HIV infected children of the post-intervention group subjected to ART prophylactic treatment at the first prenatal visit.

Furthermore, increases in regular nutritional assessments during visits after the enrollment in HIV service and in INH prophylaxis rates during the post-intervention period were reported. The effectiveness of the new pathway of care with regard to monitoring malnutrition and the prophylaxis against tuberculosis, respectively, was also documented. On the other hand, the less frequent TB treatment delivered in the post-intervention group suggested a potential controversial impact of the intervention on the global clinical management of concurrent co-morbidities.

It remains controversial how the new pathway of taking charge of HIV infected children resulted in a significant decreasing of CD4 count and Haemoglobin monitoring at the beginning of ART. One explanation of this difference is that performances require more time and commitment as compared to the simple administration of a single therapy and being that the CD4 count was not necessary for the initiation of ART within the Option B+ scenario, it could have been neglected in the post-intervention periods.

Moreover, having been Option B+ and TS implementation concomitant, our study design is not able to isolate the different effects of each specific factor.

For the aforementioned reasons, it is difficult to make a reliable interpretation of the whole result and this represents the main drawback of the study.

Other limitations of our results could be linked to the limited time period available for the comparison - which should be extended in order to extensively assess the effectiveness of the intervention - and to the retrospective nature of the study. In fact, even if pre-post intervention study is often the most feasible option for conducting public health impact evaluations in real world settings, particularly for exploring health services, socio-economic, political or ethic domains, the availability of data is not collected for the specific study, but derives from registries, which is often a major barrier in using it in a retrospective manner [17].

Moreover, records from LHF registries were often incompletely filled in and poorly maintained, mainly because health workers were steadily overloaded, without enough time – and probably without proper training - to provide an adequate completion of health records. As a consequence, for many patients the records were unavailable or incomplete, resulting in missing data for some variables. In addition, the low number of HEI accessing the health services [6] contributed to the restriction of the number of patients enrolled.

Furthermore, the difficulty in controlling important confounding variables, due to the lack of randomization typical of pre-post intervention design [18–20], could not be balanced with an appropriate statistical analysis because of the overall low quality of the database available.

Lastly, no evidence was provided of the availability of a suitable screening protocol for other relevant communicable diseases, such as hepatitis, to implement appropriate health control strategies in the local health settings [21].

However, to our knowledge, this is the first study assessing the effectiveness of TS from clinical officers to nurses in delivering paediatric antiretroviral treatment to Mozambique, and trying to increase the value of data available from local health facilities.

According to available literature, it is clear that TS is a potentially effective approach to address the human resource limitations and to scale up the ART coverage and retention in care for both adults and children [16, 21, 22], however, for a more comprehensive evaluation of quality of care provided, more attention should be paid to human attitude, motivation and training of the personnel involved [23, 24].

Conclusions

According to our findings, the proposed new pathway of taking charge of HIV infected children under 5 years old supports the provision of the continuum of care. Furthermore, the introduction of the TS from physicians to MCH nurses may have a positive impact on the management of patients affected by HIV and other relevant infectious diseases in the considered context, in particular a decrease in the mean time from the referral to ARCC to the initiation of ART and an increase in Isoniazid (INH) prophylaxis were observed. On the contrary, our findings were controversial for the performance of the nutrition assessment and the CD4 count at the initiation of ART. This suggests how, even if it could be considered appropriate and sustainable to involve nurses in the care of all HIV patients, including both children and their mothers, TS alone may be considered to play a role in the improvement of the global effectiveness of care for HIV infected children only if integrated in a wider range of public health measures including specific pre- and post-lauream education programs for physicians and nurses [25–28].

In conclusion, further studies conducted on a larger scale and in a longer time period are needed to assess the extensive impact of TS on both specific clinical outcomes and on retention in care of HIV infected children in developing countries.

Abbreviations

AFB: Acid Bacilli Fast; ARCC: At Risk Child Clinic; ART: Antiretroviral treatment; ARV: Antiretroviral; CIDI: Centre of Infectious Disease; CNBS: Comité Nacional de Bioética para Saúde; CTZ: Cotrimoxazole; HEI: HIV Exposed infants; HHS: HIV Health Service; HIV: Human Immunodeficiency Virus; INH: Isoniazid; LHF: Local health facilities; MCH: Mother and Child Health; OPD: Outpatients department; OSM: One stop model; PCR: DBS Polymerase chain reaction using dried blood spots; PMCT: Prevention of Mother to Child Transmission; TB: Tuberculosis; TS: Task Shifting; UCM: Catholic University of Mozambique; WHO: World Health Organization

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Availability of data and materials

The data that supports the findings of this study are available on demand from the authors upon reasonable request and with permission of Doctors with Africa CUAMM.

Authors' contributions

All individuals listed as authors have contributed substantially to designing, performing or reporting the study and every specific contribution is indicated as follows. Conception and design of the study: CM, DP, GP, WM. Data collection: KC, GM, DP. Statistical analysis: CM, JM, DP. Interpretation of data: CM, FDG, WM. Manuscript writing and drafting: CM, FDG, GM, DP, WM. Revision of the manuscript: CM, FDG, DP, GP, AC, FV, WM. Approval of the final version of the manuscript: CM, FDG, CG, KG, AS, JM, GM, DP, GP, LM, AC, FV, WM. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethic approval of the protocol was granted by Comité Nacional de Bioética para Saúde (CNBS) of Mozambique (Ref. 260/ CNBS/15). No individual consent to participate was required as all the analyses were made on aggregated data.

Competing interests

The authors declare that they have no competing interests.

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Surgical diseases and HIV status in patients at Central Hospital of Beira, Mozambique

PAPER

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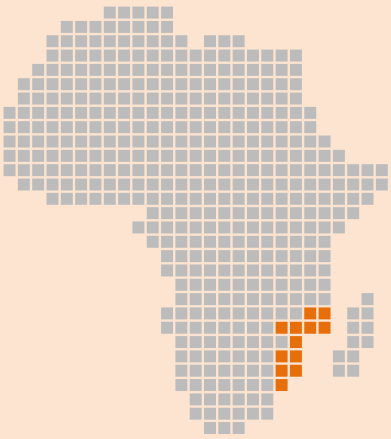

Abstract

HIV-infected patients with surgical conditions are at greater risk of developing post-operative complications than those without HIV.

This study assessed the main surgical pathologies occurring in both HIV-infected and non-HIV-infected patients in the surgical division of Mozambique's Beira Central Hospital (BCH).

A total of 237 adult patients were admitted to the surgical division of BCH from January to December 2017. Most of the operations (174; 73.4%) involved the abdomen, followed by those involving the perineum (42; 17.7%) and the chest (21; 8.8%).

Our data analysis showed that HIV-infected patients were more likely to undergo emergency operations than those without HIV; they were also hospitalized longer, probably due to the seriousness of their illnesses and the longer recovery periods necessitated by their already poor health conditions. Even so, no deaths were recorded in either of the two groups during the patients' hospitalizations, an indication of the efficiency of the surgical interventions looked at in the study.

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Original article

SURGICAL DISEASES AND HIV STATUS IN PATIENTS AT CENTRAL HOSPITAL OF BEIRA, MOZAMBIQUE.

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ABSTRACT

HIV-positive patients with surgical diseases are at a higher risk than HIV-negative patients of developing post-surgery complications. The goal of this study was to evaluate the main surgical pathologies among HIV positive and HIV negative patients hospitalized in the surgical ward of the Hospital Central da Beira (HCB) in Mozambique.
Were collected data before and after surgical procedures in all consecutive adult patients (> 18 years old) admitted and hospitalized at the Surgical Ward of the HCB from January to December 2017.
Overall, a total of 237 adult patients were admitted to the surgical ward of Hospital Central of Beira, Mozambique. We reported all surgical information collected from patients. The most frequent surgical site for the operation was the abdomen (n.174; 73.4%), followed by perineum (n.42; 17.7%) and thorax (n.21; 8.8%). For health professionals working in surgery wards, data on the most frequent postoperative complications in HIV-positive patients will offer useful tools for the follow-up of those patients.

1. Introduction

Human immunodeficiency virus (HIV) has a significant impact on surgery, especially in Africa (1).
In fact, surgical interventions are a common component in the management of patients with HIV or suffering from the clinical consequences of acquired immunodeficiency syndrome (AIDS) (2).
Effective antiretroviral therapy (ART) has significantly increased longevity among HIV-infected patients and the resulting increase of life expectancy has allowed more HIV-positive patients to undergo surgery (2).
For these reasons there is a need for health workers to focus on surgical pathologies in HIV patients in terms of feasibility and outcomes (3).
According to WHO, in 2015 about 35.3 million people were living with HIV worldwide and many of these people had already developed AIDS(4). Mozambique has the 8th highest prevalence of HIV in the world, with a 11.5% prevalence of HIV infection in adults between the ages of 15 and 49 (5).
It is observed that with the increase of HIV prevalence, the prevalence of pathologies that to date were considered rare increases as well.

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In addition, the clinical presentation of the pathologies in HIV patients has been shown to be different from the clinical presentations of the same pathologies in HIV-free patients (6,7). HIV-infected patients do not show signs and symptoms that are useful for the preoperative diagnosis of HIV-related surgical pathologies (7). These findings show that there is a need to diagnose surgical pathologies in patients with HIV and their immediate treatment to improve their prognosis (8)

Moreover, HIV-positive patients with surgical pathologies are at a higher risk of developing post-surgery complications than HIV-negative patients, such as sepsis and surgical site infection. (9).

The majority and quality of the data regarding HIV and surgery come from high income countries. There is no data in Mozambique on the main surgical pathologies in patients with HIV and on their main postoperative complications. Beira is the capital of the Sofala province, one of the 5 Mozambican provinces in the country with the highest HIV prevalence (15.5%) (5).

Knowing the main surgical pathologies and the different clinical manifestations that affect patients with HIV, will allow to pay more attention in the follow-up visits of the patients and to administer the proper attention in advance, thus improving the prognosis of these patients.

The goal of this study was to evaluate the main surgical pathologies among HIV positive and HIV negative patients hospitalized in the surgical ward of the Hospital Central da Beira (HCB) in Mozambique.

2. Methods

This is an observational, prospective study conducted at the Surgical Department of Hospital Centrale da Beira, to analyze the prevalence of main surgical pathologies.

To this purpose, a trained nurse collected the data before and after the surgical procedures in all consecutive adult patients (> 18 years old) admitted and hospitalized at the Surgical Ward of the HCB from January to December 2017.

In particular, the data collected before surgery included the demographic profile, HIV status, comorbidities, surgery indication, clinical presentation and clinical examination; while patient outcomes, surgical complications and hospital-stay lengths were registered at discharge. Moreover, on the day of discharge patients were also instructed by the study team to return after 7 days for the follow-up visit.

Mean with standard deviations and median with ranges for the continuous variables and proportion and frequencies for the categorical variables were calculated as descriptive statistics. The study sample was stratified by HIV status in two groups, and the comparison between them was analyzed using the X-square and t student when appropriate. IBM SPSS version 21 was used for the statistical analyses.

Ethical approval

The study was approved by the Comité Nacional de Bioetica para a Saúde/ National Bioethics Committee for Health by the protocol Ref: 55/CNBS/16.

Written informed consent was obtained from each patient enrolled.

3. Results

Overall, a total of 237 adult patients (n.141, 59.5% male, n.107, 45.1% under 40) were admitted to the surgical ward of Hospital Central of Beira, Mozambique.

The prevalence of HIV patients in the whole sample was of 46% (n.109).

Table 1 lists demographic and clinical characteristics of all patients, stratified by HIV positivity.

Almost half of all patients (n. 134, 56.5%) were referred to the surgical ward from other hospitals, while the remaining were transferred from other wards. BMI was low (<18) in 28.2% (n.67) of patients, while normal (18 - 25) in 66.2% (n.157) and high (>25) 5.5% (n.13) patients.

The following comorbidities were reported among the patients: gastro-enteric diseases (n.31; 13%), hypertension (n.21, 8.9%), hepatitis (n.20; 8.4%), psychiatric diseases (n.11; 4.6%), diabetes (n.9; 3.8%), TB (n.6; 2.5%) and dermatologic disease (n.3; 1.3%).

Forty-six per cent (n.109) of patients reported symptoms, with an average of 5.2 (1-10) days and a pain scale median value of 7.8.

Differences between the HIV positive and HIV negative patients were observed for distribution of age classes, the under 40-year-old patients were more frequent in the HIV + group (n.65, 60.7%; p-value: 0.00), and of comorbidities with hepatitis and psychiatric disease. In fact, hepatitis prevalence was more frequent in the HIV positive patients (n.16, 80.0%; p-value: 0.01), and the same was for psychiatric diseases (n.8, 72.7%; p-value: 0.07). Moreover, symptoms were reported more frequently in the HIV group (n.71, 65.1%; p-value: 0.00).

Table 1. Demographic and clinical information of patient enrolled at surgical ward of Beira Hospital stratified by HIV positivity.

Table 2 reports all surgical information collected in patients, also stratified by HIV status. The most frequent surgical site for the operation was the abdomen (n.174; 73.4%), followed by perineum (n.42; 17.7%) and thorax (n.21; 8.8%).

The prevalence of surgical diagnosis in our sample was: 21.5% inguinal hernia (n.51), 19.4% peritonitis (n.46), 8.8% perianal fistula (n.21), 8.8% hemorrhoids (n.21), 8.0% hydrocele (n.19), 6.3% epigastric hernia (n.15), 5.5% appendicitis (n.13), 5.5% vaginal-bladder fistula (n. 13), 3.8% bilateral gynecomastia (n.9), 3.4% thyroid goiter (n.8), 2.9% colon carcinoma (n.7), 2.9% breast carcinoma (n.7), 1.7% esophagus (n.4), 1.2% pancreas carcinoma (n.3).

Comparing the distribution of the above mentioned surgical diagnoses in the two groups of patients, HIV patients presented 41.2% (n.21) of inguinal hernia cases, 45.6% (n.21) of peritonitis, 66.7% (n.14) of perianal fistula, 47.6% (n.10) of hemorrhoids, 36.8% (n.7) for hydrocele, 40.0% (n.6) of epigastric hernia, 53.8% (n.7) of appendicitis, 69.2% (n. 9) of vaginal-bladder fistula, 77.7% (n.7) of bilateral gynecomastia, 62.5% (n.5) of thyroid goiter, 42.8% (n.3) of colon carcinoma (n.3), 57.1% (n.4) of breast carcinoma, 25.0% (n.1) of esophagus, 66.6% (n.2) of pancreas carcinoma (table 2).

Emergency intervention was performed in 37.5% (n.89) of the cases with a median length of hospitalization of 9 (range: 5 - 24) days.

HIV patients more often underwent emergency surgery (n.60, 67.4%, p-value: 0.00) than the HIV negative patients, and their hospitalization was also longer (11 days, range 7-24 versus 8 days, range 5 – 19).

		Tot n.237 (100.0%)	HIV + n. 109 (46.0%)	HIV – n. 128 (54.0%)
Surgical site	Thorax	21 (8.8)	14 (66.6)	7 (33.4)
	Abdomen	174 (73.4)	79 (45.4)	95 (54.6)
	Perineum	42 (17.7)	16 (38.0)	26 (62.0)
Diagnosis	Peritonitis	46 (19.4)	21 (45.6)	25 (54.4)
	Inguinalhernia	51 (21.5)	21 (41.2)	30 (58.8)
	Ginecomastia bilateral	9 (3.8)	7 (77.7)	2 (22.3)
	Vaginalbledder fistula	13 (5.5)	9 (69.2)	4 (30.8)
	Esophagus carcinoma	4 (1.7)	1 (25.0)	3 (75.0)
	Colon carcinoma	7 (2.9)	3 (42.8)	4 (57.2)
	Breast carcinoma	7 (2.9)	4 (57.1)	3 (42.9)
	Pancreas carcinoma	3 (1.2)	2 (66.6)	1 (33.4)
	Hemorrhoids	21 (8.8)	10 (47.6)	11 (52.4)
	Hydrocele	19 (8.0)	7 (36.8)	12 (63.2)
	Epigastrichernia	15 (6.3)	6 (40.0)	9 (60.0)
	Perianal fistula	21 (8.8)	14 (66.7)	7 (33.3)
	Thyroidgoiter	8 (3.4)	5 (62.5)	3 (37.5)
	Appendicitis	13 (5.5)	7 (53.8)	6 (46.2)
Days of hospitalization (median - range)		9 (5 - 24)	11 (7-24)	8 (5 - 18)
Emergency surgery		89 (37.5)	60 (67.4)	29 (32.6)
Good clinical conditionatdischarge		237 (100.0)	109 (46.0)	12 (54.0)

Table 2. Surgical information and diagnosis' prevalence of patient enrolled at Surgical Ward of Beira Hospital stratified by HIV positivity.

HIV information of HIV positive patients is listed in Table 3.

The median of years from HIV diagnosis was 2.9 (1-5), and 71.5% (n.78) of patients received a regular HIV follow up. All 109 (100%) HIV patients were under ARV therapy; the therapeutic scheme was tenofovir/lamivudine/efavirenz (TDF/3TC/EFV) for 80.7% (n.88) of patients, and zidovudine/lamivudine/nevirapine (AZT/3TC/NVP) for the remaining 19.3% (n.21). The median of years from ARV initiation was 2.6 (1-4).

HIV information		
Years from HIV diagnosis (median, range)		2.9 (1-5)
HIV follow up (n, %)		78 (71.5)
Patients under TARV (n, %)		109 (100)
Years form TARV initiation (median, range)		2.6 (1-4)
Type of ARV	TDF+3TC+EFV (n, %)	88 (80.7)
	AZT +3TC +NVP (n, %)	21 (19.3)

Table 3. HIV information of the 109 HIV positive patients enrolled at surgical ward of Beira Hospital, Mozambique.

All patients, regardless their HIV status, were alive and with good clinical conditions when they were discharged.

4. Discussion

Our study had the goal of reporting the main surgical pathologies in patients hospitalized at the Central Hospital of Beira with a particular focus on HIV positive patients.

Favorable surgical outcomes have been reported among HIV-infected patients undergoing surgical procedures. The most frequent surgical pathologies seen in HIV patients were inguinal hernia, gynecomastia probably as a collateral effect of ART, vaginal bladder and perianal fistula, thyroid goiter and appendicitis. The data on cancer is interesting, with pancreas and breast carcinoma as the most prevalent types of tumors.

HIV patients underwent emergency surgery more often than the HIV negative patients, and also their hospitalization was longer, probably due to the higher severity of diseases and the longer time needed to recover from the surgery (10,11).

For health professionals working in surgery wards, data on the most frequent postoperative complications in HIV-positive patients will offer useful tools for the follow-up of those patients. In our study we were not able to complete a follow up at 30 days but no deaths were recorded in both groups during the hospital stay, which could be a attributed to good surgery results (12,13).

Surgical interventions, particularly in low-income countries, are effective also from an economic point of view for their ability to prevent long-term disabilities. However, this consideration must be contextualized in a setting with high HIV incidence, where many patients still await ART and without a cost-effective method for staging HIV subjects (12,13).

Limited data is available on surgery performed on HIV positive patients in developing countries, especially in Eastern Africa.(14,15,16)

In particular, in Mozambique, a scarce resource setting, with high incidence of HIV and TB, there is limited data available about surgery and outcome of these patients (17,18).

Several studies conducted in hospitals to assess the impact of HIV on surgical pathologies have revealed that HIV infection does not affect the healing time of a surgical wound (19). The immunological status of patients with HIV has been reported as one of the main contributing factors for patients' poor prognosis (10,20). Unfortunately we didn't have CD4 count of our HIV patients. Furthermore, our HIV patients were all on ART and they probably had hidden complications.

This study presented some limitations: difficulty in understanding the signs and symptoms for cultural reasons, even if the data collection form was designed to overcome this problem and the role of local nurses minimized the risk of underreporting. In addition, it was impossible to collect data on the control visit recommended at 7th day after discharge, since a high number of patients wasn't present for follow up, so we could not report this result. To better understand our report it should be considered that all admitted patients were under ART, who may present hidden clinical differences between HIV patients and non-HIV patients, and that the CD4 number or percentage was not considered to further describe this patients from a clinical point of view. More studies on surgery in low-income countries, especially in Mozambique, are need to better understand the different surgical pathologies of HIV patients, treatment and outcome.

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Prevalence and Predictors of Malaria in Human Immunodeficiency Virus Infected Patients in Beira, Mozambique

PAPER

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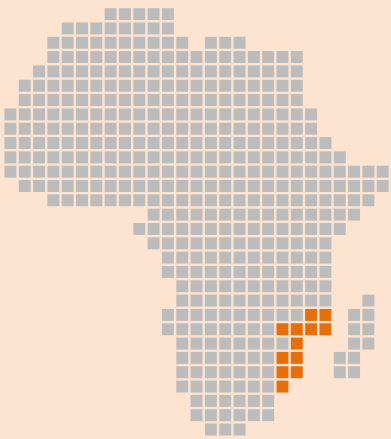
Mozambique



Abstract

Despite the progress that has been made in the treatment of malaria and acquired immunodeficiency syndrome (HIV/AIDS), these two infectious diseases are still the most common in the world, causing millions of deaths annually. Mozambique, in particular, has one of the prevalences rates of HIV/malaria co-infection in sub-Saharan Africa; even so, little research has been done there on the topic.

The aim of this study was to assess malaria prevalence and to identify positive predictors to the diagnostic test in HIV patients admitted to the São Lucas Health Center in Beira, Mozambique's second largest city. Conducted from January to December 2016, it involved 701 adult patients infected with HIV, 232 (33%) of whom tested positive for malaria. The data collected also showed that most of the patients were unemployed (76.3%), aged under 40 (72.0%) and had HIV-positive partners (22.4%).

Despite the study's limitations, the data that emerged from it revealed a high prevalence of malaria in the HIV-positive individuals who made use of the country's health centers, confirming the heightened vulnerability of such patients to malaria and other infectious diseases.

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Prevalence and Predictors of Malaria in Human Immunodeficiency Virus Infected Patients in Beira, Mozambique

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Abstract: Co-infection between malaria and HIV has major public health implications. The aims of this study were to assess the malaria prevalence and to identify predictors of positivity to malaria Test in HIV positive patients admitted to the health center São Lucas of Beira, Mozambique. A retrospective cross-sectional study was performed from January 2016 to December 2016. Overall, 701 adult HIV patients were enrolled, positivity to malaria test was found in 232 (33.0%). These patients were found to be more frequently unemployed (76.3%), aged under 40 (72.0%), with a HIV positive partner (22.4%) and with a CD4 cell count <200 (59.9%). The following variables were predictors of malaria: age under 40 (O.R. = 1.56; 95%CI: 1.22–2.08), being unemployed (O.R. = 1.74; 95%CI: 1.24–2.21), irregularity of cotrimoxazole prophylaxis's (O.R. = 1.42; 95%CI: 1.10–1.78), CD4 cell count <200 (O.R. = 2.01; 95%CI: 1.42–2.32) and tuberculosis comorbidity (O.R. = 1.58; 95%CI: 1.17–2.79). In conclusion, high malaria prevalence was found in HIV patients accessing the out-patients centre of São Lucas of Beira. Our findings allowed us to identify the profile of HIV patients needing more medical attention: young adults, unemployed, with a low CD4 cell count and irregularly accessing to ART and cotrimoxazole prophylaxis.

Keywords: malaria prevalence; HIV; HIV-malaria co-infection; malaria predictors in developing countries; cotrimoxazole prophylaxis; Mozambique

1. Introduction

Despite improvements, malaria and acquired immune deficiency syndrome (AIDS) are two of the most important infectious diseases worldwide [1]. Malaria is on the list of AIDS-related opportunistic infections and the highest occurrence of human immunodeficiency virus (HIV) and malaria cases are reported in sub-Saharan countries [2]. Particularly, HIV infection is expected to increase the morbidity and mortality attributed to malaria, reducing the immune response against *Plasmodium* spp. and, consequently, leading to a more frequent occurrence of clinically severe malaria cases [3]. Interestingly,

the use of cotrimoxazole (CTX) prophylaxis and antiretroviral therapy (ART) in HIV-infected patients seems to provide a protective effect from malaria [4].

Mozambique is one of the sub-Saharan African countries with the highest incidences of HIV co-infection associated to endemic malaria [5,6]. In Mozambique, *Plasmodium falciparum* infection accounts for 90% of all malaria cases, followed by *P. malariae* and *P. ovale* responsible of about 9% and 1%, respectively. In 2015, the confirmed cases of malaria were 8,520,376 [5]. Furthermore Mozambique has one of the highest incidences of HIV worldwide with an estimated national prevalence of 12.5% in the age-group 15–49 and the estimated number of deaths of 62,000/years [6].

However, the number of studies on prevalence and clinical manifestations of HIV- malaria co-infection in Mozambique is limited [7,8]. The aims of our study were: (i) to verify the prevalence of malaria in HIV patients and (ii) to identify predictors of positivity to malaria test in HIV patients admitted to the health center of São Lucas of Beira, the second largest city of Mozambique.

2. Materials and Methods

A retrospective observational cross-sectional study was designed and implemented to analyze data of patients accessed the health centre of São Lucas of Beira, Sofala, Mozambique, from January 2016 to December 2016.

The health center of São Lucas provides access to free care and treatment of HIV/AIDS patients in an out-patients setting. For each new admitted patient, medical history is collected and the HIV status is checked with the HIV Rapid Test and, if positive, confirmed by western blot. Each consecutive consultation includes full clinical examination, (including HIV status according to WHO), ART therapy, cotrimoxazole prophylaxis, CD4+ T cell count, partner HIV status, co-morbidities (diabetes, hypertension and tuberculosis) and other sexual transmitted infections (STI), including genital herpes, condyloma, syphilis, gonorrhea and candidiasis. With regard to ART therapy and cotrimoxazole prophylaxis, information on regularity of their administration are also collected. In case of clinical suspicion of diabetes or tuberculosis, specific diagnostic protocol according to WHO guidelines is applied to confirm the diagnosis [9].

Malaria screening is performed using the Malaria Rapid Diagnostic Test (RDT) kit, as described by the manufacturer's (Standard Diagnostics Bioline, 2013). The confirmation of RDT results is obtained by blood smear microscopy [10]. All patients with a positive malaria blood slide and/or rapid diagnostic test are considered as infected with malaria.

A sample size estimation was performed using the following formula [11]:

$$n = \frac{Z^2 x\, p(1-p)}{e^2} \quad (1)$$

where Z = 1.96, p = prevalence of malaria among people living with HIV (PLWHIV): 25.9% [12], e = error rate: 0.05.

A convenience sampling of at least 298 PLWHIV was estimated. All HIV/AIDS adult patients (>18 years) that consecutively accessed the health center for a medical consultation or to collect their antiretroviral (ARV) drugs from January 2016 to December 2016 were identified through the patients' registry and were recruited in the study.

2.1. Statistical Analysis

Categorical variables were reported as absolute and relative frequencies (percentages). Chi-square test (with the Yates' correction as required) was used to compare categorical variables. A logistic regression model was implemented as follows: Malaria positivity was considered as dependent variable and each one of the available factors at the baseline evaluation were used as independent variables (univariate analysis). In the multivariate analysis all the factors with a p-value < 0.10 at the univariate analyses were included. Multicollinearity among covariates was assessed through the variance inflaction factor (VIF), taking a value of 2 for excluding a covariate. However, no variable was

excluded according to the previous criterion. Odds Ratios (ORs) as adjusted Odds Ratios (Adj-ORs) with their 95% confidence intervals (CIs) were used to measure the association between factors at the baseline (exposure) and Malaria positivity (outcome).

All statistical tests were two-tailed and statistical significance was assumed for a p-value < 0.05. Analyses were performed by using the SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA).

2.2. Ethics Approval

Ethical approval of the protocol was achieved by District Health Authority in Beira, the Health District Direction (protocol reference: 189/17), Mozambique and (as this study used secondary data) informed patient consent was not required.

3. Results

A total of 701 adult HIV positive patients (n = 430, 61.3% females; n = 421, 60.0% under 40 years old) were enrolled in the study. The demographic and HIV related characteristics, overall and according to the malaria test result (positive versus negative), are summarized in Table 1. A positive malaria test was found in 232 (33.0%) patients. These patients, compared to the negative ones, were more frequently unemployed (n = 177; 76.3%), aged under 40 (n = 167; 72.0%), with a HIV positive partner (n = 52; 22.4%) and with a CD4 cell count <200 (n = 139; 59.9%), being all of these differences statistically significant (p-value: <0.05). By contrast, malaria negative patients resulted were more frequently receiving cotrimoxazole prophylaxis (n = 302; 64.3%), under ART (n = 360; 77.2%), and to be more regular in taking it ART (n = 261; 72.5%) (p-value: <0.05). No statistical differences between the two groups were observed for gender (p-value: 0.38) and HIV stage defined by the WHO (p-value: 0.38).

Table 1. Demographic and HIV related characteristics of 701 HIV positive patients, stratified by malaria test results.

	Total	**Malaria Test Result**		***p*-Value**
		Positive	**Negative**	
	***n*. 701 (100%)**	***n*. 232 (33.0%)**	***n*. 469 (77.0%)**	
Sex				
Female	430 (61.3)	137 (59.0)	293 (62.5)	0.38
Male	271 (38.7)	95 (41.0)	176 (37.5)	
Age				
<40 years	421 (60.05)	167 (72.0)	254 (54.1)	<0.05
≥ 40 years	280 (39.95)	65 (28.0)	215 (45.9)	
Occupation				
Unemployed	350 (49.92)	177 (76.3)	173 (36.8)	<0.05
Employed	351 (50.07)	55 (23.7)	296 (63.2)	
Partner' HIV status				
Positive	79 (11.3)	52 (22.4)	27 (5.8)	
Negative	281 (40.0)	110 (47.4)	171 (36.4)	<0.05
Missing	341 (48.7)	70 (30.2)	271 (57.8)	
HIV Stage by WHO				
I-II	322 (45.93)	112 (48.2)	210 (44.7)	<0.05
III-IV	379 (54.07)	120 (51.8)	259 (55.3)	
ART				
Yes	463(66.1)	103 (44.3)	360 (77.2)	<0.05
No	238 (33.9)	129 (55.7)	109 (22.8)	
Regularity of ART				
Yes	271 (58.53)	10 (19.4)	261 (72.5)	<0.05
No	192 (41.47)	93 (80.6)	99 (27.5)	

Table 1. *Cont.*

	Total	Malaria Test Result		*p*-Value
		Positive	Negative	
	***n*. 701 (100%)**	***n*. 232 (33.0%)**	***n*. 469 (77.0%)**	
CD4+ T cell count				
< 200	245 (34.9)	139 (59.9)	106 (22.6)	<0.05
>200	456 (65.1)	93 (40.1)	363 (77.4)	
Cotrimoxazole prophylaxis				
Yes	353 (50.3)	51 (22.0)	302 (64.3)	<0.05
No	348 (49.7)	181 (88.0)	167 (35.7)	
Regularity of cotrimoxazole prophylaxis				
Yes	251 (71.10)	10 (19.6)	241 (79.8)	<0.05
No	102 (28.90)	41(80.4)	61 (20.2)	

Table 2 reports the distribution of co-morbidities, stratified by malaria test result. Considering the whole sample, hypertension was found in 83 patients (11.8%), diabetes in 15 (2.1%), tuberculosis in 97 (13.8%) and other STIs in 188 (26.8%). Comparing the two groups, patients were more frequently affected by tuberculosis in the malaria positive group (n.61; 26.3%) (*p*-value: <0.05). Conversely, no statistically significant difference was highlighted between the two groups for hypertension, diabetes and other STIs.

Table 2. Distribution of co-morbidities among the 701 HIV positive patients enrolled, stratified by Malaria test results.

	Total	Malaria Test Result		*p*-value
		Positive	Negative	
	***n* = 701 (100%)**	***n* = 232 (33.0%)**	***n* = 469 (77.0%)**	
Hypertension				
Yes	83 (11.84)	21 (9.0)	62 (13.2)	0.10
No	618 (88.15)	211 (91.0)	407 (86.8)	
Diabetes				
Yes	15 (2.13)	3 (1.3)	12 (2.3)	0.41
No	686 (97.86)	229 (98.7)	457 (97.7)	
Tuberculosis				
Yes	97 (13.83)	61 (26.3)	36 (7.7)	<0.05
No	604 (86.16)	171 (73.7)	433 (92.3)	
Other STI *				
Yes	188 (26.81)	71 (30.6)	117 (24.9)	0.13
No	513 (73.18)	161 (69.4)	352 (75.1)	

* STI: sexual transmitted infections.

The multivariate model considered the effects on malaria (dependent variable) of age (<40 years old), occupational status (unemployed), partner HIV positivity, being under ART, regularity of ART, CD4+ T cell count < 200, being under cotrimoxazole prophylaxis, irregularity of cotrimoxazole prophylaxis and presence of tuberculosis comorbidity. The following variables resulted predictive of malaria positivity (Table 3): age under 40 (O.R. = 1.56; 95%CI: 1.22–2.08), being unemployed (O.R. = 1.74; 95%CI: 1.24–2.21), irregularity of cotrimoxazole prophylaxis (O.R. = 1.42; 95%CI: 1.10–1.78), CD4 cell count < 200 (O.R. = 2.01; 95%CI: 1.42–2.32) and tuberculosis comorbidity (O.R. = 1.58; 95%CI: 1.17–2.79).

Table 3. Predictors of positivity at Malaria Test in HIV positive patients.

Characteristics	Univariate Analysis OR	Multivariate Analysis Adj-OR
Age < 40	1.28 (1.06–1.78)	1.56 (1.22–2.08) *
Partners HIV positivity	0.36 (0.08–0.83)	0.42 (0.08–1.03)
Unemployed	1.85 (1.35–2.45)	1.74 (1.24–2.21) *
ART	0.64 (0.38–0.78)	0.74 (0.50–1.03)
Regularity of ART	0.75 (0.49–0.92)	0.51 (0.28–0.85)
CD4+ T cell count < 200	1.91 (1.34–2.19)	2.01 (1.42–2.32) *
Cotrimoxazole prophylaxis	0.53 (0.41–0.83)	0.58 (0.43–0.90)
Irregularity of Cotrimoxazole prophylaxis	1.80 (1.50–2.00)	1.42 (1.10–1.78) *
Tuberculosis	1.31 (1.06–1.66)	1.58 (1.17–2.79) *

* Statistically significant values; OR: Odds Ratio; Adj-OR: Adjusted Odds Ratio; ART: antiretroviral therapy.

4. Discussion

This cross-sectional study aimed to estimate the prevalence of malaria and to identify its predictors in HIV patients accessing to the health center of São Lucas of Beira, an endemic malaria area. Malaria and HIV are two of the most challenging global health issues for developing countries, especially for Mozambique, where malaria accounts for 29% of all deaths, closely followed by AIDS, responsible of 27% of the mortality in the general population [13,14]. Moreover, it is well know that these two infectious diseases are closely linked each other. In HIV patients, during malaria co-infection, it has been reported to cause an increase in plasma HIV-1 RNA levels and a decline in the CD4+ T cell count [15]. On the other hand, HIV co-infection is associated with increased mortality in areas of stable malaria transmission, making both malaria severity and HIV important risk factors for death [16].

However, to the best of our knowledge, only a few studies have evaluated the epidemiological aspects of HIV and Malaria co-infection in Mozambique [12–17], and none of them have explored the HIV non-hospitalized population.

Malaria prevalence in our study population was 33.0%, being higher when compared to the 25.9% reported among HIV patients hospitalized at Central Hospital of Beira and to the 9.8% of HIV patients hospitalized at Central Hospital of Maputo in 2008 [17]. In the same direction, our study documented a higher malaria occurrence, if compared to similar studies conducted in other developing countries, such as Ghana (11.75%) [18], and Nigeria (18.5%) [19]. These differences could be due to the different study periods, considering that malaria transmission is seasonal, and has different endemicity levels.

Moreover, although it is well known than HIV patients are more susceptible to malaria, in this study we identified a further more vulnerable group, consisting of young and unemployed patients with a low CD4 cell count, irregular in taking cotrimoxazole prophylaxis and with a previous history of tuberculosis. This evidence is in line with the current literature [20,21]. In fact, correlation between age and level of malaria transmission is well known also among HIV negative patients: IgG levels, tending to increase with the age [22–24], influence the severity of malaria and immune response.

Again, according to the literature, the patients enrolled in our study undergoing regularly to ART were less susceptible to malaria. This effect could be explained by the non-adherence to ART that can increase the risk of opportunistic infection such as malaria, being included in the list of AIDS-related opportunistic infections by CDC since 2009 [25,26]. Likewise, also cotrimoxazole prophylaxis was just described as an important factor in reducing malaria incidence [12] and our data confirmed this hypothesis. Of interest, WHO recommends to stop cotrimoxazole in clinically stable patients with evidence of immune recovery and/or viral suppression under ART, while it should be continued in patients living in areas with high malaria and bacterial infection prevalence [27].

Another aspect emerging from our data is the role played by tuberculosis and health determinants such as socio-economic status in the interaction between HIV and malaria [28]. In fact, it is clear that poverty represents one of the major obstacle to the global burden control, leading to unfavourable outcomes most of all in these categories of patients [29–31]. Finally, our study also confirmed that

having a HIV positive partner is a risk factor for malaria, since the behavioural determinant could be correlated both in the HIV transmission between the couple, the adherence to the ART therapy, the prophylaxis with cotrimoxazole and the proper use of the mosquito net [32–37]. On this basis, an appropriate couple-based care strategy should be integrated and implemented at the same time HIV behavioural and medical interventions. However, a further comparison with HIV negative patients could have been useful in order to better understand of the role of the HIV infection itself in the differences reported. Unfortunately, information on HIV negative patients were not available from our database.

The major limitations of this study are related to the cross-sectional design and to the typology of patients included in the study: since the study enrolled non-hospitalized patients, the possibility of self-medication for malaria could have biased the prevalence detected. In addition, the lack of data on pregnancy status, haemoglobin values and other health outcomes, did not allow a more comprehensive interpretation of results, so when HIV and malaria infection occur together a higher risk of complications should be considered.

Our findings allowed us to identify the profile of HIV patient needing more medical attention: young adults, unemployed, with a low CD4 cell count and irregularly accessing to ART and cotrimoxazole prophylaxis.

5. Conclusions

Despite the noted limitations, our study documented a very high malaria prevalence in a population of HIV subjects accessing an out-patients center in Mozambique, allowing us, at the same time, to better understand the profile of these patients that are highly vulnerable to co-infection. These findings could assist decision makers in efforts to plan HIV and malaria prevention interventions in low income countries and in settings with high endemicity. In particular, a more extensive use of cotrimoxazole for preventing and protecting opportunistic infections associated to malaria should be advocated with regard to young and unemployed HIV patients.

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Potential Diagnostic Properties of Chest Ultrasound in Thoracic Tubercolosis – A Systematic Review

PAPER

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Abstract

The aim of this study was to analyze the role and effectiveness of chest ultrasound in the diagnosis of tuberculosis (TB). There were an estimated 10.4 million new cases of TB worldwide in 2015, 1.4 million of which resulted in death. In order to achieve the World Health Organization's End TB Strategy by 2035, early detection measures will be of critical importance, especially in low-resource settings. Indeed, one of the main reasons for the failure to diagnose TB is the limited availability of diagnostic tools.

Our objective here was to analyze the existing literature on the use of chest ultrasound in thoracic TB in order to understand whether it is an effective diagnostic tool.

We identified five main areas for the use of chest ultrasound:
- Detection of pleural effusions;
- Assessment of pleural effusions;
- Biopsy support;
- Identification of pathological mediastinal lymph nodes in children;
- Identification and assessment of pulmonary complications.

The use of chest ultrasound appears to be effective, particularly in low-resource settings where access to radiological techniques is limited.

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Review

Potential Diagnostic Properties of Chest Ultrasound in Thoracic Tuberculosis—A Systematic Review

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Abstract: *Background*: Chest ultrasound (CUS) has been shown to be a sensitive and specific imaging modality for pneumothorax, pneumonia, and pleural effusions. However, the role of chest ultrasound in the diagnosis of thoracic tuberculosis (TB) is uncertain. We performed a systematic search in the medical literature to better define the potential role and value of chest ultrasound in diagnosing thoracic tuberculosis. *Aim*: To describe existing literature with regard to the diagnostic value of chest ultrasound in thoracic tuberculosis. *Methods*: MEDLINE, EMBASE, and Scopus databases were searched for relevant articles. We included studies that used chest ultrasound for the diagnosis or management of any form of thoracic tuberculosis, including pulmonary, pleural, mediastinal, and military forms. *Results*: We identified five main fields of chest ultrasound application: (1) Detection, characterization, and quantification of TB; (2) detection of residual pleural thickening after evacuation; (3) chest ultrasound-guided needle biopsy; (4) identification of pathologic mediastinal lymph nodes in children; and (5) identification of parenchymal ultrasound patterns. Effusion was also detected, in early stages, with signs of organization in 24–100% of patients. A low to moderate (10–23%), false negative rate was reported for chest ultrasound-guided needle biopsy. CUS was able to identify mediastinal lymph nodes in as many as 67% of patients with negative chest radiography. *Conclusions*: Very few studies with important methodological limitations analyze the role of chest ultrasound in the diagnosis of TB. The scarce available data suggests potential targets of future diagnostic or feasibility trials, such as the detection of tuberculosis–related pleural effusion, residual pleural thickening, lymphadenopathy, TB parenchymal patterns, or the use of CUS in biopsy guidance.

Keywords: tuberculosis; lung ultrasound; low-resource settings

1. Introduction

In 2015, an estimated 10.4 million patients were newly diagnosed with tuberculosis (TB) worldwide, with 1.4 million cases resulting in death [1]. To achieve the End TB 2035 target [1] of a 90% reduction in the TB incidence rate by 2035, an acceleration of the present decline rate is urgently needed. Early and accurate diagnosis in high- and low-resource settings is the first pillar of the End TB strategy and is pivotal in enabling early treatment [2].

One of the main reasons for the under-detection of TB is the limited availability of diagnostic methods [3]. Moreover, when a diagnostic apparatus is available, many patients present with non-specific symptoms and negative laboratory exams. This delays diagnosis and aggravates prognosis.

The diagnosis of active TB has always used a composite approach, uniting radiology with three other technologies: Microscopy (sputum smears), culture-based methods, and molecular tests [4]. Unfortunately, facilities using these technologies are not always available in resource-limited settings, especially in peripheral health centers.

Point-of-care chest ultrasonography (CUS), intended for lung, pleural, and mediastinal ultrasonography, is becoming an attractive, non-invasive medical imaging modality in both affluent and resource-limited settings [5]. A recent consensus standardized terminology and indications, regarding critical care lung ultrasound [6]—a method which evolved as a highly sensitive and specific imaging tool for diagnosing chest conditions, such as pneumothorax, pneumonia, and pulmonary edema. Resource-limited settings are of special interest, as radiological equipment and expertise are scarce, or even absent, due to their high costs or poor maintenance. A focused assessment of extra-pulmonary TB has been also proposed [7]. However, the role of lung, and more broadly, chest ultrasound in defining TB has been scarcely investigated. It is currently unclear if CUS could play a clinically-relevant role in diagnosing or excluding active tubercular chest lesions.

The aim of this review is to describe existing studies that have used CUS for the diagnosis of thoracic TB, to ascertain whether it represents a useful tool for the diagnosis and follow up of TB.

2. Methods

This systematic review was conducted, following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [8] statement. The methodological quality of each study was critically evaluated, using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS 2) [9].

2.1. Search Strategy

Two investigators (FG and LP), independently and unaware of the other investigator's decisions, searched PubMed, EMBASE, and Scopus for studies assessing the role of lung ultrasound in thoracic TB. Searches were carried out without language restrictions and from the database's inception until April 2017. Any inconsistencies that remained after discussion were resolved by consensus with a third author (NV), available for mediation. In PubMed, we used the following search strategy: (tuberculosis) AND (ultrasound OR ultrasonography) OR (miliary OR lung OR chest) AND/OR (recovery OR pattern OR diagnosis OR effusion). A similar search strategy was run in EMBASE and Scopus. Reference lists of included articles and those relevant to the topic were hand-searched for identification of additional, potentially-relevant articles.

2.2. Study Selection

We included all studies reporting patient data (including original studies, case-reports, and case series) using chest ultrasound for the diagnosis or management of any form of thoracic tuberculosis, namely its pulmonary, pleural, mediastinal, and miliary forms. Studies were excluded if they (1) used ultrasound for non-thoracic organs or (2) used endoscopic ultrasound. Studies were included, irrespective of the methodology employed. This was to ensure that a comprehensive understanding of the available evidence was achieved.

2.3. Data Extraction and Analysis

The two authors (FG, LP) independently extracted data, using a standardized spreadsheet. Any disagreement was resolved by consensus with a third author (DP). The following information was extracted: (i) Study population characteristics (i.e., author, year, number of participants, mean age, and percentage of females); (ii) study design and inclusion criteria; (iii) details of the ultrasound procedure; (iv) diagnostic criteria used for detecting TB and the final diagnosis made (pulmonary, pleural, or mediastinal TB); and (v) the anatomical site of investigation (pleural cavity, mediastinum, or lung).

The extracted information was organized in tables, describing each study's characteristics, methods, and its main results. Patient characteristics—such as age, number of participants, and number of female cases—were summarized as the mean or proportions, where appropriate. Due to the different design of the studies included, the purely descriptive aim of 8 of the 12 studies, and the high heterogeneity of the outcomes reported, we decided not to meta-analyze the selected studies, instead reporting the main findings as descriptive results. Where some degree of diagnostic accuracy was reported, we calculated it as the percentage of patients with a positive ultrasound (US) examination, over the total of confirmed or suspected TB patients.

3. Results

The search identified 4442 non-duplicate records. After title and abstract screening, as well as a full text review, 12 studies were included, as shown in Figure 1 [10–20], with one study included from the reference screening of a previous article [21].

3.1. Study and Patient Characteristics

Study and patient characteristics are summarized in Table 1. The 12 analyzed studies included 300 participants, with a mean age of 32, 46% of which were females. We found that four studies were conducted in Asia, five in Europe, and three in Africa. Hemi-thoraxes (costophrenic recesses) were the most common site analyzed (n = 5), followed by the mediastinum (n = 4) and lung parenchyma (n = 3). Reference methods for the confirmation of tuberculosis strongly differed across studies.

3.2. Main Findings

The main findings of the included studies are reported in Table 2. We found that five main fields of application of chest ultrasound in the field of thoracic TB emerged. The first concerned the diagnosis of pleural effusions, initially investigated in 1989, in 21 young subjects [10]. Effusions seemed to facilitate the determination of underlying lung lesions [12], while CUS could detect pleural effusions in early stages [16]. Secondly, CUS seemed to be accurate in detecting residual pleural thickening after evacuation [20].

A third use of chest ultrasound focused on biopsies of TB lesions, as reported in three studies. In two studies, some degree of accuracy could be extrapolated, which resulted in moderate to high (76–90%) rates of success [13,21].

The fourth application aimed at identifying pathological mediastinal lymph nodes in children with suspected mediastinal disease, as reported by three studies, all in the pediatric setting [14,15,21] with variable diagnostic performance (40–100%). Only one study monitored the response after treatment, using the reduction of lymph node volume as an indicator for treatment success [14].

Finally, CUS was used to describe parenchymal patterns in one study, which only enrolled patients with miliary TB [18] and reported on only one case [19].

The qualitative assessment of the included studies showed a predominance of high or unclear risk of bias and concern over applicability, across all features analyzed, especially with regards patient selection and the reference standard used.

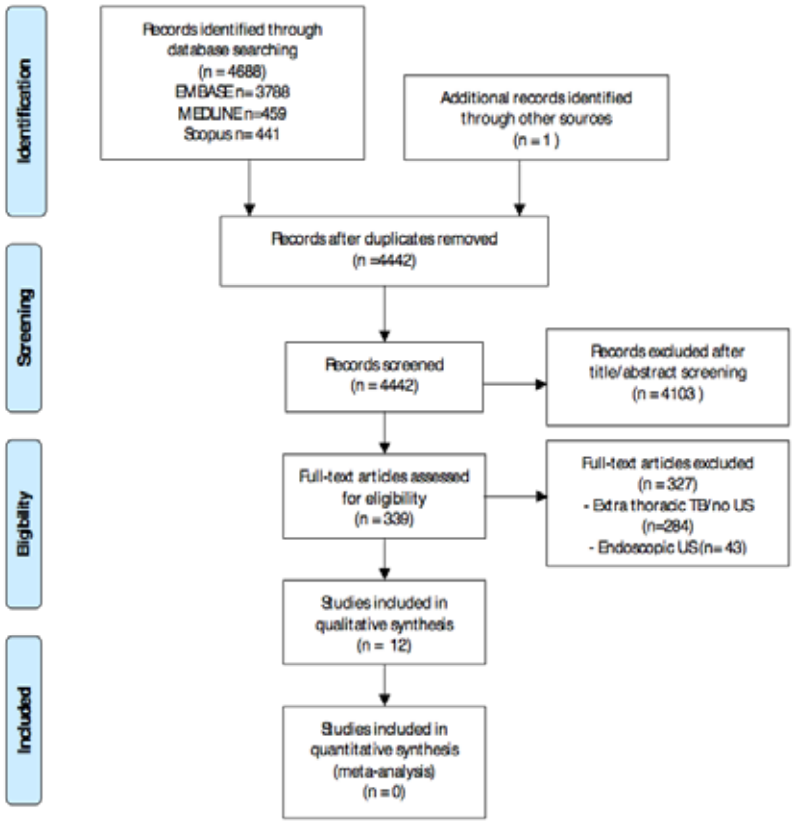

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram. Abbreviations: Tuberculosis (TB) and ultrasound (US).

Table 1. Descriptive characteristics of the study participants, study design, and chest ultrasound (CUS) techniques used.

Author, Year	Country	Study Design	N of Participants	Mean Age	Percentage of Females	Diagnostic Criteria for TBC	Final Diagnosis Made	Details of Ultrasound Procedure	Site of Investigation
Martinez, 1989 [10]	Spain	Case series	21	22.5	57	Microbiological	TB pleurisy	identification of effusion	Hemi-thoraxes
Akhan, 1992 [11]	Turkey	Case series	20	30.5	35	Pleural fluid analysis positive for MT	TB pleurisy	identification of effusion	Hemi-thoraxes and pleural line
Yuan, 1993 [12]	China	Case series	13	53.5	NA	Culture of MT	Pulmonary TB	percutaneous US-guided biopsy	Lung lesions
Gulati, 2000 [13]	India	Case series	26	35.0	31	Composite§	TB-lymphoadenopathy	percutaneous US-guided FNAB	Mediastinum
Bosch-Marcet, 2004 [21]	Spain	Retrospective	32	6	47	Chest radiography/CT	TB-lymphoadenopathy	identification of lymphoadenopathy	Mediastinum
Bosch-Marcet, 2007 [14]	Spain	Retrospective	57	6	NA	Chest radiography	TB-lymphoadenopathy	identification of lymphoadenopathy	Mediastinum
Moseme, 2014 [15]	South Africa	Pilot study	30	6	NA	Not specified	TB-lymphoadenopathy	identification of lymphoadenopathy	Mediastinum
Ahuja, 2014 [16]	India	Case report	1	27	100	Culture of MT	TB pleurisy	identification of effusion	Hemi-thoraxes
Bahr, 2014 [17]	Egypt	Case series	2	NA	NA	Biopsy positive for TB	Pulmonary and TB pleurisy	percutaneous US-guided biopsy	Hemi-thoraxes and Lung lesions
Hunter, 2016 [18]	South Africa	Case series	10	33	50	Sputum positive	Pulmonary TB	Lung US	Lung
Heuvelings, 2016 [19]	Netherlands	Case report	1	44	0	Chest radiography/Bal positive for MT	Pulmonary TB	Lung US	Lung
Lai, 2016 [20]	China	Prospective study	87	64.2	32	Pleural fluid analysis positive for MT	TB pleurisy	identification of pleural effusion and RPT	Hemi-thoraxes

Abbreviations: Mycobacterium tuberculosis (MT), ultrasonography (US), tuberculosis (TB), fine-needle aspiration biopsy (FNAB), bronchoalveolar lavage (BAL), residual pleural thickening (RPT), and not available (NA). §Combination of clinical, imaging, and laboratory parameters + FNAB result.

Table 2. Main findings of the studies included.

Author, Year	Sensitivity of US Procedure *	Main Findings
Martinez, 1989 [10]	Not applicable	First study to propose ultrasound as a useful method for characterizing TB-related pleural effusion. US revealed winding or filiform structures in all patients associated with exudates having high fibrin and protein content.
Akhan, 1992 [11]	Not applicable	90% of patients with TB-related effusion demonstrated regular pleural thickening (1–13 mm). A total of 30% had pleural nodules and 90% of the effusions presented delicate, complete septations.
Yuan, 1993 [12]	90%	US-guided aspiration biopsy provided the diagnosis in 9 out of 10 patients. US findings of pulmonary TB with unusual radiographic appearances were even more diverse than the plain radiographs had depicted. While the US findings of hypo-, iso-, or hyperechoic consolidations and fluid bronchograms were not specific for pulmonary tuberculosis, US indicated the most appropriate area for aspiration.
Gulati, 2000 [13]	76%	A total of 20 out of 26 patients with mediastinal tuberculosis could be diagnosed by guided FNAB. No procedure-related complications were recorded. US-guided FNAB was falsely negative in 6 patients.
Bosch-Marcet, 2004 [21]	90.5%	US showed lymphoadenopathy in 67% of children with a normal chest radiograph and in 90.5% of children with chest radiographic images, compatible with TB.
Bosch-Marcet, 2007 [14]	Not applicable	US examination detected mediastinal lymphadenopathy in all children and a reduction in volume, after 3 months of treatment in 80.9% of children. Mediastinal sonography appears to have been a valuable tool for the diagnosis of TB and in the monitoring of response to treatment, in children.
Moseme, 2014 [15]	40%	Pilot feasibility study showing how mediastinal sonography could detect mediastinal lymphadenopathy in 12 out of 30 children with suspected primary TB. Care was warranted with the deeper aorto-pulmonary zones, as they were harder to visualize.
Ahuja, 2014 [16]	Not applicable	A bedside lung US was the key factor in the early diagnosis of pleural effusion and subsequent patient management.
Bahr, 2014 [17]	Not applicable	In patients with undiagnosed pleural effusion, US-guided pleural biopsies aided in the differential diagnosis of 80% of cases, indicating a tuberculous effusion in 2 out of 30 patients (6.7%).
Hunter, 2016 [18]	Not applicable	Interstitial pattern with B-lines disseminated in multiple lung areas and a pattern of bilateral, diffuse sub-pleural granularity as typical changes seen in lungs of all patients with miliary TB.
Heuvelings, 2016 [19]	Not applicable	Lung ultrasound on a single patient revealed a subpleural consolidation with "shred signs," compatible with infiltrative TB disease.
Lai, 2016 [20]	Not applicable	A complex, septated sonographic pattern was a useful sign to predict the development of residual pleural thickening, 1 year after the start of anti-TB treatment (PPV 84%, NPV 94%).

Abbreviations: Computer tomography (CT), ultrasound (US), positive predictive value (PPV), and negative predictive value (NPV). * was calculated as % of a positive US examination, for the chosen endpoint, over the total of confirmed or suspected TB patients. Not applicable in qualitative studies.

4. Discussion

The main finding of our systematic review is that the few available studies on chest ultrasound have focused on five fields of interest: detection of pleural effusion, assessment of residual pleural thickening, the helpfulness of trans-thoracic needle biopsy, assessment of mediastinal lymphadenopathies, and detection of pulmonary involvement in miliary TB. To our knowledge, this is the first review summarizing evidence for the use of chest ultrasound in the diagnosis of thoracic tuberculosis.

Surprisingly, apart from a single reported case, we found no study analyzing parenchymal ultrasound patterns, typical of pulmonary TB. Considering the pulmonary involvement of TB has been extensively studied by other radiological means [22], we expected to find evidence to include or exclude CUS as an alternative imaging technique in active TB. In the wider field of chest ultrasound, lung ultrasound (LUS) has gained acceptance for the diagnosis of consolidations and interstitial syndromes [23], hence its potential role in defining TB-related, pneumonic infiltrates. However,

there appears to be scant available data at the moment, analyzing the use of LUS in the definition of TB parenchymal infiltrates.

The only study that attempted to report lung patterns describes the presence of B-lines and subpleural granularity, but only enrolled ten patients with miliary TB, which is distinct from pulmonary TB. Additionally, B-lines are, by definition, a highly non-specific sign of interstitial involvement, hence their role must be confirmed before LUS can be used to differentiate TB from other interstitial and alveolar lung diseases. Further, the presence, severity, and distribution of subpleural consolidation in patients with sole pulmonary involvement is still unknown.

There is an increasing interest in employing chest ultrasound in low- and middle-income countries [24]. Chest ultrasound has a relatively steep learning curve: It is ionization-free and is increasingly available [25] at reasonable costs. Moreover, it can be portable and operated with rechargeable batteries. Ultrasound gel, the only routine supply item needed, can easily be produced locally [26], thus making it an attractive option in resource-limited settings. On the other hand, inter-observer variability and diagnostic errors represent important pitfalls, and should be investigated specifically for TB. While the conditions for a wider implementation are favorable, none of the studies were performed in low-income countries. This observation, added to the paucity of available evidence, indicates that the use of CUS for the diagnosis of thoracic TB is still a clinical niche.

No conclusions can be drawn on diagnostic accuracy, as we did not find any clinical trial that compared CUS versus other imaging modalities. In the search for early diagnosis techniques, high negative predictive values become an important endpoint to target. If the benefits of point of care ultrasonography can be transposed to the diagnosis and management of TB—a disease that may yield highly unspecific signs [12]—it remains yet to be challenged by an adequately-powered, diagnostic trial.

The strength of our review stems from the strict search performed and pragmatic clinical questioning. Limitations of the review are the paucity of available data and extreme heterogeneity of the studies included, in terms of aim, methodology, and outcomes. The low or unclear quality of many of the included studies also greatly limits generalizations. Additionally, only five studies [12–15,21] compared the result of the CUS technique to a reference standard for the diagnosis of TB. Most importantly, no prospective studies comparing CUS to other imaging modalities in diagnosing TB were identified.

5. Conclusions

There is a striking scarcity of studies analyzing the use of chest ultrasound as an imaging technique to aid TB diagnosis. CUS is a promising imaging technique for the detection of TB-related effusion, residual pleural thickening, mediastinal lymphadenopathy, and trans-thoracic biopsy guidance. CUS may prove beneficial, especially in low-income countries, where incidence is high and radiological techniques are scarce. Further research is urgently needed to define pulmonary TB patterns, the feasibility of CUS, and diagnostic accuracy.

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Abbreviations

CUS	chest ultrasound
TB	tuberculosis

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The hidden burden of measles in Ethiopia: how distance to hospital shapes the disease mortality rate

PAPER

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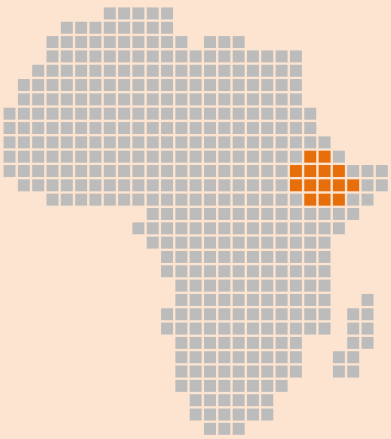

Abstract

Carried out in Ethiopia by Doctors with Africa CUAMM and the Bruno Kessler Foundation (Trento) in cooperation with local health centers, this study analyzed a sequence of annual measles outbreaks in the Oromia Region in order to identify their impact, both evident and hidden, on the region's inhabitants.

We used a mathematical model to calculate and assess the spread of the disease and the related mortality rate, attempting to identify individuals who were unable to access hospital care and reviewing the distance that patients had to travel to access care. Our findings showed that proximity to health centers plays a key role as a determinant of treatment: hospital admissions dropped sharply when patients had to travel more than 20-30 km to reach a facility.

Lack of access to hospital care translated into "missed" (i.e. unobserved) deaths and severe cases of disease: just 2% of total estimated deaths, in fact, were recorded at Wolisso Hospital, indicating that 98% occurred elsewhere in the region due to lack of access to treatment.

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The hidden burden of measles in Ethiopia: how distance to hospital shapes the disease mortality rate

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Abstract

Background: A sequence of annual measles epidemics has been observed from January 2013 to April 2017 in the South West Shoa Zone of the Oromia Region, Ethiopia. We aimed at estimating the burden of disease in the affected area, taking into account inequalities in access to health care due to travel distances from the nearest hospital.

Methods: We developed a dynamic transmission model calibrated on the time series of hospitalized measles cases. The model provided estimates of disease transmissibility and incidence at a population level. Model estimates were combined with a spatial analysis to quantify the hidden burden of disease and to identify spatial heterogeneities characterizing the effectiveness of the public health system in detecting severe measles infections and preventing deaths.

Results: A total of 1819 case patients and 36 deaths were recorded at the hospital. The mean age was 6.0 years (range, 0–65). The estimated reproduction number was 16.5 (95% credible interval (CI) 14.5–18.3) with a cumulative disease incidence of 2.34% (95% CI 2.06–2.66). Three thousand eight hundred twenty-one (95% CI 1969–5671) severe cases, including 2337 (95% CI 716–4009) measles-related deaths, were estimated in the Woliso hospital's catchment area (521,771 inhabitants). The case fatality rate was found to remarkably increase with travel distance from the nearest hospital: ranging from 0.6% to more than 19% at 20 km. Accordingly, hospital treatment prevented 1049 (95% CI 757–1342) deaths in the area.

Conclusions: Spatial heterogeneity in the access to health care can dramatically affect the burden of measles disease in low-income settings. In sub-Saharan Africa, passive surveillance based on hospital admitted cases might miss up to 60% of severe cases and 98% of related deaths.

Keywords: Mathematical model, Sub-Saharan Africa, Access to health care, Case fatality rate, Measles epidemic, Infectious diseases

Background

Measles is one of the most contagious vaccine-preventable viral diseases and represents an important cause of child mortality in sub-Saharan Africa [1, 2]. Despite considerable progress has been made during the last decade in measles mortality reduction [3], the persistent circulation of measles in the WHO African Region [1, 4–6] reflects the challenge of achieving sufficiently high herd immunity levels in areas with limited financial resources.

In low-income countries, a strong heterogeneity both in the measles case fatality rate [47] and in the access to health care infrastructures has been widely documented [8–10], although rarely quantified and little understood [8–12].

In particular, some recent epidemiological studies, focusing on a variety of illness conditions, have shown that larger travel distances to large health care facilities are associated with lower hospital admission rates [8–10] and higher mortality [8, 9, 12]. However, these studies

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do not always differentiate between causes of hospitalization and death [11] and few recent works have documented measles mortality in sub-Saharan Africa [13]. As a matter of fact, the burden of disease is still often estimated on the basis of admitted hospital cases, representing a biased sample that does not reflect the severity of measles within the community [7].

In recent years, recurrent measles outbreaks, primarily affecting children below 5 years of age [1], have been reported in several areas of Ethiopia [1, 14], including the Oromia Region [4]. In Ethiopia, the national Expanded Programme on Immunization was established in 1980 and consists of the first dose of measles-containing vaccine (MCV1) administered at 9 months of age. Routine immunization of infants is supplemented by planned campaigns at 2- and 5-year intervals [3], aimed at increasing vaccination coverage and providing the opportunity for a second dose of vaccine to children who did not respond to the first one [3].

Here we analyze a sequence of annual measles epidemics, with 1819 hospitalized cases and 36 deaths, occurring from January 2013 to April 2017 in the South West Shoa Zone of the Oromia Region. Specifically, we describe the epidemiological characteristics of the observed epidemic, providing estimates of the disease transmissibility, incidence, and mortality at population level. In addition, we investigate the spatial heterogeneity characterizing both the detection and treatment of measles infections as a consequence of travel distance to the nearest hospital. The performed analysis highlights the potential hidden burden of disease caused by the heterogeneous access to primary health care in the region.

Methods

Study population and measles case patients

This study was conducted in the South West Shoa Zone of the Oromia Region in Ethiopia (Fig. 1a), with an estimated population of 1,341,702 inhabitants in 2014, of whom 50.3% were men and 49.7% were women. The main hospital is located in Woliso town, 114 km southwest of the capital Addis Ababa, representing the nearest hospital for 521,771 individuals living within an area of 30 km radius from Woliso town (53,065 inhabitants). The hospital has 200 beds with an annual average bed-occupation rate of 84%; single-patient air-borne infection isolation rooms are not available in the hospital.

Data on age, sex, residence at woreda (i.e., district) and kebele (i.e., neighborhood) level, date of hospital admission, and death/discharge of measles case patients from 2013 to 2017 were obtained from the registers of Woliso hospital. Incidence of hospitalizations by woreda and kebele were calculated by assuming population projections for the 2014, based on the 2007 census conducted by the Central Statistical Agency of Ethiopia (Table 1) [15]. Travel distances to the Woliso hospital for different kebeles and woredas were obtained from administrative hospital records on distances of all health posts and largest villages distributed in the main hospital's catchment area (see Table 1). The case fatality rate (CFR) for hospital admitted cases was calculated as the percentage of fatal cases among measles patients recorded. Routine vaccination coverage for this area was derived from administrative records: on average, 88% of children are routinely vaccinated against measles at 9 months of age. Two immunization campaigns were conducted in the area from May 29 to June 5, 2013, and from March 13 to March 20, 2017, targeting children 9–59 months of age [16]; the achieved vaccination coverage is unknown. In 2016, the vaccination status of case patients was assessed for 295 children in the age group 9 months to 5 years.

Patients' records related to different illness conditions recorded at the Woliso hospital between 2014 and 2016 were considered to estimate hospitalization incidence over time and to assess differences in the access to health care and related outcomes with respect to travel distances from the hospital.

Collected data consisted of routine health data and medical records, were encrypted and anonymous, and did not contain any information that might be used to identify individual patients; therefore, the study did not require informed consent.

Synchrony of local epidemics

Synchrony in the timing of epidemics across different woredas was assessed by calculating the cross-correlation of time series at different time lags. The aim of this analysis is twofold: (i) to evaluate whether the observed seasonal pattern is an artifact of averaging asynchronous local epidemics and (ii) to support the hypothesis that observed measles cases were the result of a unique synchronous epidemic with similar epidemiological characteristics across different woredas.

The modeling approach

The baseline analysis combines results of a dynamic transmission model, calibrated on the time series of hospitalized measles cases occurring between 2013 and 2017, with a spatial regression analysis, providing estimates of the measles hospitalization rate at different distances from the Woliso hospital. We restricted the analysis to measles cases from Woliso, Wonchi, Ameya, and Goro woredas, which represent the main hospital catchment area, consisting of 521,771 inhabitants and accounting for 83.1% of recorded case patients. Under the assumption of homogeneous mixing transmission, the baseline model provided estimates

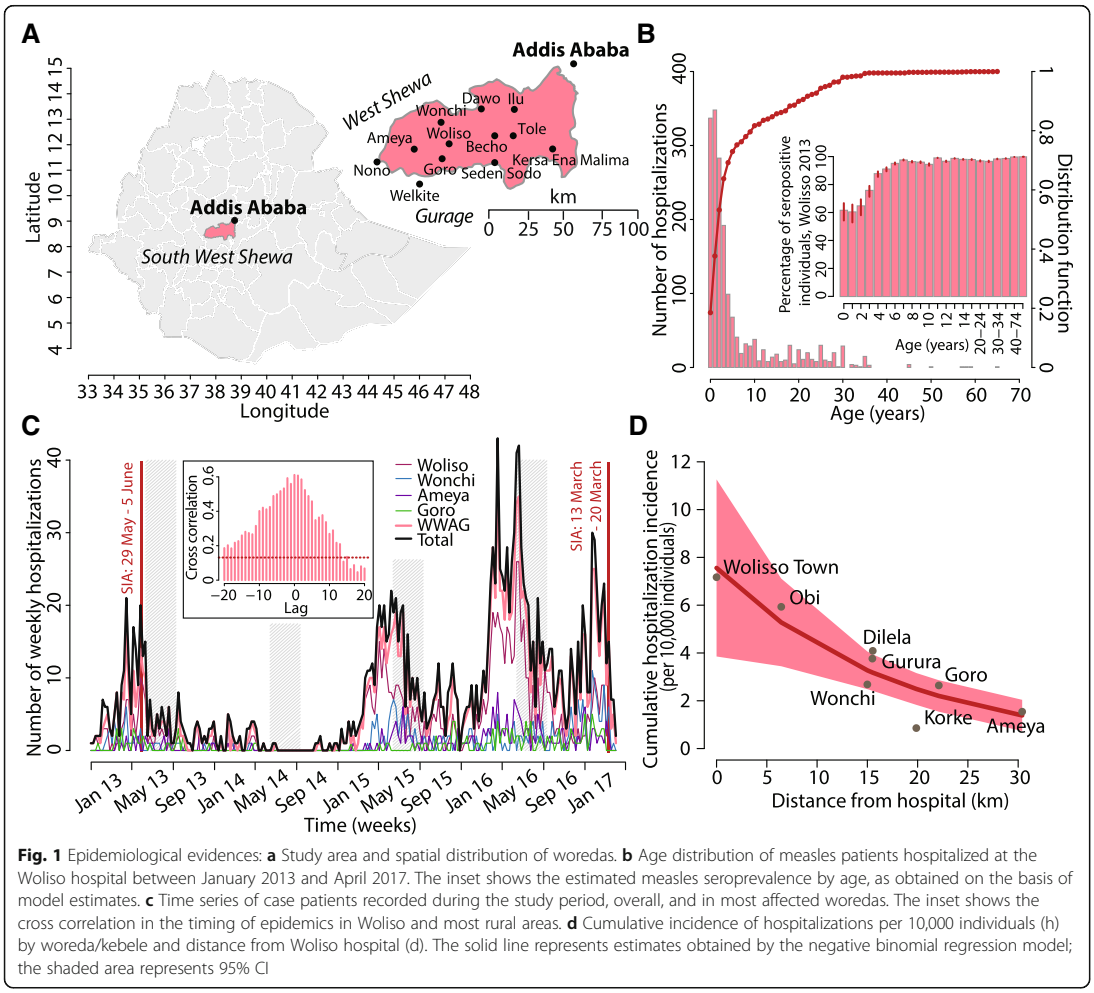

Fig. 1 Epidemiological evidences: **a** Study area and spatial distribution of woredas. **b** Age distribution of measles patients hospitalized at the Woliso hospital between January 2013 and April 2017. The inset shows the estimated measles seroprevalence by age, as obtained on the basis of model estimates. **c** Time series of case patients recorded during the study period, overall, and in most affected woredas. The inset shows the cross correlation in the timing of epidemics in Woliso and most rural areas. **d** Cumulative incidence of hospitalizations per 10,000 individuals (h) by woreda/kebele and distance from Woliso hospital (d). The solid line represents estimates obtained by the negative binomial regression model; the shaded area represents 95% CI

of the basic reproductive number (R_0), the age-specific immunity profile, and the average measles incidence in the considered area. The estimated total number of infection cases in the population was disaggregated into smaller spatial units (woredas and kebeles), by assuming the same incidence rate across all spatial units and proportionally to the population size of each spatial unit. A regression model was applied to counts of observed hospitalized cases in each spatial unit to estimate the corresponding hospitalization rate; distance from the hospital was used as the independent variable and the estimated total number of cases in each spatial unit as offset. Obtained results were used to quantify the hidden burden of measles disease.

In the rest of this section, we detail the dynamic transmission model, the performed spatial analysis, how we calculated the hidden burden of disease, and the performed sensitivity analyses.

The dynamic transmission model

Measles transmission dynamics between 2013 and 2017 is simulated through a deterministic, non-stationary, age-structured transmission model. In the model, the population is stratified in 86 1-year age classes, according to available data on the age distribution of the Ethiopian population in 2013 [17]. The crude birth rate of the population is 0.0325 years^{-1}; individuals die according to age-specific mortality rates as reported between

Table 1 Measles cases patients. Epidemiological characteristics of measles cases admitted to Woliso hospital (South West Shewa Zone, Oromia Region, Ethiopia) from January 1, 2013, to April 9, 2017

Mean age (years)	6.1 (SD 8.9; range 0–65)				
Deaths	36/1819 (2.0%)				
Females	855/1819 (47.0%)				
Vaccinated measles patients (2016)	120/295 (40.6%)				
Hospital main catchment area					
Woreda	Kebele	Patients	Deaths	Population	Distance (km)
Woliso	All kebeles	843	19	209,321	0–19.9
Woliso	Woliso town	379	8	52,849	0
Woliso	Obi	91	5	15.341	6.4
Woliso	Dilela	182	3	48,353	15.5
Woliso	Gurura	141	0	34,477	15.5
Woliso	Korke	50	3	58,301	19.9
Wonchi	All kebeles	296	1	110,275	15.0
Goro	All kebeles	147	3	55,640	22.1
Ameya	All kebeles	226	5	146,535	30.4
Woredas outside the hospital main catchment area					
Becho		41	3	91,116	33.7
Welkite (Gurage Zone)		31	1	55,097	40.1
Seden Sodo		19	1	82,969	45.0
Dawo		23	0	101,133	49.5
Ilu		19	0	75,326	55.9
Tole		48	0	75,438	73.6
Nono (West Shoa Zone)		45	1	108,356	82.7
Kersa Ena Malima		1	1	97,761	137.0
Other		80	1	Unknown	Unknown

2013 and 2015 and reflecting a crude mortality rate of 0.0083 days^{-1} [17]. The population of any age a is divided into five epidemiological classes: individuals protected by maternal antibodies (M_a), susceptible individuals (S_a), exposed individuals (E_a), infectious individuals (I_a), and individuals who acquired immunity against measles through either vaccination or natural infection (R_a).

We assume that newborn individuals are protected against measles infection for 6 months on average by the passive transfer of maternal immunity [1], after which they become susceptible to the infection.

Susceptible individuals can acquire infection after contact with an infectious individual under the assumption of homogeneous mixing and become exposed without symptoms; at the end of the latent period, lasting 7.5 days on average, infectious individuals can transmit the infection for 6.5 days on average; the resulting generation time is 14 days [18]. After recovery, individuals are assumed to gain lifelong immunity. Newly infected individuals are hospitalized with a certain, age-independent, probability p_h, representing the average hospitalization rate in the main hospital catchment area.

Seasonal variations in the transmission rate are considered: during school holidays, overlapping with the rainy season [14], the transmission rate is decreased by a factor r.

Routine vaccination of children is simulated at 9 months of age [3] with homogenous coverage across woredas at 88%. The latter estimate was obtained by administrative records on infant immunization occurring between 2013 and 2016 in the main hospital catchment area. Vaccine efficacy at the first dose of routine administration is assumed at 85% [19].

The follow-up campaigns conducted in 2013 (from May 29 to June 5) and in 2017 (from March 13 to March 20), targeting children 9–59 months of age [16], are also considered. The coverage of the 2013 supplementary immunization activities (SIAs), c_S, was estimated among free model parameters. Vaccine efficacy during SIAs is assumed to be 95% [19].

Epidemiological transitions are described by the following system of ordinary differential equations:

$$\begin{cases} M_a'(t) &= bN(t)-\mu M_a(t)-(\varepsilon_R c_R(t,a)+\varepsilon_S c_S(t,a))M_a(t)-d(t,a)M_a(t) \\ S_a'(t) &= \mu M_a(t)-(\varepsilon_R c_R(t,a)+\varepsilon_S c_S(t,a))S_a(t)-\beta(t)S_a(t)I(t)/N(t)-d(t,a)S_a(t) \\ E_a'(t) &= \beta(t)S_a(t)I(t)/N(t)-\omega E_a(t)-d(t,a)E_a(t) \\ I_a'(t) &= \omega E_a(t)-\gamma I_a(t)-d(t,a)I_a(t) \\ R_a'(t) &= \gamma I_a(t)+(\varepsilon_R c_R(t,a)+\varepsilon_S c_S(t,a))(S_a(t)+M_a(t))-d(t,a)R_a(t) \\ H_a'(t) &= p_h \omega E_a(t) \\ I(t) &= \sum_{a=0}^{85} I_a(t) \\ H(t) &= \sum_{a=0}^{85} H_a(t) \\ N(t) &= \sum_{a=0}^{85} [M_a(t)+S_a(t)+E_a(t)+I_a(t)+R_a(t)] \end{cases}$$

where t represents time and a the individuals' chronological age; $b(t)$ and $d(t,a)$ are the crude birth and the age-specific mortality rates at time t; $1/\mu$ is the average duration of protection provided by maternal antibodies; $1/\omega$ and $1/\gamma$ are the average duration of the latent and the infectivity periods; $c_R(t,a)$ and $c_S(t,a)$ are the coverage associated with the first-dose routine vaccination and SIAs for individuals of age a, at time t; ε_R and ε_S represent the vaccine efficacy associated with routine vaccination of infants and SIAs. Specifically, c_S denotes the vaccinated fraction of individuals who were not yet immunized by natural infection or routine programs. $N(t)$ and $H(t)$ represent the total population of the hospital main catchment area and the cumulative number of hospitalized measles cases at time t; p_h is the fraction of measles infections that are hospitalized, and $\beta(t)$ is the measles transmission rate defined as follows:

$$\beta(t) = \begin{cases} r\,\beta, & \text{1st Jun} < t < \text{12th Sep} \\ \beta, & \text{otherwise} \end{cases}$$

At the end of the year, the chronological age of individuals is incremented by 1. The number of hospitalized measles cases in a time interval $[t_1,t_2]$ is computed as $H(t_2) - H(t_1)$.

Model estimates were obtained by simulating measles transmission between January 1, 2013, and March 20, 2017. Simulations are initialized on January 1, 2013. As the result of past natural infection and immunization campaigns, only a fraction s_0 of the population is assumed to be susceptible to the infection. The age distribution of susceptibles at the beginning of 2013 was assumed to mirror the age distribution of hospitalized cases between January 2013 and March 2017. Specifically, the initial fraction of susceptible and immune individuals in each age group are $S_a(0) = N_a s_0 Z_a / \sum_{a=0}^{85} Z_a$ and $R_a(0) = N_a - S_a(0)$, respectively, where N_a is the number of individuals of age a at the beginning of 2013 in Woliso, Ameya, Goro, and Wonchi [17] and Z_a is the observed total number of hospitalized measles cases of age a.

Free model parameters (s_0, β, r_β, p_h, c_S) were calibrated using a Markov Chain Monte Carlo (MCMC) approach based on the negative binomial likelihood of observing the weekly number of hospitalized case patients reported between January 1, 2013, and the beginning of the 2017 SIA. The scale parameter defining the negative binomial distribution was jointly estimated with other free parameters within the MCMC procedure. Details are provided in the Additional file 1.

Reproduction number and disease elimination

The fundamental quantity regulating disease dynamics is the basic reproduction number (defined as $R_0 = \langle\beta\rangle/\gamma$, where $\langle\beta\rangle$ is the average of $\beta(t)$ over the year), which represents the average number of secondary infections in a fully susceptible population generated by a typical index case during the entire period of infectiousness. The larger the R_0, the higher the disease transmissibility. If $R_0 > 1$, the infection will be able to spread in a population. Otherwise, the infection will die out. For endemic diseases like measles, R_0 provides insights into the proportion p of population to be successfully vaccinated to achieve disease elimination; the equation $p = 1-1/R_0$ is widely accepted (e.g., [5, 18, 20]). For instance, if $R_0 = 10$, at least 90% of children have to be routinely immunized to eliminate the disease.

Spatial analysis

A negative binomial regression was used to study the relationship between incidence of hospitalization by kebeles/woredas and distance from Woliso hospital. Specifically, the observed number of hospitalized cases from each spatial unit is the response variable, the distance from the hospital is the independent variable, and the estimated total number of measles cases in each spatial unit (as estimated by the transmission model) is used as the offset.

Detailed origin of patients at the kebele level was used to better identify the travel distances for patients living within the Woliso woreda, where the hospital is located (Table 1).

In the negative binomial regression, we assume that counts of hospitalized cases h_i (the response variable) associated with a given location i are distributed as a negative binomial of mean μ_i determined by the number of infection in the location c_i (the offset) and the distance of location from the hospital d_i (the regressor) as follows:

$$\mu_i = \exp(\ln(c_i) + b_1 + b_2 d_i)$$

where b_1, b_2 are unknown parameters that are estimated from the observed hospitalized cases h_i.

In order to take into account the uncertainty on incidence estimates obtained with the dynamic model, 10,000 draws from the posterior distribution of incidence estimates associated with 10,000 samples of the posterior distribution of free model parameters were considered to generate a distribution of regression model fits. Obtained results therefore account for the combined uncertainty due to the regression model and the dynamic transmission model.

We investigate the spatial variation in the incidence of hospitalized patients in the population as a consequence of different illness conditions. The aim is to characterize the relationship between hospitalization and distance from the hospital. The relative risk of being hospitalized at different distances from the hospital was computed by considering the incidence of hospitalization in each kebele/woreda divided by the incidence of hospitalized cases from Woliso town. The relative risk was fitted by an exponential function using distance as the independent variable (i.e., by fitting a linear model to the logarithm of the relative risk without intercept). Finally, a proportional test was used to assess possible statistical differences in the case fatality rate at hospital between cases coming from different sites.

The hidden burden of disease

Persons living in Woliso town do not have distance barriers to access to the Woliso hospital. The probability of severe disease after measles infection was therefore computed as the fraction of measles patients from Woliso town that have been hospitalized for two nights or more among all measles infections estimated by the transmission model for this spatial unit. For severe cases, we indicate here those cases that from a clinical point of view are physiologically unstable and require supportive care (fluid resuscitation, oxygen, etc.) that can be provided only inside a well-resourced hospital. The resulting probability of developing severe measles illness p^s was used in combination with the estimated number of measles infections at different kebeles and woredas c_i to estimate the potential number of severe cases occurring at different distances from the hospital as $p^s c_i$. For each considered spatial unit i, missed severe cases were computed as the difference between the estimated number of severe cases and the number of patients recorded at the hospital, namely $m_i^s = p^s c_i - h_i$. Missed severe cases were considered untreated and counted as additional deaths. The overall number of deaths caused by measles was estimated as the sum of missed deaths and measles deaths observed among hospital admitted patients. Averted deaths due to hospital treatment were estimated by considering all severe cases $p^s c_i$ as counterfactual deaths that would have occurred in the absence of adequate treatment.

Sensitivity analyses

A variety of sensitivity analyses were conducted to evaluate to what extent some crucial assumptions made in the above described analysis may affect the obtained results.

We evaluated whether the assumption of decreased transmissibility during school holidays (or rainy season) is necessary to explain the observed pattern, by fitting a model with constant transmission rate against the time series of measles hospitalized cases.

Since the fraction of immunized individuals during the SIA in 2013 is unknown, we also considered two alternative models with $c_S = 0$ (SIA not conducted in 2013 in the considered area) and $c_S = 0.92$ (the highest coverage reported for past campaigns, namely 92% [3]).

We explored whether the assumption of homogeneous mixing, consisting in applying the same transmission rate to all age groups, can affect the model ability in reproducing the observed epidemiological patterns. To do this, we fitted the time series of cases with a transmission model encoding age-specific contacts as recently estimated for Ethiopia by Prem et al. [21]. In this case, increased mixing in schools corresponds to higher transmission rate among school-age children.

Models' performances were assessed through the Deviance Information Criterion (DIC).

A sensitivity analysis was also conducted by fitting a transmission model to the time series of measles cases observed in Woliso, Wonchi, Ameya, and Goro separately. Specifically, a single epidemic was simulated in the four woredas simultaneously, by assuming the same initial conditions and by assuming that populations from different locations mix homogeneously. All epidemiological parameters were assumed to be equal across different woredas, but a different hospitalization rate was considered for each woreda.

An additional sensitivity analysis was performed to test whether estimates on the spatial variation of the hospitalization rates change when patients recorded from all woredas of the South West Shoa Zone are considered or when patients' sex is considered.

Finally, estimates on the overall number of measles deaths and on the overall case fatality rate were estimated by relaxing the assumption that all missed/untreated severe measles cases die.

Details are provided in Additional file 1.

Results

Measles case patients

A total of 1819 case patients were recorded in Woliso hospital from January 1, 2013, to April 9, 2017 (Table 1). Of these, 855 (47.0%) were female and 964 (53.0%) were male; 1512 patients (83.1%) were resident in the main hospital's catchment area, consisting of Woliso, Wonchi, Goro, and Ameya woredas. The mean age was 6.0 years (range, 0–65); 1259 case patients (69.2%) were aged ≤ 4 years and 1486 (81.7%) were aged ≤ 10 years (Fig. 1b). Records obtained during 2016 show that vaccinated admitted cases between 9 months and 5 years of age were 40.6%. In sub-Saharan Africa, different immunization rates may correspond to rural and urban areas [22, 23]. However, by looking at the vaccination status of hospitalized measles cases, though only recorded for a small fraction of cases, we found that the fraction of vaccinated individuals among measles cases was not significantly different across woredas (proportional test p value, 0.663) and consistent with administrative records of routine coverage in the area (see Additional file 1). This simple analysis partially supports the assumption of homogeneous coverage in the main catchment area.

The CFR based on hospital admitted cases was 1.98% (36/1819, 95% credible interval (CI) 1.43–2.72). The mean age of fatal cases was 3.3 years (range, 0–30). The time series of case patients is shown in Fig. 1c. Epidemic peaks were observed in June of 2013, 2015, and 2016, with marked incidence decrease after closure of schools for holidays and at the beginning of rainy seasons. A much lower number of case patients was recorded in 2014. In 2017, the epidemic peak was observed in late winter with marked incidence decrease after the conducted SIA (13–20 March).

Measles transmissibility and seasonal patterns in measles circulation

Simpler transmission models with $r = 1$, $c_S = 0$, or $c_S = 0.92$ and the one based on heterogeneous mixing by age were all ruled out by the DIC analysis. Best model performances were obtained with the baseline transmission model. Remarkably, even if based on the assumption of homogeneous mixing, the baseline transmission model well reproduced the number of measles cases observed over time, among different age groups: 0–6 years, 7–14 years, and > 15 years (details in Additional file 1). Interestingly, we found that considering different transmission rate by age groups, as a consequence of heterogeneous mixing by age, does not improve the model ability in reproducing the observed time series of measles cases. The average reproduction number estimated with the baseline transmission model was $R_0 = 16.5$ (95% CI 14.5–18.3).

A strong seasonal pattern of transmission was consistently observed across the different woredas. Significant synchrony in the timing of epidemics in Woliso and most rural areas was observed (inset of Fig. 1c and Additional file 1), so that the observed seasonal pattern was not an artifact of averaging asynchronous local epidemics. Model estimates suggest an average decrease in the force of infection of 27.8% (95% CI 21.6–33.2) between June and September, corresponding to school holidays and the rainy season.

The estimated average hospitalization rate in the main hospital's catchment area was 12.4% (95% CI 10.9–14.1), similar to results found in [24]. Accordingly, 12,194 infections (95% CI 10,723–13,872), corresponding to a disease incidence of 234 per 10,000 individuals (95% CI 206–266), may have occurred in the area from January 1, 2013, to March 13, 2017.

The coverage of the 2013 SIA among residual susceptible individuals was estimated to be 18.7% (95% CI 11.9–24.3). The percentage of susceptible individuals at the beginning of 2013 was estimated to be 6.5% (95% CI 6.0–7.3). By assuming that the age distribution of observed measles cases mirrored the distribution of susceptible individuals across different age segments, we estimated the corresponding age-specific immunity profile of the population. This analysis showed that about 40% of children aged ≤ 2 years were not immunized against measles, while less than 10% of individuals aged > 5 years were susceptible to measles (inset of Fig. 1b).

Spatial analysis

Differences in the case fatality rate among hospital admitted patients from different sites were not found statistically significant (see Fig. 2b). Significantly different cumulative incidences of hospitalizations by woreda and kebele were observed, with the largest values at 71 per 10,000 inhabitants in Woliso town (Fig. 1d). Cumulative incidence of hospitalizations by kebele/woreda was significantly correlated to travel distance from Woliso (Pearson $\rho = -0.90$, $p = 0.003$) (Fig. 1d).

Estimated measles hospitalization rate dramatically decreases with travel distance from the hospital: from 31.0% (95% CI 15.9–45.0) in Woliso town to 5.7% (95% CI 3.0, 8.1) at 30 km from the hospital (Fig. 2a). Remarkably, similar estimates were obtained by fitting the transmission model to cases observed in Woliso (Woliso town and Obi, Dilela, Gurura, and Korke kebeles), Wonchi, Ameya, and Goro separately (see Additional file 1). In this case, estimates of woredas' specific hospitalization rates range between 6.1% (95% CI

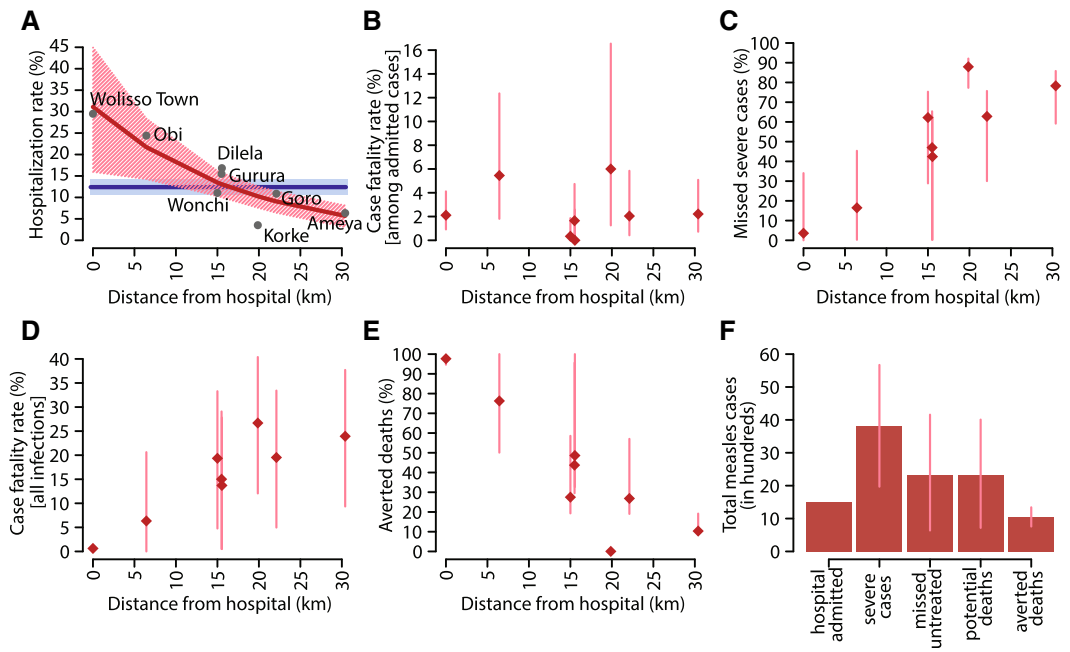

Fig. 2 The hidden burden of measles disease. **a** Point estimates of the hospitalization rate at different distances from the Woliso hospital (in gray) and results from the negative binomial regression (mean in dark red and 95% CI in light red); estimates of the average hospitalization rate in the area as obtained with the transmission model are shown in blue (solid line represents the mean, shaded area represents 95% CI). **b** average CFR among hospital admitted cases across different sites (red diamonds); vertical bars represent 95% CI as obtained by exact binomial test. **c** Estimates of the proportion of untreated and missed severe cases over distance (diamonds represent the mean estimates; vertical bars represent 95% CI). **d** Estimates of the overall measles case fatality rate at different distances from the hospital; CFR is obtained as the fraction of estimated deaths over the estimated number of measles infections across different sites (diamonds represent the mean estimates; vertical bars represent 95% CI). **e** Estimated percentage of averted deaths due to hospital treatment as obtained by considering all severe cases as counterfactual deaths that would have occurred in the absence of adequate treatment (diamonds represent the mean estimates; vertical bars represent 95% CI). **f** Cumulative number of cases between 2013 and 2017 stratified in observed hospital admissions, estimated severe cases, missed untreated cases, overall potential deaths computed by assuming that all severe untreated cases died, and averted deaths due to hospital treatment (vertical bars represent 95% CI)

5.7–6.5) in Ameya and 15.9% (95% CI 15.0–17.0) in Woliso, with an average hospitalization rate in the hospital catchment area of 12.7% (95% CI 11.1–14.1) that is consistent with estimates obtained with the baseline model (see Additional file 1).

Similar results were also obtained when all woredas of the South West Shoa Zone were considered, although it is likely that measles cases occurring beyond 30 km from Woliso town have been partially detected, recovered, and treated in other health care facilities. A sensitivity analysis suggested that males had a higher access to health facilities with respect to females. However, the impact of distance on individuals' access to care was found to not depend on the individual sex.

Interestingly, we found that the relative risk of hospitalization at the Woliso hospital associated with different illness conditions and health care treatments decreases with distance as well (see Additional file 1). These results suggest that the estimated decrease in measles hospitalization with the distance from the hospital is ascribable to inequalities in access to health care due to travel distances from the nearest hospital. These results, combined with those coming from the cross-correlation analysis of time series of cases from distinct woredas, suggest that observed measles cases were the result of a unique synchronous epidemic with similar epidemiological characteristics across different woredas. More details are provided in Additional file 1.

The hidden burden of disease

The probability of severe illness once infected, based on measles inpatients from Woliso town, resulted in 0.30 (95% CI 0.16–0.43). The total number of severe measles cases in the Woliso hospital catchment area was consequently estimated to be 3821 (95% CI 1969–5671), only 1512 of which have been recorded among hospital

admissions (Fig. 2c, f). By assuming that all untreated severe measles cases died, a total number of 2337 deaths (95% CI 716–4009) were estimated, 28 of which were detected at the hospital. Accordingly, 98% of deaths remained unobserved.

By estimating for each site the overall number of infected cases, the number of severe cases, and deaths, we found that the overall case fatality rate in the whole area (defined as the number of deaths per measles infection) might have been as high as 18.4% (95% CI 5.9–30.2).

Averted deaths due to hospitalization in the main hospital's catchment area resulted to be 1049 (95% 757–1342). However, our results suggest that hospital effectiveness in preventing deaths dramatically reduces with travel distance from the hospital, becoming negligible beyond 20–30 km from the hospital (Fig. 2e). Our estimates suggest that the case fatality rate increases from 0.62% (95% CI 0.60–0.65) in Woliso town to more than 20%, on average, for sites that are more than 20 km far from the hospital (Fig. 2d).

The estimated number of deaths and the resulting CFR in the main catchment area decrease with the fatality rate assumed among severe cases that were not hospitalized (see Fig. 3). However, if only half of the severe cases that were not hospitalized are assumed to die, the estimated average number of measles deaths exceeds 1100, only 3% of which were recorded at the hospital; the estimated CFR among all infections results larger than 9% (see Fig. 3).

Discussion

The epidemic in South West Shoa Zone highlights that measles still represents a major public health issue in Ethiopia. The synchrony of local epidemics and the consistent negative relationship between hospitalization incidence for different illness conditions and the distance from the referral hospital support the hypothesis of a large epidemic, spreading in the entire zone with similar transmission characteristics, but characterized by a significant heterogeneity in access to health care infrastructures.

The estimated average reproduction number of the observed epidemic was $R_0 = 16.5$ (95% CI 14.5–18.3), slightly larger than values recently found for Niger (4.7–15.7) [20] and Zambia (12.6) [5]. Accordingly, the herd immune level required in the area to progress towards measles elimination is around 94%, far beyond possible achievements with routine administration of a single dose at 85% of vaccine efficacy [19, 25] and coverage at 88%. In particular, the estimated age-specific serological profile is consistent with estimates recently provided for Ethiopia [26], showing that, in 2015, 60% of susceptible individuals in Ethiopia were less than 5 years of age. These results suggest critically low immunization rates in recent birth cohorts.

Our analysis highlighted a significant reduction of measles transmission between June and September.

Such a reduction may reflect changes in contact rates induced by either school closure or rainfalls. Indeed, in the Oromia Region, school holidays occur during the rainy season [14]. Changes in measles transmission during this period was already observed in Ethiopia [14], and the decrease in measles circulation caused by rainfalls was suggested for other African countries [6], possibly due to relatively low connectivity or an increase in urban density during the dry season as a consequence of migration from agricultural areas. As already observed in Niger [6], the strong seasonality in measles

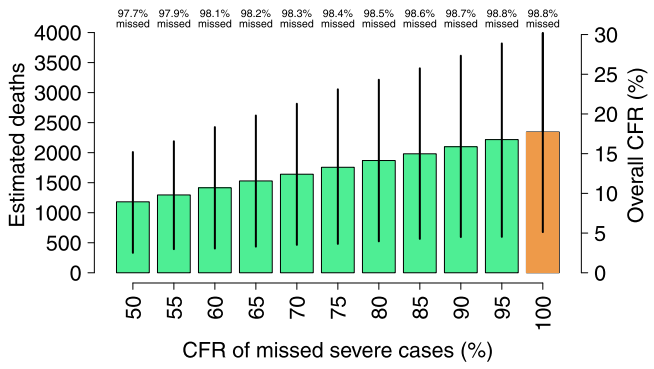

Fig. 3 Sensitivity analysis. Total number of measles deaths (scaled on the left) and overall measles case fatality rate (scaled on the right) in the main hospital catchment area as estimated for different values of the fatality rate among severe cases that were not hospitalized. Estimates obtained with the baseline assumption are shown in orange. Vertical bars represent 95% of credible intervals. Percentages shown on top of the figure represent the estimated average proportions of deaths that were not reported at the hospital obtained with different values of the fatality rate among missed/untreated severe cases

transmission, combined with variations in vaccine uptake and in fertility rates may lead to erratic epidemiological patterns [27], characterized by frequent stochastic fadeouts, and irregular large epidemics. Occasional large outbreaks may be followed by years of very few cases, with inter-epidemic periods of unpredictable length and frequency, during which the high fertility characterizing the country can produce a fast, possibly unnoticed, recruitment of susceptible individuals [6, 26–28]. These considerations apply also to the South West Shoa Zone.

We found that the 2013 SIA might have reached less than 20% of residual susceptible individuals, which is much lower than the observed 75% reduction in the susceptible proportion produced by the first regional SIA conducted in southern Ethiopia in 1999 [29] and than the coverage levels estimated for SIAs conducted in other sub-Saharan countries (66–77%) [30]. The low impact of 2013 vaccination campaign with respect to past SIAs might have been influenced by problems in cold chain operations or vaccine maintenance [25] and the short duration of this campaign. However, the low impact of 2013 SIA may also reflect difficulties in immunizing individuals who escaped routine programs and past immunization efforts, especially through vaccination activities performed as a response strategy to ongoing epidemics [31].

Remarkably, we found that hospitalization rates and the effectiveness of passive surveillance based on hospital admissions, in both detecting measles and preventing measles-related deaths, dramatically decrease with travel distances from the hospital, becoming negligible beyond 20–30 km from the hospital. In particular, our estimates suggest that measles hospitalization rate decreases by about 80% within a 30-km travel distance from the hospital. These results are consistent with what observed in Kenya where all-cause admission rates were found to decrease by 11–20% with every 5-km increase in distance from the hospital [10]. A decrease of hospital admissions with increasing distance from the hospital was also found when estimating the global and regional burden of severe acute lower respiratory infections [32].

The overall estimated cumulative incidence was 2.34% (95% CI 2.06–2.66) of the population in less than 5 years. CFR among hospitalized cases was 1.98% (95% CI 1.43–2.72). However, while only 36 deaths were recorded at the hospital, the spatial epidemiological analysis performed highlighted that the observed epidemics may have caused about 2300 additional deaths, consisting of severe cases that did not received any hospital treatment. These results suggest that the overall case fatality rate among all measles infections might have been between 5 and 30%, significantly higher than published estimates for epidemics occurred in 2005–2006 in Niger, Chad, and Nigeria, namely 4.2–8.1% [13]. Obtained estimates for the measles CFR are consistent with those obtained for low-income countries during outbreaks occurring in isolated populations (above 15%) [7]. The assumed CFR among untreated measles cases essentially reflects our estimate of the percentage of most severe cases (around 30%), and it is in line with estimates of measles CFR in Ethiopia dating back to more than 30 years ago (around 27%) [7]. Estimates obtained on the total number of deaths and on the overall case fatality rate strongly depend on the assumption that all unobserved severe measles cases died. On the one hand, this represents a worst-case scenario. On the other hand, it is worth considering that cases here defined as severe are those with critical complications requiring to occupy, for two or more consecutive nights, one out of the 200 beds of a hospital in Ethiopia serving a potential catchment area of roughly 1.3 Million people and representing the closest well-resourced heath facility that can provide adequate treatments and supportive care for 521,771 inhabitants.

Obtained results are supported by spatial trends we identified in the relative risk of being hospitalized as a consequence of other illness conditions (see Additional file 1) and are consistent with what observed in previous studies on a variety of illness conditions [10, 22]. The role of distance as a barrier to health care access and affecting individuals' mortality has been well documented by recent population-based studies [8, 9], although most of them do not differentiate between causes of death [11] and between levels of care available in facilities [11], and none of these are focused on measles. In particular, a cross-sectional survey recently conducted in Ethiopia highlighted that children who lived more than 30 km from the health center had a two- to threefold greater risk of death than children who lived near to the health center [8]. Similar results were found when considering either traveling distances or travel times [8]. In rural Tanzania, direct obstetric mortality was found to be four times higher at 35 km from hospital [11]. Finally, geographical clusters of acute abdominal conditions in India were found to have a nine times higher mortality rate and significantly greater distance to a well-resourced hospital [12].

All these epidemiological evidences suggest that what was observed for measles in the South West Shoa zone may likely affect other diseases and characterize other low-income settings of sub-Saharan Africa. Obtained results highlight that epidemiological estimates, based on hospitalization records only, may dramatically underestimate the burden of measles and should be carefully considered to design adequate and effective surveillance activities. More, in general, as already suggested in [10, 11], disease burden estimates based on hospital data

may be strongly affected by distance from the hospital, although the amount of underestimation of disease burden may differ by disease [10, 11] and region considered.

The analysis has several limitations that should be considered in interpreting the results. The most important ones relate to the short observational period, the limited area considered, and the difficult task of quantifying unobserved severe measles cases. In particular, we assume that severe cases occurring within the main hospital's catchment area that have not been reported at the Woliso hospital were not treated at all for measles disease. Although past studies have not found any association between child mortality and distance to small health facilities (e.g., health posts) [8], most severe infections might have seek treatment at hospitals that are more distant than the Woliso one. In addition, factors other than distance such as individual sex, age, family's income, and geographical heterogeneity in incidence levels of comorbidities and social support provided to families might have strongly affected the access to health care and the disease outcome of patients coming from different locations [9]. Finally, misclassification of measles patients may always occur [7]. These limitations make it particularly difficult to reliably quantify untreated cases and estimate their fatality rate and the number of measles deaths, especially in absolute terms [7]. Other limitations of the proposed approach are determined by the lack of suitable data to model heterogeneous vaccination coverage within the hospital main catchment area, possible changes in the measles hospitalization rates over time, variations in the individual transmission rate of hospitalized cases, and seasonal variations of the population density as a consequence of migration flows between rural and urban areas.

Conclusions

The carried out analysis represents a first attempt to investigate the impact of spatial heterogeneity in hospital accessibility on measles epidemiology, to quantify the hidden burden of measles in low-income settings, and to assess the effect of hospitalization in preventing death from severe measles disease. Epidemiological patterns identified through the performed analysis should be tested in other settings and may strongly depend on both levels of care available in health facilities [11] and infection rates in the considered community. If similar results will be confirmed, geographical heterogeneity in the hospitalization rates should be taken into account when estimating the burden of diseases and the effectiveness of the public healthcare system [7].

Additional file

Additional file 1: Supporting material. Model details, sensitivity analysis, and additional results. (PDF 8654 kb)

Abbreviations

CFR: Case fatality rate; CI: Credible interval; DIC: Deviance Information Criterion; MCMC: Markov Chain Monte Carlo; MCV1: First dose of measles-containing vaccine; R_0: Basic reproductive number; SIA: Supplementary immunization activity; WHO: World Health Organization

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Availability of data and materials

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

Authors' contributions

PP, SP, GP, FM, and SM conceived of the study. TF, RF, ML, AT, GS, GP, and FM collected the data. PP, SP, GP, FM, and SM analyzed the data. PP and SM performed the experiments. PP drafted the first version of the manuscript. All authors contributed to the interpretation of the results and edited and approved the final manuscript.

Ethics approval and consent to participate

The study did not require informed consent as collected data consisted of routine health data and medical records were encrypted and anonymous and did not contain any information that might be used to identify individual patients.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

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The implementation of Universal Test and Treat Programs: one-year experience from Test & Treat Project in Shinyanga and Simiyu Regions, Tanzania

POSTER PRESENTATION

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Authors
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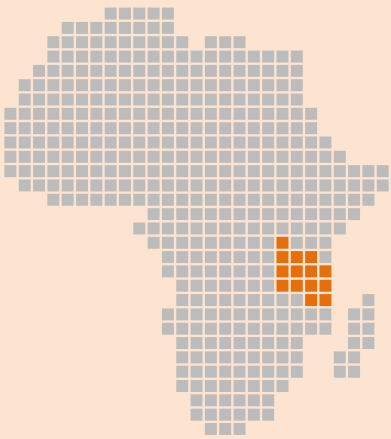
Focus country
Tanzania



Background
A poster aimed at presenting the Test & Treat Project in Shinyanga and Simiyu regions, northwestern Tanzania. In these regions the HIV prevalence is 5.9% and 3.9%, respectively.
The evaluation concerns a community model of HIV care encompassing both Universal Test and Treat and Differentiated Care in four Care and Treatment Centres

Description
Community-based HIV testing services and sensitization campaigns were implemented in public areas, factories, schools, and worship places based on a "hamlettesting" strategy. HIV testing was also offered routinely to all clients attending health facilities (HFs). All people tested HIV+ during a testing campaign were referred to a CTC through community health workers who represented a key component in linkage to care.

Conclusion
Conclusions/Next steps One-year data of Test & Treat Project in Tanzania demonstrate the potential of TCs to increase the overall testing coverage in a short time frame and preferentially include male clients. Linkage to care remained a challenge. Viral suppression was achieved in majority of clients on treatment. Determinants that underlie these initial results are being studied with the aim to develop a sustainable Tanzanian blueprint for the UNAIDS 90-90-90 goals.

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The implementation of Universal Test and Treat Programs: one-year experience from Test & Treat Project in Shinyanga and Simiyu Regions, Tanzania

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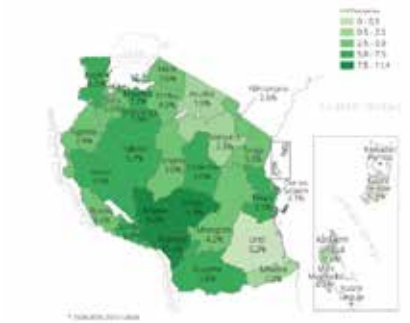
Background

The Test & Treat Project is conducted in Shinyanga and Simiyu regions, in northwestern Tanzania. In these regions the HIV prevalence is 5.9% and 3.9%, respectively. We evaluate a community model of HIV care encompassing both Universal Test and Treat and Differentiated Care in four Care and Treatment Centres (CTCs). Here we report twelve-month findings on HIV testing, linkage to care and viral suppression.



THIS TANZANIA HIV IMPACT SURVEY A DROP THAT COUNTS 2016-2017

Description

Community-based HIV testing services and sensitization campaigns were implemented in public areas, factories, schools, and worship places based on a "hamlet-testing" strategy. HIV testing was also offered routinely to all clients attending health facilities (HFs). All people tested HIV+ during a testing campaign were referred to a CTC through community health workers who represented a key component in linkage to care.

Outreach activity in a rural area of Simiyu Region

Lessons learned

From May 2017 to April 2018, 86,744 clients were tested through the testing campaigns (TC), while 25,944 were tested at the project's (HFs). More men were tested in the TC compared to HFs (56% *vs* 44%; p<0.001). Overall 2,021 (1.8%) HIV+ clients were identified (male 39%). Of these, 953 (47%) were identified by TC and 1,068 (53%) by HFs. 15,554 (14%) children <15 years were tested. Of these, 65 (0.4%) were HIV+. Among the HIV+ clients identified through TCs, 138 (13%) were already aware of their HIV status. Data on testing by age groups and sites are reported in the figures below. By 31 March 2018, 352 (43%) newly diagnosed clients identified in TC were linked to a CTC. More women were linked than men (45% vs 40%). Linkage was higher in Shinyanga than Simiyu (47% *vs* 38%; p=0.003). Among 3,014 patients on ARV at the four project CTCs, 1,745 (58%) had documented viral load (VL) results. Of these, 1,592 (91%) had VL <1,000 cp/ml, while 1,440 (82%) had VL <50 cp/ml.

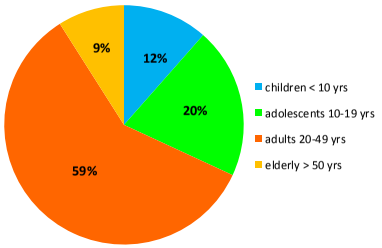


Figure 1. Testing activity by age groups (May 2017 - April 2018)

Conclusions/Next steps

One-year data of Test & Treat Project in Tanzania demonstrate the potential of TCs to increase the overall testing coverage in a short time frame and preferentially include male clients. Linkage to care remained a challenge. Viral suppression was achieved in majority of clients on treatment. Determinants that underlie these initial results are being studied with the aim to develop a sustainable Tanzanian blueprint for the UNAIDS 90-90-90 goals.

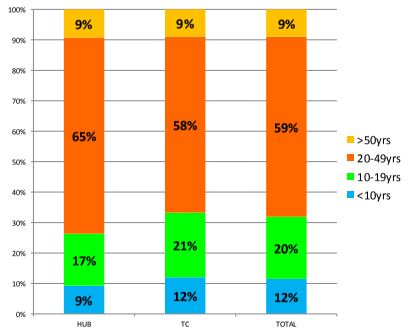


Figure 2. Age groups by site of testing
(May 2017- April 2018)

Test & Treat HIV Project • Huduma kwa Wote

We thank the people living with HIV who have participated in this research. Our fight against HIV and AIDS is indebted to people living with HIV both past and present.

GILEAD aighd St Stephen's AIDS TRUST MEDICI CON L'AFRICA CUAMM Doctors with Africa

Presented at the 22nd International AIDS Conference – Amsterdam, the Netherlands

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Transdisciplinary Systems Map of Causes Leading to HIV Drug Resistance

POSTER PRESENTATION

Conference
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Presentation date
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Authors
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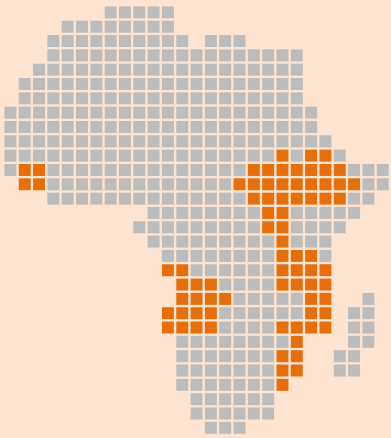
Focus country
Multi-Country



The poster starts assessing that HIV Drug Resistance (HIVDR) is a Wicked Problem: for this reason it requires a transdisciplinary approach. The study aimed to create an overview of all factors contributing to HIVDR and how they are interrelated and to create the first transdisciplinary systems map of causes leading to HIVDR.

The poster shows a Preliminary Systems Map of Causes Leading to HIVDR; 32 drivers of HIVDR and 130 connections have been identified from interviews and literature review.

In particular, the core of the systems map describes sufficient suppression of viral load as a combination of sufficient drug levels and an efficient drug combination. Each of those drivers is influenced by other factors related to access to treatment, adherence and the healthcare system. HIVDR drivers directly associated with the core are mainly pharmaceutical, biological, healthcare system-related and adherence-related, whereas preliminary results suggest that local experts indicate different drivers to be the core of HIVDR such as poverty, gender inequality, education and stigma.

Transdisciplinary Systems Map of Causes Leading to HIV Drug Resistance

A Kiekens[1], JS Lushaba[2], MR Jordan[3,4], JC Louw[5], AM Vandamme[1,6]

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Hypothesis: HIV Drug Resistance (HIVDR) is a Wicked Problem

- **Wicked problem**: no single definition, more than one explanation, no model solution, causes have roots in different fields of science and every wicked problem is a symptom of another problem (Rittel et al. 1973).
- Wicked problems require a **transdisciplinary approach** (Figure 1).

Figure 1: Schematic overview of the differences between disciplinarity, multidisciplinarity, interdisciplinarity and transdisciplinarity.

- **Several fields are crucial in the quest to prevent HIVDR**: biology (molecular basis of HIVDR), pharmaceutics (drug related), psychology (adherence and stigmatization), etc.
- We aimed to create an overview of all factors contributing to HIVDR and how they are interrelated and to create **the first transdisciplinary systems map of causes leading to HIVDR.**

Methods

- Combination of **literature review and semi-structured interviews** (Vandenbroeck et al. 2007) with international and local experts from different fields (currently N=10) (Table 1).
- Identification of drivers of **HIVDR** and links between drivers.
- **Mapping** of drivers of HIVDR and their connections using the KUMU software (e.g. for obesity see Vandenbroeck et al. 2007).
- Expert review.

Disciplines of International Experts	Progress Code	Disciplines of Local Experts	Progress Code
Epidemiology	A	Induna (community head)	B
Virology	A	Traditional healer	B
Bioinformatics	A	Healthcare worker	B
Medicine	A	Villager	B
Public Health	A	Nurse	B
Pharmacy	A	High school teacher	B
Psychology	A	Religious Leader	B
Anthropology	A	People living with HIV	C
Visual Methodology	A	Local hospital technician	C
NGO representative	A		
Sociology	C		
Philosophy	C		
Economy	C		

Table 1: overview of interviewees by discipline. Progress codes: A) experts were interviewed and data are included in the results; B) experts were interviewed, but data are not included in the results, C) experts to be interviewed.

Results: Preliminary Systems Map of Causes Leading to HIVDR

- **32 drivers** of HIVDR and **130 connections** between drivers were identified.
- Preliminary mapping reveals how some HIVDR drivers influence each other and suggests that projects aimed at a specific driver may have a positive or negative effect on other drivers. Further mapping is in progress.

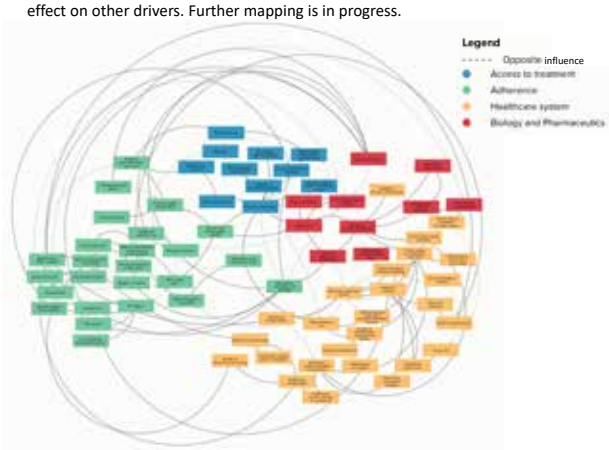

Figure 2: Preliminary systems map of causes leading to HIVDR. The 32 drivers of HIVDR and the 130 connections identified from interviews and literature review are displayed in the form of a systems map. Elements are colored according to their category: access to treatment, adherence, biology and pharmacy, and healthcare system

Results: continued

- Drivers are divided into **four categories**: 1) access to treatment, 2) adherence to treatment, 3) biology and pharmaceutics and 4) healthcare system, as in figure 2. The strong interconnection between these four categories indicates that when one category is approached, its link to the others should be kept in mind.

Discussion: Core Map

Figure 3: Systems map from figure 1 with the core highlighted.

- The core of the systems map describes **sufficient suppression of viral load** as a combination of **sufficient drug levels** and an **efficient drug combination** (Figure 3). Each of those drivers is influenced by other factors related to access to treatment, adherence and the healthcare system.
- HIVDR drivers directly associated with the core are mainly **pharmaceutical, biological, healthcare system-related and adherence-related,** whereas preliminary results suggest that local experts indicate different drivers to be the core of HIVDR such as **poverty, gender inequality, education and stigma**.

Conclusions

- HIVDR is a **wicked problem** with various interconnected drivers which stem from different disciplines. A shared, **transdisciplinary**, approach to preventing HIVDR should be developed (Hadorn et al. 2008).
- Wicked problems cannot be solved by one single solution. A **continuous collaboration between disciplines** is necessary to minimize emergence and transmission of drug resistant HIV. It is critical to **involve local experts** and **people living with HIV** in the identification of solutions in order to understand their perception of the problem and to align scientific research with it.
- We suggest the map can be used to identify the part(s) of the HIVDR problem with the **highest solution-potential** for further research.

Future

- People living with HIV and local experts from three different study sites will be interviewed at 2 sites in South Africa (one rural and one urban) and one urban site in Tanzania.
  A comparison of identified HIVDR drivers and connections will be made between international and local experts and between study sites.
  Development of a theoretical framework, which can be used to facilitate the identification of local HIVDR drivers and possible solutions for a specific site.

Preliminary Findings:

- Greater scientific attention is needed to characterize the impact of **stigma, poverty, gender inequality and education** on the emergence and transmission of drug resistant virus.

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Protocol and Operative Procedures for the implementation of a Decentralized HIV Service Delivery Model in North-Western Tanzania: Test & Treat Project in Shinyanga and Simiyu Regions

POSTER PRESENTATION

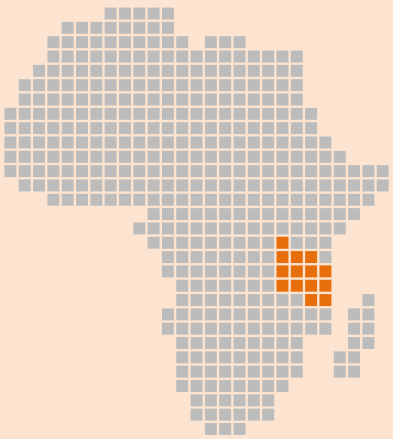
Conference
Tanzania Health Summit

Location
Dar Es Salaam – Tanzania

Presentation date
November 13th – 14th 2018

Authors
De Nardo P., Bortolani A., Rinke de Wit T., S Hermans S., E Gentilotti E., de Klerk J., Novello G., Pellizzer G., Sips I., Mfinanga S., Kwezi E., Somi E., Desderius B., Pozniak A.

Focus country
Tanzania



Background
The latest recommendation to "treat all diagnosed with HIV" challenges the capacity of health systems, especially in low and middle resource countries. Differentiated ART delivery models are promising approaches to simplify and adapt HIV services across the treatment cascade. Nonetheless, their efficacy and sustainability could be greatly influenced by social and cultural factors and need to be addressed through a setting-based approach. The Test & Treat Project in Shinyanga and Simiyu Regions, Tanzania aims to implement a model of HIV care encompassing both Universal Test and Treat and Differentiated Care.

The study is currently ongoing in four HIV clinics (CTC) located in Shinyanga and Simiyu Regions and the poster reports the protocol and preliminary data of a decentralized HIV services delivery model (SDM). The intervention is based on a client-centred approach through peer-to-peer support.
This intervention study assesses the effectiveness of a (hybrid) differentiated SDM in a resource-poor setting with low health care coverage. The Test & Treat club model seems to be a promising sustainable client-centred approach for PLHIV and for reducing unnecessary burdens to clients and the health facilities. The project approach is meant to serve as a proof of successful implementation of club model, which could be put in place and scaled up in other Tanzanian regions. Clinical, social and economic analyses will provide data on its feasibility and sustainability in the study sites, thus informing on the issues to be addressed while scaling up the model at the country level.

Protocol and Operative Procedures for the implementation of a Decentralized HIV Service Delivery Model in North-Western Tanzania: Test & Treat Project in Shinyanga and Simiyu Regions

P De Nardo[1], A Bortolani[1], T Rinke de Wit[2], S Hermans[2], E Gentilotti[1], J de Klerk[2], G Novello[1], G Pellizzer[1], I Sips[2], S Mfinanga[3], E Kwezi[1], G Somi[4], B Desderius[5], A Pozniak[6] and the Test & Treat Study Group

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5 Bugando Medical Centre, Mwanza, Tanzania

6 Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom

Introduction

The latest recommendation to "treat all diagnosed with HIV" challenges the capacity of health systems, especially in low- and middle- resource countries. Differentiated ART delivery models are promising approaches to simplify and adapt HIV services across the treatment cascade. Nonetheless, their efficacy and sustainability could be greatly influenced by social and cultural factors and need to be addressed through a setting-based approach.

We thank the people living with HIV who have participated in this research.

Methods

The Test & Treat Project in Shinyanga and Simiyu Regions, Tanzania aims to implement a model of HIV care encompassing both Universal Test and Treat and Differentiated Care. The study is currently ongoing in four HIV clinics (CTC) located in Shinyanga and Simiyu Regions. Here we report the protocol and preliminary data of a Decentralized HIV services delivery model (SDM). The intervention is based on a client-centred approach through peer-to-peer support. It consists of: 1. recruitment of three key persons, each with specific tasks: a clinician based at an HIV clinic, a club nurse, and a club responsible personnel (a community health worker or an "expert client"); 2. identification of clients eligible for the differentiated SDM according to protocol inclusion criteria for stable clients; 3. constitution of clubs of 25-30 people living with HIV based on geographical criteria as well as members' preferences; 4. scheduling of club meetings for drug refill, symptoms' screening, adherence counselling, health education sessions, etc. 5. scheduling of biannual clinician consultations and routine laboratory monitoring at CTC as well as annual HVL monitoring. The primary outcome is the proportion of HIV-infected people on ART maintaining virological suppression within the club model over the whole intervention period (measured at 12, 24, and 36 months). Secondary outcomes include qualitative and quantitative indicators, economic outcomes and social indicators.

Tab 1. Characteristics of the CLUBs established

	N. Clubs	N. Clients	Wards covered	CTC Average distance (Km)	Average club size
Shinyanga DC	18	325	7	16 (3-25)	18 (10-32)
Shinyanga MC	12	90	7	5 (3-7)	8 (4-13)
Total	30	415	14	11 (3-25)	13 (4-32)

Results

By October 2018, 29 clubs were established for a total of 14 wards covered within the districts of Shinyanga DC and Shinyanga Municipality (Tab 1). A total number of 415 clients (with 60% of the members being males and an average age of 40) were involved. The average club size is 13 clients. Four PLHIV were referred back to the CTC. Among these, only one was affected by an opportunistic infection (TB), while one patient was lost to follow up.

Discussion

This intervention study assesses the effectiveness of a (hybrid) differentiated SDM in a resource-poor setting with low health care coverage. The Test & Treat club model seems to be a promising sustainable client-centred approach for PLHIV and for reducing unnecessary burdens to clients and the health facilities.
The project approach is meant to serve as a proof of successful implementation of club model, which could be put in place and scaled up in other Tanzanian regions. Clinical, social and economic analyses will provide data on its feasibility and sustainability in the study sites, thus informing on the issues to be addressed while scaling up the model at the country level.

Our fight against HIV and AIDS is indebted to people living with HIV both past and present.

Universal coverage and equity

Assessing the feasibility of community health insurance in Uganda: A mixed-methods exploratory analysis

PAPER

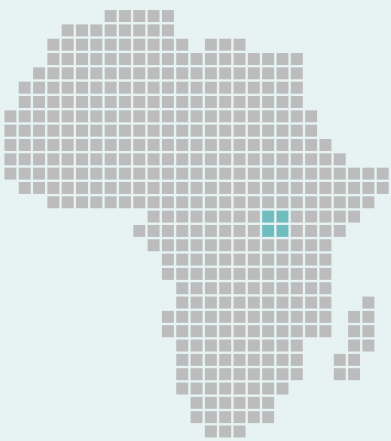
Authors
Biggeri M., Nannini M., Putoto G.

Published in
Social Science & Medicine, January 2018

Link
https://doi.org/10.1016/j.socscimed.2018.01.027

Topic
Universal coverage and equity

Focus country
Uganda



This paper is not available as open access, which is why only an abstract is posted. If you would like to read the entire paper, please go to the web page given and follow the instructions.

Abstract

Community health insurance (CHI) is an innovative tool for providing financial protection and facilitating access to health services for poor rural populations in middle- and low-income countries.

Within the framework of the different types of community prepayment schemes that can be implemented in limited-resource settings, CUAMM conducted a feasibility study in the rural district of Oyam, Uganda, from October to December 2016 in order to assess the practicality of implementing a CHI scheme there.

We surveyed 180 households to investigate the key factors impacting the community's access to health services. In addition to demographic and socio-economic parameters, we analyzed morbidity statistics, people's behavior in the event of illness and maternity, the methods they used to cover health care expenses, their degree of ability and willingness to take part in a CHI scheme and the pre-existence in the area of mutual aid groups. We also carried out 40 interviews with key technical and political authorities from the district to explore the role that community leaders might play in implementing such a scheme.

Through our analysis of the data collected we were able to verify the presence of key feasibility factors for launching a micro-insurance scheme in the area. Health care seemed to be quite important for the community, which was also well aware of the heavy cost of accessing it. Its members found the quality of the services provided by local health facilities to be acceptable, and trusted the health workers providing them.

Our study, therefore, demonstrated how a well-designed micro-insurance scheme could serve as a viable tool for expanding access to health care and offering financial protection to local communities such as the one in Oyam.

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Assessing the feasibility of community health insurance in Uganda: A mixed-methods exploratory analysis

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Keywords:
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Feasibility study
Health policy
Mixed-methods
Community health financing
Community health
Health economics

ABSTRACT

Community health insurance (CHI) aims to provide financial protection and facilitate health care access among poor rural populations. Given common operational challenges that hamper the full development of the scheme, there is need to undertake systematic feasibility studies. These are scarce in the literature and usually they do not provide a comprehensive analysis of the local context.

The present research intends to adopt a mixed–methods approach to assess ex-ante the feasibility of CHI. In particular, eight preconditions are proposed to inform the viability of introducing the micro insurance. A case study located in rural northern Uganda is presented to test the effectiveness of the mixed–methods procedure for the feasibility purpose. A household survey covering 180 households, 8 structured focus group discussions, and 40 key informant interviews were performed between October and December 2016 in order to provide a complete and integrated analysis of the feasibility preconditions. Through the data collected at the household level, the population health seeking behaviours and the potential insurance design were examined; econometric analyses were carried out to investigate the perception of health as a priority need and the willingness to pay for the scheme. The latter component, in particular, was analysed through a contingent valuation method.

The results validated the relevant feasibility preconditions. Econometric estimates demonstrated that awareness of catastrophic health expenditures and the distance to the hospital play a critical influence on household priorities and willingness to pay. Willingness is also significantly affected by socio–economic status and basic knowledge of insurance principles. Overall, the mixed-methods investigation showed that a comprehensive feasibility analysis can shape a viable CHI model to be implemented in the local context.

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Doctors with camper vans (CUAMM): itinerant primary healthcare service for migrant farm workers in the Foggia (Apulia) area

POSTER PRESENTATION

Original title
Medici col camper (Cuamm): servizio itinerante di assistenza sanitaria di base ai braccianti agricoli del foggiano

Conference
XV Congresso della Società Italiana di Medicina delle Migrazioni

Location
Catania, Italy

Presentation date
April 18th – 21st, 2018

Authors
Cavagna C., Raho L., Schiavone M., Marotta C., Volpe A., Zacchè I., Cotugno S., Di Gennaro F., Laforgia R., Pellizzer G., Putoto G.

Focus country
Italy

In October 2015, a Bari-based group of Doctors with Africa CUAMM volunteers set up and began providing an itinerant primary healthcare service to migrant farm workers living in four makeshift encampments (known locally as "ghettoes") in Foggia, in Italy's southern Apulia region.
Our poster presents data on the activities carried out in more than two years of service, including indications as to the trust of the beneficiaries (percentage of return visits; average number of daily visits). The overall health picture of the farm worker population suggests that while providing the latter with such a targeted service is of critical importance, it needs to be paired with further initiatives to protect both them and their families.

MEDICI COL CAMPER (CUAMM): SERVIZIO ITINERANTE DI ASSISTENZA SANITARIA DI BASE AI BRACCIANTI AGRICOLI DEL FOGGIANO

AUTORI

Cavagna C.[1], Raho L.[1], Schiavone M.[1], Marotta C.[1], Volpe A.[1], Zacchè I.[1], Cotugno S.[1], Di Gennaro F.[1], Laforgia R.[1], Pellizzer G.[1], Putoto G.[1]

1. Medici con l'Africa Cuamm

INTRODUZIONE

A partire da ottobre 2015, un gruppo di volontari dell'ONG Medici con l'Africa CUAMM - gruppo Bari, in collaborazione con la ONLUS Prof Nicola Damiani ha organizzato e offerto un servizio itinerante di assistenza sanitaria di base presso 4 insediamenti (Ghetti) di migranti braccianti agricoli presenti nel foggiano (Ghetto Ghana - Località Tre Titoli - Cerignola); Ghetto Bulgari (Borgomezzanone - Manfredonia); Ghetto Pista (Borgomezzanone - Manfredonia); Casa Sankara-Arena (San Severo).

AZIONE

Il servizio viene svolto ogni domenica, a rotazione tra i 4 Ghetti, da un massimo di 6 operatori (2 medici, 1 infermiere, 3 volontari di diversa formazione, 1 driver) attraverso un camper adibito ad ambulatorio mobile. La comunità viene avvisata con anticipo settimanale grazie alla collaborazione di altre associazioni presenti in loco e con i referenti dei Ghetti che si occupano della divulgazione interna agli stessi, mediante volantini e passaparola.

Nel giorno di attività, arrivati al Ghetto ci si posiziona in un punto preventivamente concordato tale da facilitarne l'accesso da parte di tutti. L'attività ambulatoriale inizia intorno alle ore 12 circa. All'esterno del camper, viene organizzato un *triage* per rendere l'accesso ordinato e con priorità di visita. Sul camper rimane un medico, un infermiere e un volontario addetto alla registrazione della visita. L'ambulatorio rimane aperto a fino al tramonto, per una media di 5 h/die. Sono stati analizzati i dati descrittivi degli accessi registrati da ottobre 2015 a gennaio 2018.

RISULTATI

Nei 28 mesi di attività svolti, sono state effettuate in totale 79 giornate di servizio per un totale di 3.150 accessi (media 40 accessi/die). Di questi, il 60% era una prima visita, mentre il 40% era un accesso ripetuto. Il numero totale di pazienti visitati è stato di 1.890 (81% M). La fascia d'età maggiormente rappresentata è stata quella dei 15-30 anni (78,7%). Il 34% dei pazienti ha dichiarato di avere un documento di riconoscimento valido. I principali motivi di accesso documentati sono riferibili alle seguenti categorie: 46% sintomatologia osteo-muscuscolare e/o da affaticamento; 18,8% odontoiatrico; 10,2% sintomi respiratori/influenzali; 8,1% dermatologico; 3,9% ostetrico/ginecologico; 3,9% trauma; 3,6% cardiovascolare; 2,4% sintomi oftalmici; 1,2%dimetabolici; 0,6% psicologici. L'88% degli accessi ha richiesto un intervento farmacologico; le classi farmaceutiche maggiorante utilizzate sono state: Fans, Antibiotici, Gastroprotettori, Adiuvanti, Topici. Il 5% non ha richiesto alcun tipo di intervento, mentre il 7% ha richiesto un'assistenza complessa, quindi una presa in carico da parte del Sistema Sanitario Regionale.

CONCLUSIONI

L'attività sanitaria svolta presso i Ghetti ha dimostrato, dalla percentuale di accessi ripetuti e dal numero medio di visite/die, come le comunità destinatarie nutrano una buona fiducia nel servizio offerto. Il bisogno di salute emerso con maggiore frequenza è riferibile ad una sintomatologia correlabile alle specifiche attività di lavoro svolte, nonché alle condizioni abitative e igienico-sanitarie caratteristiche dei Ghetti stessi. In conclusione, dal profilo di salute emerso dalla nostra esperienza, si può evincere come una risposta sanitaria specifica per questa popolazione sia indispensabile, ma che da sola non sia sufficiente. Necessarie ed urgenti sono azioni intersettoriali coordinate volte alla tutela integrata dei braccianti agricoli e delle loro famiglie.

Questa pubblicazione è stata realizzata con il contributo della Agenzia Italiana per la Cooperazione allo Sviluppo. I contenuti di questa pubblicazione sono di esclusiva responsabilità di Medici con l'Africa Cuamm e non rappresentano necessariamente il punto di vista dell'Agenzia.

Network initiatives to help build a new culture of health in Italy's Veneto Region: the "Train of Health"

POSTER PRESENTATION

Original title
Iniziative di rete per diffondere una nuova cultura della salute in Regione Veneto: il Treno della Salute

Conference
51st Italian Conference SITI – Italian Society for Hygiene

Location
Riva del Garda, Italy

Presentation date
October 17th – 20th 2018

Authors
Bertoncello C., Bennici S. E., Fonzo M., Baldovin T., Russo F., Putoto G., Baldo V.

Focus country
Italy

Chronic-degenerative diseases are a leading cause of morbidity and mortality worldwide. Co-promoted by Doctors with Africa CUAMM and Railroad Workers with Africa, the "Train of Health" initiative offered free checkups in a "medical center" set up in a train traveling through the seven provinces of Italy's northern Veneto region.

The aim of the initiative was to identify and provide counseling on health risk factors such as smoking, hypertension, fasting hyperglycemia, hypercholesterolemia and excess weight. It spurred a good level of community engagement, with the participation of 838 individuals from all seven provinces including some who failed to take advantage of the services provided by the region's healthcare system and who were therefore at greater risk than others.

51 CONGRESSO NAZIONALE SItI RIVA DEL GARDA 17-20 OTTOBRE 2018

VENERDÌ 19 OTTOBRE 2018

DALLE 13:30 ALLE 14:30

PITCH SESSIONE 5

Promozione della Salute e Lotta al Tabagismo

Iniziative di rete per diffondere una nuova cultura della salute in Regione Veneto: il Treno della Salute

C. Bertoncello [1], S.E. Bennici [1], M. Fonzo [1], T. Baldovin [1], F. Russo [2], G. Putoto [3], V. Baldo [1]

[1]Unità di Igiene e Sanità Pubblica - DSCTV - Università di Padova

[2]Direzione Prevenzione sicurezza alimentare veterinaria - Regione Veneto - Venezia

[3]Programmazione e ricerca operativa - Medici con l'Africa CUAMM - Padova

INTRODUZIONE

Le malattie cronico-degenerative costituiscono la principale causa di mortalità e morbosità. L'iniziativa "Il treno della salute", promossa dai Medici con l'Africa – CUAMM, attuata grazie al coinvolgimento di Ferrovieri con l'Africa, la Direzione Prevenzione – Sicurezza Alimentare – Veterinaria del Veneto, ha offerto controlli sanitari gratuiti per la rilevazione dei fattori di rischio e counseling per migliorare la propria salute. Lo scopo dello studio è indagare le caratteristiche della popolazione che ha aderito, rispetto alla popolazione generale del Veneto, ed il ruolo dell'iniziativa nell'ambito degli interventi di promozione della salute.

MATERIALI E METODI

L'iniziativa si è snodata nelle stazioni delle sette province venete. I partecipanti comprendono chi transitava per la stazione e chi vi si è recato appositamente per partecipare. Sono stati valutati i fattori socio-demografici, di rischio (fumo, ipertensione, iperglicemia a digiuno, ipercolesterolemia, eccesso ponderale) e protettivi (adesione agli screening, consumo di frutta e verdura, attività fisica). I risultati ottenuti dall'elaborazione dei dati raccolti sono statti confrontati con i dati ISTAT e della Sorveglianza PASSI.

RISULTATI

Hanno partecipato 838 persone, provenienti da tutte le province. I partecipanti, rispetto alla popolazione del Veneto, presentano una maggiore percentuale del sesso maschile (54% vs 49%), di stranieri (17% vs 10%) e di disoccupati (7% vs 4%). Le classi d'età più rappresentate sono quelle tra i 50 e i 69 anni, seguite da quella tra i 20 e i 29. Sei partecipanti su 10 possiedono uno o due fattori di rischio, il 13,6% 3 e l'1,5% 4. Si conferma un rischio maggiore nel genere maschile, a bassi livelli di istruzione e che aumenta con l'età. Rispetto ai dati PASSI, a eccezione dell'abitudine al fumo, i partecipanti presentano una maggiore prevalenza di fattori di rischio, mentre, per l'aderenza agli screening, per quanto la percentuale sia comunque elevata a conferma dell'efficacia degli interventi nel Veneto, si attesta ad un valore inferiore rispetto ai dati della popolazione generale. La maggioranza (60%) ha dichiarato di mangiare una o due porzioni di frutta e verdura al giorno e un consumo più consistente è associato al sesso femminile, all'età superiore a 50, alla nazionalità italiana e al non essere disoccupati.

CONCLUSIONI

L'iniziativa ha registrato una buona adesione, i soggetti che si sono sottoposti allo screening costituiscono uno spaccato a rischio: l'iniziativa ha intercettato delle persone che sfuggono in parte alla maglia dei servizi, risulta quindi utile e complementare per raggiungere in futuro più elevati livelli di salute nella popolazione.

Nutrition

Quality of care for children with acute malnutrition at health center level in Uganda: a cross sectional study in West Nile region during the refugee crisis

PAPER

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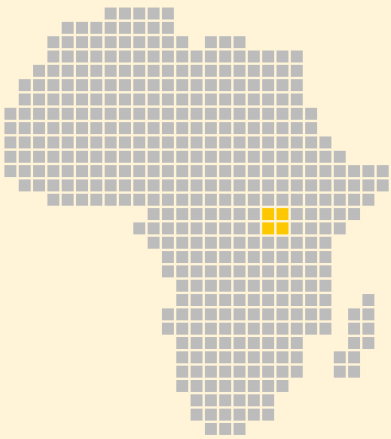

Abstract

Uganda's Arua District is home to some of the country's largest refugee camps. The prevalence of moderate and severe acute malnutrition in children residing there is higher than the national estimates (10.4% and 5.6%, respectively, versus 3.6% and 1.3%).

This study assessed the quality of care provided in six health facilities in the district to acutely malnourished children. The overall scores were mediocre, revealing a number of gaps including a lack of adequately-skilled personnel, case mismanagement, the unavailability of basic supplies including therapeutic foods for children, and the absence of consolidated links with local communities.

Our findings suggest that the quality of care provided by the district's health centers to malnourished children falls well below the recommended standards. It is critical, therefore, to find effective ways to improve their adherence to national guidelines and ensure the provision of therapeutic foods, ongoing service monitoring and the creation of more robust links with communities by way of health worker activities in villages.

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RESEARCH ARTICLE Open Access

Quality of care for children with acute malnutrition at health center level in Uganda: a cross sectional study in West Nile region during the refugee crisis

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Abstract

Background: Arua district, in Uganda, hosts some of the largest refugee camps in the country. The estimated prevalence of moderate and severe acute malnutrition in children is higher than the national estimates (10.4 and 5.6% respectively, compared to 3.6 and 1.3%). This study aimed at assessing the quality of care provided to children with acute malnutrition at out-patient level in such a setting.

Methods: Six facilities with the highest number of children with malnutrition were selected. The main tool used was the National Nutrition Service Delivery Assessment Tool, assessing 10 key areas of service delivery and assigned a score as either poor, fair, good or excellent. Health outcomes, quality of case management and data quality were assessed from the health management information system and from the official nutrition registers.

Results: All facilities except two scored either poor or fair under all the 10 assessment areas. Overall, 33/60 (55%) areas scored as poor, 25/60 (41%) as fair, 2/60 (3.3%) as good, and none as excellent. Main gaps identified included: lack of trained staff; disorganised patient flow; poor case management; stock out of essential supplies including ready-to-use therapeutic foods; weak community linkage. A sample coverage of 45.4% (1020/2248) of total children admitted in the district during the 2016 financial year were included. The overall mean cure rate was 52.9% while the default rate was 38.3%. There was great heterogeneity across health facilities in health outcomes, quality of case management, and data quality.

Conclusion: This study suggests that quality of care provided to children with malnutrition at health center level is substandard with unacceptable low cure rates. It is essential to identify effective approaches to enhance adherence to national guidelines, provision of essential nutritional commodities, regular monitoring of services and better linkage with the community through village health teams.

Keywords: Acute malnutrition, Children under 5 years, Quality of care, Quality assessment, Health center

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Background

Under-nutrition is a major cause of morbidity in children under 5 years [1]. The most recent estimates indicate that 52 million children under 5 years are diagnosed with wasting and 17 million with severe wasting and of these, 26.9% occur in Sub-Saharan Africa [1].

In Uganda, under-nutrition is considered a condition of public health importance [2]. National estimates report that 3.6% children suffer from moderate acute malnutrition (MAM) while 1.3% have severe acute malnutrition (SAM) [3]. However, this prevalence is heterogeneous across regions. For instance, the West Nile region, currently considered as a humanitarian setting and hosting refuges from South Sudan and Congo [4, 5] has the highest reported prevalence of MAM and SAM in the country at 10.4 and 5.6% respectively [3]. This is far above the target identified by the World Health Assembly which adopted the goal of reducing and maintaining the prevalence of wasting in children to under 5% by 2025 [6, 7].

Uganda is committed to reducing malnutrition and has identified this as a key part of its strategy for becoming a middle-income country by 2040 [8]. Actions to address malnutrition were included in the National Development Plan 2015/2016–2019/20 [9] and in the Uganda Nutrition Action Plan 2011–2016 for multi-sectoral support [10]. The Ministry of Health (MoH) developed the Integrated Management of Acute Malnutrition (IMAM) guidelines in 2006 and updated them in 2011 [11] and 2016 [2], in line with the WHO recommendations. The guidelines provide details for the management of children with both MAM and SAM at health facility level and include recommendations for screening and follow up at community level. Support has been provided from both international and local stakeholders especially the procurement and distribution of therapeutic foods and basic nutritional equipment [10, 12].

However, several studies have shown that adopting guidelines, providing training and basic equipment per se do not actually ensure that care is delivered according to set standards [13–17]. Assessments of the quality of nutritional services in other settings have highlighted poor adherence to guidelines leading to substandard health outcomes [14, 15, 18]. Therefore identifying areas of substandard quality of care is an important step towards improvement of health services [18–23]. In Uganda there is limited published literature on the performance of health facilities offering nutritional services, especially in a refuge setting. The aim of this study was to carry out an assessment of the quality of care provided to children admitted with acute malnutrition at out-patient therapeutic care (OTC) level in Arua district, West Nile region.

Methods

Study design, population and setting

This was a cross sectional study and is reported according to the STROBE guidelines. It was conducted between July and August 2016 in Arua district. According to the 2014 census, the estimated population in the district is 808,745 residents, [24]. By May 2017, the district was hosting approximately 174,396 refugees mainly from South Sudan and DR Congo [4]. For this assessment, six health facilities were selected out of the 55 government owned facilities based on the following criteria; those providing nutrition services, those with the highest reported number of malnourished children according to the Health Management and Information System (HMIS) data for the financial year 2016 (July 2015 to June 2016) [25] and whose staff agreed to participate. Exclusion criteria included difficult to access facilities and those without a staff assigned to be responsible for nutrition service delivery.

Data collection tools, procedures and variables

Nutrition service delivery

The Nutrition Service Delivery Assessment (NSDA) was the main tool used for this evaluation. The tool was developed by the Uganda MoH with support from external partners as the official national instrument for assessing performance of nutritional services [26]. It assesses 10 key capacity areas of nutrition service relevant at out-patient level, including: general information on service implementation, adequate human resources, provision of nutritional services, community linkage, quality improvement activities, materials and supplies, nutrition unit requirements, store management, logistics management for commodities, monitoring and evaluation. Data sources include: direct observation, documents review, interviews with health staff, village health teams (VHTs) and mothers of children diagnosed with malnutrition. For each chapter, using strict criteria specified in the tool (similar to checklists), a final judgment on the quality of the services was made and a final score assigned as one of four pre-defined categories: poor, fair, good and excellent. The tool also guides the identification of specific gaps in service delivery in each of the capacity areas.

The study team involved in the NSDA assessment included a senior paediatrician, a nutritionist and a public health expert, all experienced in the National IMAM guidelines [2] and in the use of the NSDA tool [26].

Health outcomes

Health outcomes were extracted from the HMIS by a national HMIS focal person for the review period (financial year 2016), according to six categories based on the national definitions in the IMAM guidelines [2]: 1) Cured: attaining a weight-for-height ≥ − 2 standard deviation (SD) from the mean based on the WHO 2006 standards or

mid upper circumference (MUAC) of ≥12.5 cm; 2) Non-responders: not reaching discharge criteria after three months or four months for the HIV/TB patients; 3) Defaulters: absent for 2 consecutive follow up visits; 4) Transferred to in-patient care (ITC): condition has deteriorated and requires in-patient care or not responding to treatment; 5) Transferred to to another out-patient care facility (OTC): patient transferred to other nearby OTCs or as requested by caregiver; and 6) Died: patient died while in the program.

Quality of case management and quality of data

Quality of case management and quality of data were assessed for each child enrolled in the program during the 2016 financial year using the Integrated Nutrition Register (INR) as a source of data. The INR is the official register at the health facility level where all information on malnourished children is recorded. Data extraction was conducted by a team of six data collectors, trained for this purpose, and directly supervised by a nutritionist. Data collection tools were pre-defined and pilot tested, and standard operating procedures (SOP) were developed to standardise the data extraction process. Quality of case management was assessed using the national guidelines as reference for standards [2] and using five pre-defined process outcomes:1) Correct diagnosis: correct assignment of the category of malnutrition based on weight-for-height Z-score or MUAC as follows: MAM if weight-for-height Z-score > − 3 and < − 2 standard deviation or MUAC (6 to 59 months) > 11.5 and < 12.5 cm and no bilateral pitting oedema; and SAM if weight-for-height Z-score < − 3 Standard deviation or MUAC (6 to 59 months) < 11.5 cm, bilateral pitting oedema, no medical complications and passes appetite test; 2) Correct treatment: correct treatment of cases with SAM such as: 10% glucose/sugar for hypoglycaemia at triage, Amoxicillin for bacterial infections on first day, Measles vaccination on admission (if > 9 months and not yet received), Vitamin A capsule given once at discharge, Iron and folic acid prescribed in presence of anaemia, Mebendazole/Albendazole for helminthic infections on second visit and Ready to Use Therapeutic Foods (RUFT) called Plumpy nut, as main malnutrition prescription; 3) Correct evaluation of HIV: HIV test performed on all patients following the national testing algorithm [27]; 4) Correct counselling of care givers/patients on key messages: delivery of counselling in the following area, as for the national guideline [2]: nutrition, RUFT administration, hygiene, HIV; and 5) Correct exit health outcome assigned: correct assignment of the exit criteria as for the national guideline [2] criteria, as follows: cured, non-respondent, defaulted, transfer to in-patient care or out-patient care and died.

Data quality was assessed using the following two pre-defined indicators: 1) data completeness defined for each single case as "complete" if in information on the following 15 key required fields were filled in: date, patient name, type of nutritional management, nutritional status at enrolment, HIV status at enrolment, anti-retroviral therapy services at enrolment, visit date, oedema, weight, height/length, MUAC colour, Z-score, therapeutic feeds, target exit criteria, exit outcome; and 2) internal consistency defined for each single case as "consistent" if i) the height of the child was consistent over time (ie not decreasing) and ii) the date of the visits was consistent over time (ie progressive dates in the register).

Data management

Data was collected and double entered into pre-formatted excel spreadsheets and checked for consistency and accuracy by two supervisors before analysis. The distribution of the health facility categorical parameters was presented as frequencies with respective proportions. Health outcomes were assessed against the SPHERE standards [28]. Case management and data quality indicators were assessed against a predefined target of at least 80%. Cases with missing information on health outcomes and quality of case management were counted as incorrect. A two sided p-value of < 0.05 was considered as statistically significant.

Results

Characteristics of the health facilities

The selected population sample, from the six facilities, accounted for 45.4% (1020/2248) of total caseload of malnourished children treated in Arua district during this review period (Fig. 1).

Characteristics of the health facilities are reported in Table 1. Overall, the number of children treated in each facility varied (from 318 to 61) but this was not directly proportional to the estimated population coverage (number of children diagnosed per 1000 population coverage ranging from 2.8 to 32.8).

Four out of six facilities had two or less staff assigned to the nutrition unit, with only one facility having a clinical officer involved. Overall, only one staff (7.6%) had been trained in the IMAM guidelines.

Nutrition service delivery assessment

All facilities except two scored either poor or fair under all the 10 assessment areas of the NSAD tool (Table 2). Overall, 33/60 (55.0%) areas were scored as poor, 25/60 (41.7%) as fair, 2/60 (3.3%) as good, and none as excellent. In particular, the following two areas were scored as poor in all facilities: quality improvement activities and monitoring and evaluation (see Additional file 1). Figure 2 shows a summary the distribution of the NSDA scores.

Table 3 shows the specific gaps in quality of nutritional services identified with the NSDA. Key findings included: poor organisation of services at the nutrition

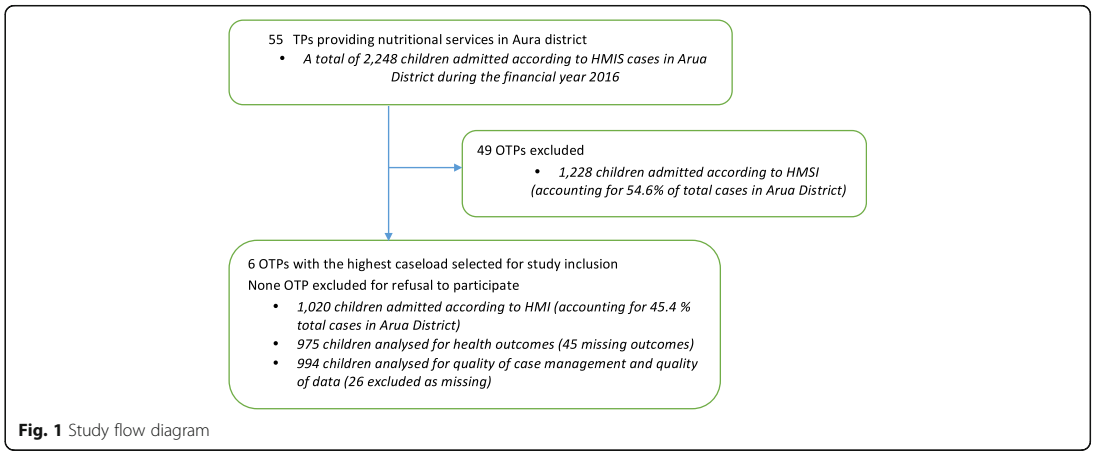

Fig. 1 Study flow diagram

service delivery point; poor case diagnosis and treatment; stock out of nutrition foods; weak community linkage mechanisms.

Of note, the assessment also identified some areas with good service delivery. All health facilities were using HMIS forms (INR and monthly quarterly reports), had basic nutrition equipment (weighing, length/height measuring scales and MUAC tapes), essential job aids (Z-score classification and counselling aids), VHTs were engaged and there was evidence of quarterly supervision conducted by district health team.

Health outcomes

The distribution of health outcomes is shown in Fig. 3. The cure rate and defaulter rate were the two health outcomes that were predominantly assigned (see Additional file 1). The overall cured rate in all the six health facilities was 52.9% while the overall defaulting rate was 38.2%. Significant heterogeneity was observed between these outcomes across health centers with the cure rate ranging from 31.2 to 74.4% and the defaulting rate ranging from 18.7 to 63.9%. During the entire study period, 37 children (4.0%) were transferred to ITC, 13 (1.3%) were classified as non-responders and only one participant (0.1%) was recorded to have died.

Quality of case management

Overall, 994 cases of malnourished children were identified in the INR and reviewed (see Additional file 1). Health facility performance on all case management process indicators was highly heterogeneous across facilities (Table 4). The rate of correct diagnosis ranged from 4.5 to 91.2%, correct treatment from 0 to 50.0%, correct HIV status assignment from 58.1 to 91.2%, correct counselling from 11.2 to 99.3% and correct exit outcome from 0 to 75.9%. The overall average rates were as follows: correct diagnosis at 34.6%; correct treatment at 19.2%; correct counselling at 47.6%; correct evaluation of HIV at 73.5% and correct exit outcome at 16.7%. None of the overall estimates for process outcomes reached the pre-defined target of 80% with a statistically

Table 1 Key characteristics of the health facilities

Variable	Health facility						
	HC 1	HC 2	HC 3	HC 4	HC 5	HC 6	Totals
Health Center level[a]	IV	III	III	III	III	III	–
Estimated population coverage	32,000	3960	22,548	13,779	2500	21,662	96,449
Children diagnosed with acute malnutrition[b]	318	292	116	151	82	61	1020
Number of staff assigned to the nutritional unit	2	2	3	1	3	2	13
Nutritional staff qualification							
Clinical officer	1	0	0	0	0	0	1
Enrolled nurse/midwife	1	1	1	0	3	2	8
Nursing assistant	0	1	2	1	0	0	4
Staff trained in IMAM guideline	1	0	0	0	0	0	1

[a]Levels of primary health care in Uganda is tiered into health center I,II,III and IV
[b]HMIS data July 2015 – June 2016 (financial year)

Table 2 Performance of health facilities in the selected capacity areas

Capacity area	Health facility Score[a]					
	HC 1	HC 2	HC 3	HC 4	HC 5	HC 6
1. General information on service implementation	Fair	Good	Fair	Fair	Fair	Fair
2. Adequate human resources	Poor	Poor	Poor	Poor	Fair	Poor
3. Provision of nutritional services	Fair	Fair	Fair	Poor	Fair	Poor
4. Community Linkagetable	Fair	Fair	Fair	Poor	Poor	Good
5. Quality improvement activities	Poor	Poor	Poor	Poor	Poor	Poor
6. Materials and Supplies	Poor	Fair	Poor	Poor	Fair	Poor
7. Nutrition unit requirements	Fair	Fair	Poor	Fair	Fair	Poor
8. Store management	Poor	Fair	Fair	Poor	Fair	Fair
9. Logistics Management for commodities	Poor	Poor	Fair	Poor	Fair	Poor
10. Monitoring and evaluation	Poor	Poor	Poor	Poor	Poor	Poor

[a]Score performance categories according to the NSDA tool: poor; fair; good; excellent [26]

significant difference when compared to this threshold (chi p-value = 0.001).

Data quality

There was high heterogeneity across health centers in data quality. Data completeness ranged from 0 to 32.1% and data consistency ranged from 0 to 87.6% (Table 4). The overall mean completeness rate was 4.4% and consistency at 20.7% with both indicators far below the pre-defined threshold of 80% (chi p-value = 0.001).

Additional analysis

No clear correlation could be found between single indicators (NSDA scores, cured rate, process outcomes, quality of data) and the type of health center (level IV vs III), or the volume of work (number of children admitted). No clear internal correlation among different indicators could

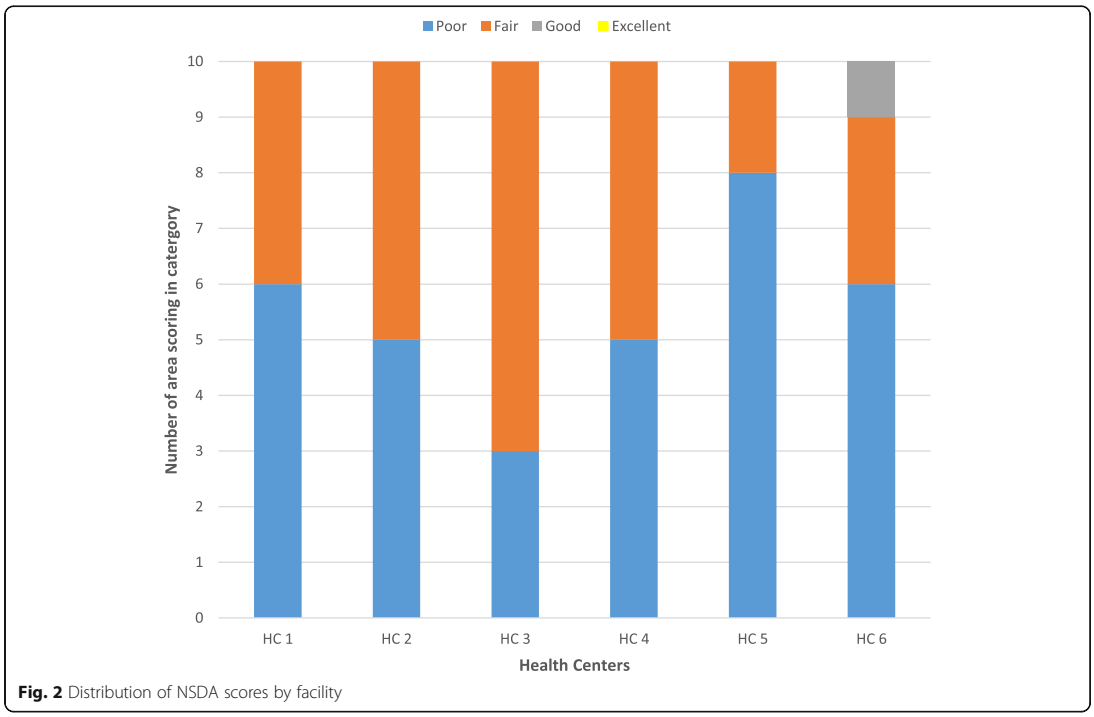

Fig. 2 Distribution of NSDA scores by facility

Table 3 Gaps in quality of nutritional services observed by capacity area

Capacity area	Observed issue
Organisation of services	Nutrition services delivered "under the tree"
	Working hours unclear
	Frequent service delays if rain
	No triage
	Chaotic organisation, no clear roles and responsibilities
	No transport for children sent In-patient Therapeutic Care (ITC)
	Working hours unclear
Case management	Triage not performed
	Mid Upper Aram Circumference (MUAC) not routinely done at all entry points (Out patients department -OPD, Tuberculosis and Anti retroviral therapy - TB/ART)
	Mis-classification SAM/MAM
	Z-score never used (only MUAC used)
	No history taking
	Comprehensive clinical examination as per the Integrated Management of Childhood Illnesses (IMCI) not performed
Treatment	Water with sugar not offered at admission
	10 key messages on RUTF not delivered
	Individual counselling never performed
	Amoxicillin, vitamine A, Iron and mebendazole not prescribed
	MAM and SAM usually treated the same
Integrated Management of childhood Illnesses (IMCI)	HIV status often indicated as unknown despite availability of testing kits
	TB rarely assessed
	Children at OPD not always assessed for nutritional status
	Children with malnutrition not assessed according to IMCI
	Staff working in out-patient care not trained in IMCI
	Old IMCI job aids in some facilities
Supplies	Stock out of RUTF observed in many facilities
	Lack of mean of transport to facilities
	Lack of timely request from facilities
Staffing	Lack of staffing with some facilities having no nutritional focal person appointed
	Lack of nutritional specific training
	Poor practices even among trained staff
	Village Health Teams (VHTs) usually not formally trained but doing the job at OTC in place of facility staff
Community linkage	VHTs screening reports not readily available
	Blank VHTs registers
	No effective means of communication between facilities and village health teams (VHTs)
	No incentives for the VHT
Quality improvement	Several supportive supervision activities are conducted on a quarterly basis, at facilities but only few are specific to nutrition

Abbreviations: *ART* Anti Retro-viral Therapy, *HIV* Human Immune-deficiency Virus, *IMCI* Integrated Management of Childhood Illness, *ITC* In-patient Therapeutic Care, *MAM* Moderate Acute Malnutrition, *MUAC* Mid-Upper Arm Circumference, *OPD* Out Patients Department, *OTC* Out-patient Therapeutic Care, *RUTF* Ready-to-Use Therapeutic Foods, *SAM* Severe Acute Malnutrition, *TB* Tuberculosis, *VHT* Village Health Teams

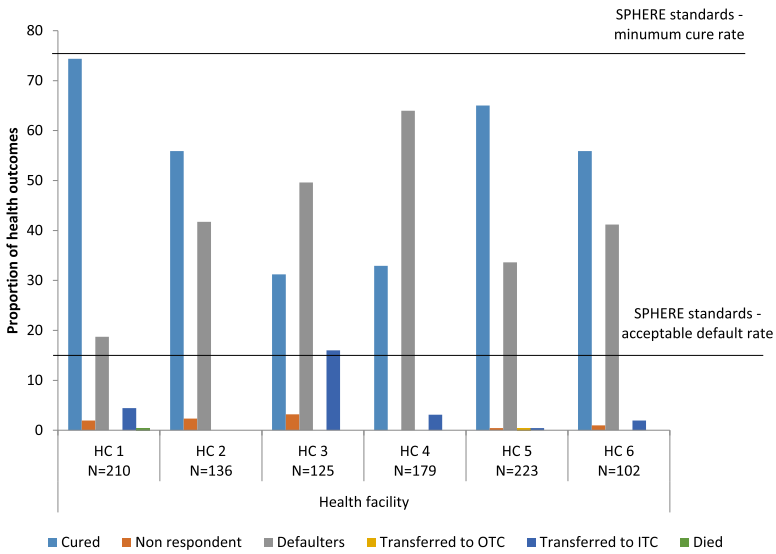

Fig. 3 Distribution of health outcomes

be found (performance of the different indicators did not seem to be directly linked to each other).

Discussion

This is the first study reporting on the performance of nutritional services for children in Arua district. The assessment shows that, even though some positive aspects were observed, there are substantial deficiencies in the quality of nutrition services at health center level in Arua district. Significant gaps were observed both by using the national tool for Nutrition Service Delivery Assessment (NSDA) and by reviewing key indicators of health outcomes, case management and data quality in the official records.

The observed health facility cure rate of 52.9% was far below the international SPHERE standards target set at above 75% [28], while the defaulting rate of 38.3%, was significantly higher than the standard's target set at below 15% (28). One of the possible reasons for this low cure rate may be the lack of adherence to guidelines for

Table 4 Case management and data quality

Variable	Health facility							
	HC 1 *N* = 194	HC 2 *N* = 137	HC 3[a] No data	HC 4 *N* = 301	HC 5 *N* = 228	HC 6 *N* = 134	Total *N* = 994	Chi *p*-value[#]
Correct process outcomes								
Diagnosis	30(15.5)	125(91.2)	–	88(29.2)	95(41.7)	6(4.5)	344(34.6)	0.001
IMAM treatment	0	0	–	151(50.0)	28(12.3)	12(9.0)	191(19.2)	0.001
Evaluation of HIV	158(81.4)	90(65.7)	–	175(58.1)	208(91.2)	100(74.6)	731(73.5)	0.001
Counselling of patients	39(20.1)	136(99.3)	–	172(57.1)	111(48.7)	15(11.2)	473(47.6)	0.001
Exit outcome assigned	19(9.8)	104(75.9)	–	31(10.3)	12(5.3)	0	166(16.7)	0.001
Data quality								
Data completeness	0	44(32.1)	–	0(0)	0(0)	0(0)	44(4.4)	0.001
Data consistency	0	120(87.6)	–	74(25.6)	11(4.8)	1(0.8)	206(20.7)	0.001

Data source: Integrated Nutrition Register
[a]Data not available in the integrated nutrition register
#*p*-value assessed against a pre-defined target of 80% achievement

case management as observed in this study. Important clinical practices such as triage, screening of all children for malnutrition, history taking, detailed examination, diagnosis of SAM and MAM, individual counselling, complementary treatment and assignment of exit outcomes were not being performed according to the IMAM guidelines [2]. Additionally, laboratory screening for HIV and TB was not routinely conducted, despite the availability of laboratory diagnostic kits. Such poor performance of quality of health service delivery has also been reported in other studies both in routine settings in Uganda [13, 15, 29, 30] and in refugee settings such as in Ethiopia [31–34].

Another key reason explaining the poor performance of case management, in addition to inadequate human resource, is the substantial lack of training of heath facility staff, both frequently observed challenges in low and middle income countries [35]. The impact of targeted training on both health workers performance and children outcomes is relatively well documented. For example, a systematic review examining the effectiveness of nutritional training of health workers showed a clear benefit in improving feeding frequency, energy intake, and dietary diversity of children [36].

Notably, almost all the assessed health facilities had basic nutritional equipment such as digital weighing scales, length/height measuring boards, MUAC tapes and essential job aids. However, the frequent stock out of RUTF, an essential nutrition management commodity, was a significant issue, a finding in line with two earlier studies conducted in other regions in Uganda [29, 30].

The observed challenges such as stock out of RUTF, poor organisation of services including irregular working hours and long waiting times and weak community linkages re-affirm some of the underlying factors explaining the very high defaulting rate observed [29]. The poor performance of VHTs especially regarding case-identification and referral of cases is an observation that deserves further scrutiny because this study was not designed to identify the causes of this occurrence. However, evidence from a systemic review on factors that influence performance of community health workers (CHWs) such as VHTs found that lack of supervision, lack of training and lack of financial incentives were the main barriers to achieving an acceptable performance from CHWs [37]. Minimizing such barriers would improve access to care and ultimately the achievement of better health outcomes. Evidence shows that barriers to access for service users may increase mortality, especially among children with SAM who actually requires urgent medical attention [38].

Poor data quality is another important but frequently reported problem in low income countries, including Uganda [39, 40]. Good quality data is the basis for evidence based decision making and two suggested approaches for improvement in such settings include better training on data quality assurance procedures and intensive supportive supervision [38–41].

As already documented, the influx of refugees into a community negatively affects the performance of health services in such settings [31, 32]. However it is also true that poor performance has been reported in settings experiencing no refugee crisis [29, 30], indicating that refugee circumstances is not the sole explanation for such a performance. This study did not aim at comparing the performance of nutritional service before and during the most recent refugee crisis In Arua, but rather at collecting baseline data for service delivery evaluation. Future studies should aim at monitoring health system performance over time while exploring the influence of different factors on key outcomes.

Limitations of this study included the relatively small sample size in terms of health facilities, however, the study sample population captured over 45% of cases of children admitted to nutritional services in Arua district. Even though most of the assessment was conducted by direct evaluation using the NSDA tool [26], health outcomes and case management were assessed using recorded data, which, by nature, are exposed to a risk of recall bias. We tried to minimised this bias in different ways such as choosing the official documents as data sources with the expectation that all information of each child with malnutrition was recorded, using trained data collectors, using pre-defined data collection variables, developing standard operating procedures and transparency during reporting of study findings.

Recommendations for policy makers derived from this study may include: hiring and training of health facility staff to fill the human resource gap; strengthening supportive supervision to improve performance at different levels (case management, timely requests of RUTF, data quality, community linkages); and conducting regular NSDA assessments to monitor progress over time. More studies are needed to identifying effective approaches to enhance adherence to national guidelines and ultimately improve health outcomes of children.

Conclusion

This assessment revealed that quality of care and health outcomes of children with malnutrition in Arua district are far below the internationally acceptable SPHERE standards. Significant deficiencies were observed under organization of service, case management, procurement, community linkage and data quality. In the future both researchers and policy makers should aim at identifying effective approaches to increase quality of care for children with malnutrition in Arua district and similar settings.

Additional file

Additional file 1: Quantitative dataset. (XLSX 57 kb)

Abbreviations

ART: Anti Retroviral Therapy; DHT: District Health Team; HC: Health Center; HIV: Human Immuno-defiency Virus; HMIS: Health Management and Information System; IMAM: Integrated Management of Acute Malnutrition; IMCI: Integrated Management of Childhood Illness; INR: Integrated Nutrition Register; ITC: In-patient Therapeutic Care; MAM: Moderate Acute Malnutrition; MoH: Ministry of Health; MUAC: Mid Upper Arm Circumference; NSDA: Nutrition Service Delivery Assessment; OPD: Out Patient Department; OTC: Out-patient Therapeutic Care; RUTF: Reay to Use Therapeutic Foods; SAM: Sever Acute Malnutrition; TB: Tuberculosis; UNICEF: United Nations International Emergency Fund; VHT: Village Health Team; WHO: World Health Organisation

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Availability of data and materials

The quantitative data generated or analysed during this study are included in this published article as its additional file. Notes from the qualitative data are available from the corresponding author on reasonable request.

Authors' contributions

ML and HW1 conceived the study idea, in collaboration with, RM, GP, GS, HW2 and PL. ML, HW1 and RM lead the design and acquisition of data, ML and HW1 conducted the analysis and interpreted the data. HW1 and ML lead the drafting of manuscript, all authors were involved during critical revision for important intellectual content. All authors read and approved for the final manuscript to be published and are accountable for all aspects of the work

Ethics approval and consent to participate

The study was approved by the Makerere University School of Public health ethical committee, Uganda National Council of Science and Technology (UNCST) and the ethical committee of the IRCCS Burlo Garofolo, Italy. All participants interviewed gave their informed consent to participate and for the information derived to be published. The HMIS extracted data was aggregated with no individual level data details obtained, all the analysis was therefore anonymous.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Chronic diseases

Frequency and pattern of gynecologic cancers from 2010 to 2014 in Beira, Mozambique

PAPER

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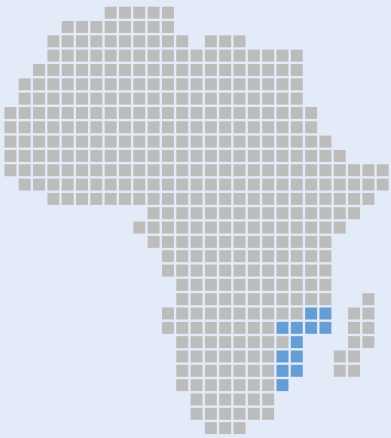

Abstract

Gynecologic cancers, especially those of the uterus and ovaries, represent a major health, social and economic burden worldwide, both in wealthier and in limited-resource countries. In middle- to low-income countries such as Mozambique, effective health policies for the prevention and care of such cancers have yet to be developed, and the data available is mostly incomplete and of poor quality.

The objective of this retrospective study was to trace the epidemiological profile of the cases of gynecologic cancer recorded from January 2010 through December 2014 in the Department of Pathology of the Beira Central Hospital in Mozambique.

43.4% of the anatomic pathology examinations performed on female patients in that time span were attributable to gynecologic cancers. The most widespread type was cervical cancer, which accounted for 86.7% of the total in 2013 and 93.3% in 2014. The high prevalence of this type of cancer, which is common in low-resource countries, points to both a lack of awareness among the population about the risk of developing the disease and the absence of primary and secondary preventive measures. Indeed, the high mortality rate from these diseases is linked both to people's inability to access prevention and screening services and to the lack of effective treatment strategies. It is essential, therefore, that gynecologic cancer awareness-raising, prevention and treatment policies be implemented to help tackle this increasingly critical problem even in limited-resource countries like Mozambique.

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Frequency and pattern of gynecologic cancers from 2010 to 2014 in Beira, Mozambique

Częstość występowania i profil nowotworów kobiecych narządów płciowych w latach 2010–2014 w mieście Beira w Mozambiku

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Abstract

Objective: Gynecologic cancers represent a large health, social and economic burden worldwide. In low-income countries, particularly in Mozambique, little data is available and no effective policies are implemented to fight these diseases. Our objective was to trace the epidemiological profile of gynecologic cancers from 2010 to 2014 in Beira, Mozambique. **Methods:** We retrospectively reviewed the registers of the Department of Pathology of Central Hospital of Beira to identify all cases of gynecologic malignancies recorded from January 2010 to December 2014. **Results:** Most of the diagnosed female cancers (43.4%) were gynecologic and, among these, cervical cancer was definitely the most commonly reported cancer every year, ranging from 86.7% in 2013 to 93.3% in 2014. **Conclusion:** As in many low-income countries, the access to screening programs for gynecologic cancer is not effective in Mozambique; therefore urgent preventive policies are crucial to address this emergent issue.

Keywords: gynecologic cancers, low-income countries, epidemiology, cervical cancer

Streszczenie

Cel: Nowotwory kobiecych narządów płciowych stanowią istotne obciążenie zdrowotne, społeczne i ekonomiczne na całym świecie. W krajach o niskich dochodach, w szczególności w Mozambiku, brak jest zarówno dostępnych danych, jak i skutecznych strategii walki z tymi chorobami. Celem badania było prześledzenie profilu epidemiologicznego nowotworów ginekologicznych w latach 2010–2014 w mieście Beira w Mozambiku. **Metoda:** Autorzy dokonali retrospektywnego przeglądu rejestrów medycznych Oddziału Patologii Szpitala Centralnego w Beirze w celu wyodrębnienia wszystkich przypadków nowotworów kobiecych narządów płciowych odnotowanych w okresie od stycznia 2010 do grudnia 2014 roku. **Wyniki:** W większości przypadków (43,4%) rozpoznane u kobiet nowotwory dotyczyły narządów rodnych, przy czym rak szyjki macicy był zdecydowanie najczęściej odnotowywanym nowotworem w każdym roku (od 86,7% w 2013 do 93,3% w 2014 roku). **Wniosek:** Podobnie jak w wielu krajach o niskich dochodach, również w Mozambiku dostęp do programów przesiewowych nowotworów narządów rodnych jest ograniczony – niezbędne jest pilne podjęcie działań prewencyjnych.

Słowa kluczowe: nowotwory kobiecych narządów płciowych, kraje o niskich dochodach, epidemiologia, rak szyjki macicy

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INTRODUCTION

Gynecologic cancers are a spectrum of malignancies affecting the cervix, vulva, ovaries, endometrium, vagina, and placenta, with a high rate of mortality worldwide, which varies significantly depending on the region, age and the stage of presentation.

Cervical cancer is the third most common cancer among women and a leading cause of mortality worldwide, with 265,653 deaths estimated in 2012[1]. Eighty-three percent of cases occur in the developing world, where cervical cancer accounts for 15% of female cancers, compared to just 3.6% in developed countries[2]. This large decline of cervical cancer incidence and mortality in high-income countries is largely credited to effective screening programs and the Pap test[3].

Vulvar neoplasia accounts for 4–5% of all malignant tumors of the female genital tract and it is estimated that more than 5,000 cases were diagnosed in the United States in 2015, with approximately 1,000 deaths[4]. In developing countries, such as Algeria and Zimbabwe, the incidence varies from 0.1 to 1.6 per 100,000 population, respectively[5]. It is usually diagnosed in older women, who often have lichen sclerosus et atrophicus or differentiated vulvar intraepithelial neoplasm but, unfortunately, the rate of diagnosed young women is on the rise due to persistent infection with HPV and HIV[6].

The term "ovarian cancer" summarizes a heterogenous group of malignant epithelial tumors and, despite advances in medicine, it remains the most fatal gynecologic malignancy[7,8]. Malignant ovarian germ cell tumors occur predominantly in girls, adolescents, and young women and are often unilateral tumors of early stage, although advanced-stage disease occurs in approximately 30% of patients[9]. Previous studies listed well known risk factors such as increasing age, family history of ovarian and breast cancer, nulliparity, and tobacco smoking[10]. Moreover, it has a strong association with breast and anal cancer and, recent studies showed the possible involvement of *BRCA2* gene mutation[11]. Subtypes of ovarian cancer can originate from the fallopian tube (high-grade serous carcinoma) or the sex cords (sex cord stromal tumors)[12,13]. Ovarian cancer incidence rates vary remarkably depending on geographic locations. Countries with the highest rates are those in Scandinavia, North America and Israel and the lowest rates were found in developing countries and Asia[14].

Endometrial carcinoma is the most common gynecologic malignancy in industrialized countries and the incidence is still rising[15]. Frequently, this cancer is diagnosed in older patients, with a higher incidence in urban rather than rural environment. Moreover, endometrial hyperplasia is frequently diagnosed in peri- and postmenopausal patients, identified due to abnormal uterine bleeding[16].

Vaginal cancer is less common, accounting for approximately 2% of all cancers of the female genital tract. It mostly affects women over 60 years, and only 10% to 15% of those under 50 years[17]. The most common types of vaginal cancer are squamous carcinoma (80% to 90%) and adenocarcinoma (4% to 10%), and recent evidence suggests the role of HPV infection[18].

Finally, gestational trophoblastic neoplasms usually occur in child-bearing age women, have high malignant and metastatic potential and can be fatal[19].

In high income countries, the survival of patients is improving due to prevention, early diagnosis and different treatment strategies, whereas most women with cancer in developing countries have advanced, untreatable disease and minimal access to anticancer therapies. Futhermore, in low-income countries, in most cases, there is no perception of the burden and the profile of these diseases. The aim of this study is to perform a retrospective analysis at the Department of Pathology of Beira Central Hospital (BCH), Mozambique, in order to trace the epidemiological profile of gynecologic cancers from 2010 to 2014.

MATERIAL AND METHODS

Setting and population

Beira is the second largest city of Mozambique with about 500,000 inhabitants, of which 17% are less than 5 years old. BCH is a 733-bed government tertiary referring and teaching hospital for the central region of the country (population of about 7 million) in Mozambique and the second hospital in the country[20].

Data collection

Data registers of BCH's Department of Pathology were retrospectively reviewed to identify all cases of gynecologic malignancies recorded from January 2010 to December 2014. Data extraction was performed by a trained external member (not involved in clinical activities or in the study design) using a piloted clinical report form in order to ensure consistent data collection regarding gynecologic diseases. Information based on the site of affliction, patient's age and histopathological diagnosis according to the International Federation of Gynecology and Obstetrics (FIGO) classification was collected.

Statistical analysis

Descriptive statistics were used to compare baseline characteristics of the study groups. The chi-square test was used for binary variables. A p-value <0.05 was considered statistically significant. All data were analyzed with SPSS 17.0 for Windows (IBM SPSS Statistics, IBM Corporation, Chicago, IL).

RESULTS

A total of 2,112 new histologically diagnosed cancer cases were registered at the Department of Pathology at the Central Hospital of Beira between January 2010 and December

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2014 (Tab. 1). Female cancers accounted for 56.3% and, among these, 517 (43.4%) were gynecologic cancers. The sites of involvement included the cervix (460 cases, 89%), vulva (30, 5.8%), ovary (9; 1.7%), endometrium (6; 1.2%) vagina (5; 1%) and placenta (7; 1.3%) (Tab. 2). Cervical cancer was definitely the most commonly reported cancer each year, ranging from 86.7% in 2013 to 93.3% in 2014. Age distribution is reported in Tab. 3. The average age of females with cervical cancer, the most representative group, was 43 ± 12.7 years, ranging from 20 to 85 years. The youngest group was represented by women with placental cancer with an average age of 29.6 ± 10.8 years (17–48 years) while the oldest one was that of endometrial cancer with an average age of 58.2 ± 18.1 (34–81 years). Only 92 histopathologically diagnosed cervical precancerous lesions were reported during 5 years (Tab. 4).

Year	Total cancer *N*	Male cancer *N* (%)	Female cancer *N* (%)	Gynecologic cancer *N* (%)*
2010	375	165 (44)	210 (56)	83 (22.1)**
2011	420	166 (39.5)	254 (60.5)****	106 (25.2)**
2012	438	185 (42.2)	253 (57.8)***	111 (25.3)**
2013	413	191 (46.2)	222 (53.8)	98 (23.7)**
2014	466	215 (46.1)	251 (53.9)	119 (25.5)**
Total	2112	922 (43.7)	1190 (56.3)	517 (24.4)**

* Percentage referred to the total cancer.
** $p < 0.01$ vs. total cancers.
*** $p < 0.05$ vs. male cancers.
**** $p < 0.1$ vs. male cancers.

Tab. 1. Distribution of cancers at Central Hospital of Beira in 2010–2014

Year	Total *N* (%)	Cervix *N* (%)	Vulva *N* (%)	Ovary *N* (%)	Endometrium *N* (%)	Vagina *N* (%)	Placenta *N* (%)
2010	83	74 (89.2)*	3 (3.6)	2 (2.4)	1 (1.2)	3 (3.6)	–
2011	106	92 (86.8)*	8 (7.6)	1 (0.9)	2 (1.9)	–	3 (2.8)
2012	111	98 (88.3)*	6 (5.4)	3 (2.7)	–	2 (1.8)	2 (1.8)
2013	98	85 (86.7)*	8 (8.2)	3 (3.1)	1 (1)	–	1 (1)
2014	119	111 (93.3)*	5 (4.2)	–	2 (1.7)	–	1 (0.8)
Total	517	460 (89)*	30 (5.8)	9 (1.7)	6 (1.2)	5 (1)	7 (1.3)

* $p < 0.01$ vs. total.

Tab. 2. Gynecologic cancer profile at Central Hospital of Beira in 2010–2014

Type	Number of cases	Mean age	Age range
Cervix	460	43 ± 12.7	20–85
Vulva	30	38.3 ± 10.2	21–65
Ovary	9	30.9 ± 13.2	13–61
Endometrium	6	58.2 ± 18.1	34–81
Vagina	5	50 ± 21.2	35–86
Placenta	7	29.6 ± 10.8	17–48
Total	517	42.5 ± 13	13–86

Tab. 3. Age distribution of gynecologic cancer at Central Hospital of Beira in 2010–2014

Year	Cases number	Mean age
2010	22	32 ± 7.2
2011	29	36.4 ± 9.9
2012	7	41.6 ± 11.3
2013	5	37.2 ± 6.6
2014	29	37.1 ± 6
Total	92	36 ± 8.3

Tab. 4. Precancerous cervical cancer lesions

CURR GYNECOL ONCOL 2017, 15 (3), p. 189–193 DOI: 10.15557/CGO.2017.0019

DISCUSSION

It is well known that gynecologic cancer, cervical cancer in particular, is very common in the developing countries with a high mortality rate[21]. The main reasons for this are the lack of prevention strategies, well-equipped diagnostic facilities and medical service as well as the lack of well-trained healthcare workers[22]. In BCH, gynecologic cancers represent over 40% of all female cancers and, among these, cervical tumors account for almost 90%. Our data are consistent with the World Health Organization (WHO), which estimates that one million-plus women worldwide live with cervical cancer and, many of them have no access to health services for prevention, curative treatment or palliative care[22]. The high prevalence of cervical cancer indicates the lack of awareness, especially among rural and poorer women, who are at an increased risk of invasive cervical cancer, because they often do not have access to crucial prevention, screening and treatment services. Moreover, from 2010 to 2014, the Department of Pathology recorded only 92 cases of precancerous lesions, rising concerns about the inequitable access to screening programs. Prevention is the strongest weapon against cervical cancer and the WHO declared vaccination and screening as an essential tool in the fight against this malignancy. It is crucial to develop effective strategies in order to prevent hundreds of unnecessary deaths. Safe and effective HPV vaccination is now available and has been adopted in many high-income countries, but only to a minimum in low income countries, such as Mozambique. Thus, preventive and vaccination campaigns need to be increased and improved in order to achieve the WHO goal of vaccinating over 30 million girls in more than 40 countries by 2020. Even though HPV vaccination reduces the risk of developing cervical cancer, regular screening remains essential. In fact, vaccination does not protect against all HPV types and, when vaccination coverage is low, non-vaccinated girls continue to be at risk.

Another important finding of our study is the diagnosis of ovarian cancer, which was low. In fact, the lack of early symptoms and high mortality rates in developing countries often lead to the lack of diagnosis. Considering the familial nature of this cancer, it will be interesting to conduct further and more adequate studies on the subject.

To the best of our knowledge, this is the first study in Mozambique focusing on gynecologic cancers. However, since it is a retrospective study in a developing country, several limitations reduce its possible impact: data are incomplete, it is not possible to calculate incidence and prevalence rates, clinical data are unavailable and, genetic and immunohistochemical relevant tests are not performed. Moreover, it is very likely that the number of diagnosed cancers is underestimated.

Despite these limitations, our findings showed a significant presence of cervical cancer in the years compared to other gynecologic tumors. Thus, considering the lack of health service for oncologic patients, it is assumed that there is a high incidence of mortality caused by this tumor both in the present and in the years to come.

Regardless of the strategies that local and national health policies will be able to implement, the *conditio sine qua non* is the force of health systems in order to guarantee access to health services. Finally, to improve and increase the impact of future interventions, an operational research approach should be implemented to win the challenges against cervical cancer and HPV infection.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the content of this publication and/or claim authorship rights to this publication.

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Successful management of a parasitic ischiopagus conjoined twins in a low-income setting

PAPER

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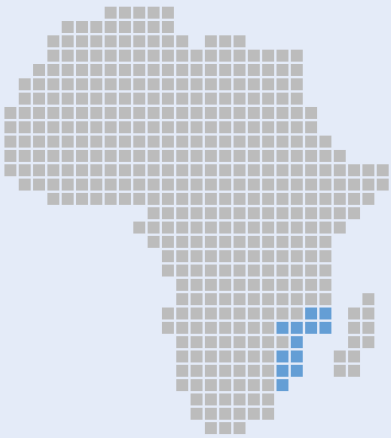

Abstract

A parasitic (or asymmetrical conjoined) twin is an embryonic anomaly that primarily affects males. It involves a rare twin malformation where tissue matter that should make up a second fetus grows within the body of the more normally-developed host twin. The solution to such cases is to surgically excise the components of the "parasitic twin" in order to ensure the most normal possible growth for the surviving one.

While the phenomenon has become increasingly rare in developed countries thanks to the possibility of prenatal diagnoses, it still arises – often with unfavorable outcomes – in limited-resource countries, due to both the absence of prenatal screening programs and the lack of means for managing such cases.

The case presented here is the first ever recorded in Mozambique, and one of the rare ones in sub-Saharan Africa to have a favorable outcome. A multidisciplinary team performed a successful surgical operation to remove two supernumerary lower limbs and seven months later, the surviving infant girl is developing normally.

We deem this experience a success based not only on the positive outcome of the surgical procedure, but also the fact that we were able to manage such a rare and complicated case in a setting where the possibility of prenatal diagnosis, specialists and adequate equipment were all unavailable.

Clinical Case Reports

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CASE REPORT

Successful management of a parasitic ischiopagus conjoined twins in a low-income setting

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Key Clinical Message

Ischiopagus parasites are fetal defects attached to a relatively normal twin by pelvis. This is the first reported case of parasitic ischiopagus twins without prenatal diagnosis successfully managed in Mozambique. A multidisciplinary team was involved in the supernumerary limbs excision. After 7 months, the infant has a normal development.

Keywords

Conjoined twins, developing country, ischiopagus, parasitic twins, surgical separation.

Introduction

A parasite conjoined (or heteropagus) twin (PCT) is a grossly defective fetus, or fetal part, attached to a relatively normal twin (the autoside) [1]. This is a rare anomaly with an incidence of <0.1 in 100,000 births and a frequency among all conjoined twins ranging from 4.5% to 15% [2].

Spencer's classification categorizes PCTs based on one of the eight anatomic sites in which symmetric conjoined twins are united: omphalopagus, thoracopagus, cephalopagus, ischiopagus, parapagus, craniopagus, and rachiopagus [1].

Ischiopagus parasites are attached to the autoside's lower abdomen and pelvis and account for about 13% of all heteropagus twins (54% male) [2].

These pathological conditions need a complex and multidisciplinary expertise, which is very hard to provide in a low-income country. To our knowledge, we report for the first time a successful case of management of heteropagus ischiopagus conjoined twins in Mozambique.

Case Presentation

A 4000-gram girl was born to a 31-year-old woman, gravida 4, para 4 in a peripheral health center in the Manica province, Mozambique, after an uncomplicated term pregnancy and was referred to the Central Hospital of Beira (CHB) for a musculoskeletal malformation.

Both the mother's personal anamnesis and the family history were uneventful. The mother was HIV and syphilis negative.

After a normal vaginal delivery, an actively crying neonate (APGAR 9-10/10) was delivered. Physical examination revealed the presence of four limbs attached to unique pelvis (Fig. 1): Medial limbs were hypotonic, hypoplastic, cold, with no active movements and with hypo-sphygmic peripheral pulses. Anatomically, normal toes were present in all four limbs. Female genitalia and perforated anus were lateralized to the right: a unique urethra, both labium minus, and a right labium majus were localized between the right lateral and medial limb,

Figure 1. Clinical presentation of the twins when arrived at CHB (presurgical separation).

while the left labium majus was localized between the left lateral and medial limb.

Inferior limb X-rays (Fig. 2A) showed the medial limbs were articulated to the ischial part of the hip. Barium abdominal X-rays and retrograde urethrocystography confirmed the presence of a unique colon (with right lateralization) and of a unique bladder with only one urethra (Fig. 2B–D). Transfontanelar and cardiac ultrasounds (US) were unremarkable and two anatomically normal kidneys were evident in abdominal US.

The patient underwent surgery on the 16th day of life. She was placed in a lithotomic position. Vesical and anorectal catheters were positioned. In order to disjoint the medial supernumerary unfunctional limbs, a transversal sovrapubic incision was performed and this allowed a better view of the viscera. The incision was extended to the articular tissue: This allowed to see the blood supply of the supernumerary limbs which was provided by some small collateral arteries of the common femoral artery. After ligation of the arteries, disarticulation of the supernumerary medial limbs from the ischial bone was performed. During surgery, a normal right lateralized uterus and vagina were found. All specimen withdrawn were sent for histopathological examination, which, however, was not performed due to lacking of reagents (Fig. 3). The wound was closed with a median longitudinal suture, following the anatomical planes, which did not allow the reconstruction of the external genitalia. The patient was in a stationary hemodynamic condition during the 6-h surgery, although she lost about 3 mg/L of hemoglobin. These data are consistent with similar procedures.

The postoperative recovery was characterized by late-onset neonatal sepsis, anemia, and pyodermitis. The infant also presented a soprainfected wound dehiscence which led to a surgery cleaning for second intention after 14 days from the first intervention.

At the age of 7 months, she is developing normally without any urinary or fecal incontinence (Fig. 4). For lateralized anus and genital area, it is planned a corrective surgery after the 12th month of life.

Discussion

We presented a rare case of PCT in a low-resource setting with limited means for diagnosis and management.

The duplication of inferior limbs, without any other associated malformations, allows several diagnoses: polymelia, caudal duplication syndrome associated with dipygus, human disorganization syndrome, and parasitic ischiopagus conjoined twins.

Polymelia is defined as the presence of accessory limbs attached to various body regions. This anomaly is usually associated with genetic factors and environmental agents (such as teratogenic agents), and it is very common in animals [3]. It usually appears as an isolated Hypotrophyc appendix attached to the body.

The association of malformations and duplications of gastrointestinal, genitourinary systems, and neural tube defects has been called caudal duplication syndrome [4]. It usually occurs with dipygus malformation and is characterized by completely duplicated legs all oriented in same direction [5].

Human disorganization syndrome is a very rare condition triggered by disorganization of morphogenetic induction resulting in anomalies of limbs (reduction or duplications, polydactyly, malformations of limb girdles), body wall defects (gastroschisis, thoracoschisis), hamartomas, and various anomalies of internal organs.

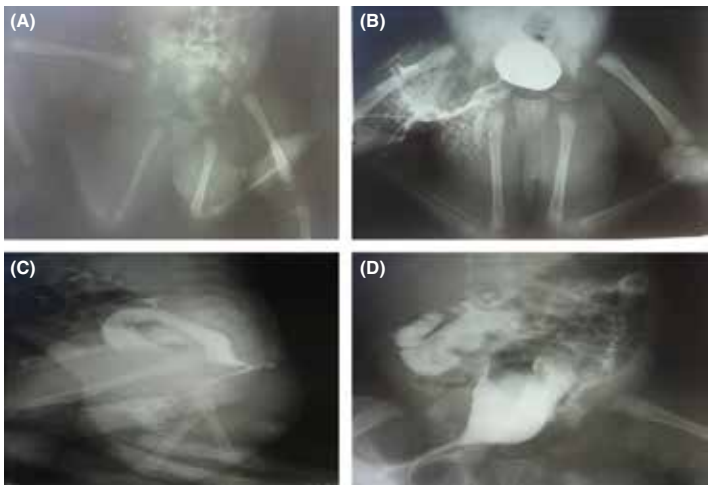

Figure 2. (A) Inferior limb X-ray: four femurs, four tibias and four fibulas, one medial pair, and one distal pair each. Medial femurs were articulated with autoside's hip to its ischial part. (B) Retrograde urethrocystography: two kidneys with hydronephrosis, two ureters, anatomically normal bladder, right lateralized urethra. (C and D) Barium abdominal X-ray: normal barium filling of the gastrointestinal tube without duplication nor dilatation or stenosis of GI tube. Right lateralization of perforated anus was evident.

Figure 3. Postsurgical specimen.

Figure 4. Clinical presentation at 7-month follow-up: She presents with a normal neurologic development: She is able to set down and to crawl. Anus and urogenital areas are lateralized to the right without any urinary or fecal incontinence.

Approximately two-thirds of cases have multiple defects [6]. Extremities anomalies usually involve one limb.

Finally, in typical ischiopagus PCTs, the parasite usually presents with some internal viscera [7–10] and often shares genitourinary organs or colon with the autoside [1, 7, 8, 10]. Moreover, it is not infrequent to find parasitic external genitalia [7, 8, 10, 11] or autoside's malformations such as defects of abdomen wall [7–10] or neural tube defects [8] (Table 1).

In our case, medial legs had a ventral and cranial orientation as seen in another case [9]. The lateralization of distal genitourinary and rectal tracts supports the fusion theory of embryologic origin of PCT [2]. The presence of parasitic viscera was not clinically or radiologically

Table 1. Review of literature about ischiopagus PCTs.

	Year	Sex	Country	Prenatal diagnoses	Autoside anomalies	Parasite	Vascular pedicle	Shared organs	Outcome	f/u
Present case	2017	f	Mozambique	No	R lateral urethra and distal GI tract, R lateral uterus, opening vagina, L labium major separated from the rest female genitalia and located in between L lateral and medial limbs.	Kidney, external genitalia,	Femoral artery	None	Alive at last f/u	7 months
Stahr N	2015	m	Switzerland	Yes	Omphalocele, R-side clubfoot, anal atresia without fistula, duplicated scrotum, two penises, hipospadia, bowel duplication		Internal iliac artery	Bladder	Alive at last f/u	4 months
Gokcen EC	2015	f	Ethiopia	No	Three kidneys, two bladders, two urethra, two uteri, two vaginas	External genitalia	Not identified	None	Alive at last f/u	1 year
Rode H	2006	f	South Africa	No	Only one kidney, opening cloaca	Deformed R arm, only one kidney, gross skeletal deformities, bowel in the chest, opening cloaca	Not identified	Bladder, terminal rectum, common rectal opening to the cloaca	Death after 6 days	
		m		No	Duplicated colon (rectovesical fistula R ending), anterior meningomyelocele	Male genitalia, urethra, one kidney, one bladder, one ureter, four vertebral bodies, bifid sacrum	Not identified	Anus	Alive at last f/u	5 months
		f		No	Not described	Anus, colon, blind-end urethra, bladder	Not identified	None	Alive at last f/u	
Corona-Rivera JR	2003	m	Mexico	No	Small L diaphragmatic defect, omphalocele, exstrophy of cloaca, lumbar meningocele	Complete L limb, lumbosacral vertebral column, spinal cord, one kidney with ureter and adrenal gland,	Major anastomosis	None	Death after 4 days	
Mahajan JK et al.	2002	f	India		Omphalocele, single ovary, and hemiuterus	Bowel, bladder, ovary x1, hemiuterus, external genitalia, patent urethra, BLE	Epigastric artery	Urinary (autoside ureter-parasite bladder)	Alive at last f/u	5 months

m, male; f, female; R, right; L, left; f/u, follow-up.

evident, but we cannot really exclude it because we did not receive any results from Pathology Service. All these data support our supposed diagnosis of parasitic ischiopagus.

This is the first case of a newborn with ischiopagus PTC managed in Mozambique. A previous case was reported in Ethiopia in a 17-year-old female [11]. In that case, on the one hand, the older age surely led to more complex surgery, due to diminished potential of remodeling, while on the other hand, the postoperative phase surely benefitted from better recovery capacity.

In our case, a multidisciplinary team was involved (radiologists, pediatric surgeons, general surgeons, neonatologists, pediatricians, anesthesiologists) in the diagnostic phase, in order to obtain a deep preoperative study of the anatomy, at the time of surgery and during postoperative recovery. Fortunately, the absence of genitourinary or gastrointestinal tracts sharing between parasite and autoside and the lack of autoside's malformations did slightly reduce the complexity of the surgery. Moreover, great intensive care in the postsurgery recovery was made in the neonatology unit.

Conclusion

In conclusion, we report the first ischiopagus PCT successfully managed in Mozambique. This is a rare case not only for the diagnosis, but also for the outcome, considering the low-income setting and the lack of prenatal diagnosis, specialists, drugs, and equipment. Moreover, rapid and effective efforts are necessary in order to increase and improve health policies and win the big challenge of health equity in developing countries.

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Ethics Approval and Consent to Participate

Once the patient was admitted to the hospital, the patient's mother signed an informed consent form that allowed the medical team to be able to use the information obtained with regard to the well-being of their child for publication. Privacy was observed at all times. Because the identities of the involved individuals are concealed, ethics approval for this particular case report was not required.

Consent for Publication

Written informed consent was obtained from the patient's legal guardian(s) for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Authorship

EC, ARM, DP: conceived and designed the study. EC and ARM: undertook the data collection. GM and DP: provided advice on study design and statistical analysis. EC: analyzed the data. EC and DP: drafted the manuscript with significant contributions from WMO, PG, DT, and LDD. All authors approved the final version of the manuscript.

Conflict of Interest

The author declares that he has no competing interests.

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Bilateral Mastectomy as Radical Treatment of Gynecomastia Secondary to Antiretroviral Therapy in a Low Income Setting: A Case Report

PAPER

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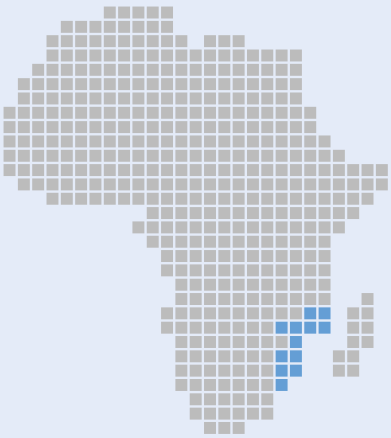

Abstract

Gynecomastia is the abnormal enlargement of the male breast that makes a man's chest appear more feminine. The condition has numerous causes, with 10-25% of cases resulting from medications such as anabolic steroids, anti-androgens, antidepressants and the antiretroviral therapy (ART) drugs used to treat HIV.

How gynecomastia is treated depends on the type and seriousness of the case in question: sometimes surgery proves necessary, especially in low-income countries where there is a relative dearth of health resources and specialized equipment.

This study reports the case of a 46-year-old man being treated with ART medications and admitted to the Beira Central Hospital in Mozambique due to a notable increase in the size of his breasts. The patient underwent a bilateral mastectomy whose outcome was positive despite the seriousness of the pathology with which he had been diagnosed.

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CASE REPORT

Bilateral Mastectomy as Radical Treatment of Gynecomastia Secondary to Antiretroviral Therapy in a Low-Income Setting: A Case Report

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Abstract Gynecomastia is a common finding in males, with an incidence that varies widely globally. In 10–25% of cases, it is caused by drugs. Its pathophysiologic mechanism includes exposure to exogenous estrogens and medications that cause hypogonadism, antiandrogenic effects and hyperprolactinemia. Gynecomastia is associated with exposure to antiretroviral therapy (ART), particularly efavirenz. Sometimes surgery may be required as treatment. We report a case of a 46-year-old man receiving ART presenting with a marked bilateral breast enlargement who underwent bilateral mastectomy as the only successful treatment in a low-income setting.

Key Points

One possible adverse drug effect of antiretroviral treatments, especially efavirenz, is male gynecomastia.

The development of prevention and early diagnosis strategies is crucial to improve treatment and patient health and to reduce health costs, especially in low-income countries given the large number of patients with HIV in these countries.

Surgery can be a solution, especially in low-income countries facing late-stage disease and a lack of specialized health professionals and equipment.

Introduction

Gynecomastia is the enlargement of male breast tissue in men and is frequently observed in newborns, adolescents, and older men [1].

It should be differentiated from breast carcinoma and pseudogynecomastia, which is characterized by fat deposition without glandular proliferation.

Physiological gynecomastia, occurring in almost 25% of cases, is benign and self-limiting; this type is observed especially in young men, up to 65% of adolescents [2].

However, several conditions, such as the use of narcotic substances and drugs may induce proliferation of male breast tissue. Moreover, true gynecomastia is a common feature often related to estrogen excess, androgen deficiency, and a high elevation of sex hormone-binding globuline (SHBG) as a consequence of different endocrine

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disorders [3]. Non-endocrine illnesses, including liver failure, chronic kidney disease, and drug side effects [1], may also cause gynecomastia.

Drug-induced gynecomastia particularly merits deep consideration as it may account for as many as 25% of all cases of gynecomastia in adults. Although the mechanism is not fully clear, it may include estrogen-like activities, stimulation of testicular production of estrogens, inhibition of testosterone synthesis or blockade of androgen action. Anabolic steroids, particularly when used during the pubertal stage, may cause significant irreversible gynecomastia [4]. The pathophysiologic mechanism includes exposure to exogenous estrogens and medications that cause hypogonadism, antiandrogenic effects, and hyperprolactinemia [5].

Drugs definitely associated with the onset of gynecomastia are spironolactone, cimetidine, ketoconazole, human growth hormone (hGH), estrogens, human chorionic gonadotropin (hCG), antiandrogens, gonadotropin-releasing hormone (GnRH) analogs, and 5-α reductase inhibitors. Other drug classes seem to be protease inhibitors, and nucleoside reverse transcriptase inhibitors, although their association with gynecomastia is based on poor-quality evidence [6]. Finally, drugs probably associated with gynecomastia include risperidone, verapamil, nifedipine, omeprazole, alkylating agents, HIV therapies, anabolic steroids, alcohol, and opioids [7].

Efavirenz is the antiretroviral treatment (ART) most clearly associated with gynecomastia as a possible adverse drug reaction, especially with prolonged exposure [8].

We report a case of advanced-stage ART-related gynecomastia, treated with surgery and managed with satisfying results in a low-income setting.

Case Report

A 46-year-old man was admitted to Beira Central Hospital (Mozambique) with marked bilateral breast enlargement (Fig. 1). He was HIV positive, had been receiving ART (tenofivir/lamivudine/efavirenz 300 mg) for the past 5 years and reported gradual breast growth over the last year. Previous diseases were unremarkable, he was in good general condition, and his vital parameters were normal. Although he had lived for many months with the discomfort of this condition, he decided to treat the disease only after consultation with a traditional healer, and after it caused marked stigmata. He had no other signs and symptoms such as nipple discharge, bleeding, or breast pain.

We were unable to perform specific laboratory tests such as those for sex hormones and tumor markers, so, after clinical examination and excluding other main causes, such as seminoma, liver diseases, and malnutrition, we clinically hypothesized the diagnosis of gynecomastia associated with ART.

Fig. 1 46-year-old HIV-positive man with gynecomastia due to antiretroviral (ART) with tenofivir/lamivudine/efavirenz admitted to Beira Central Hospital (Mozambique) and successfully treated with bilateral mastectomy

Discontinuation of HIV therapy was not feasible, and the risk of recurrence with surgical undercorrection had to be avoided. Thus, a mastectomy, with double incision approach and nipple–areola complex (NAC) free transplantation, was proposed to the patient as radical treatment of his severe bilateral gynecomastia.

Pre-operative routine laboratory tests were normal: CD4 count 440/mm^3.

The patient's chest characteristics and proportions were considered preoperatively, and the breasts were marked in a standing position: any side of lipodystrophy was noted in the patient's slim chest, no atypical thoracic conformation was detected, and severe bilateral hypertrophy with little asymmetry was noted in the context of a Simon III gynecomastia.

The NAC was removed as a full-thickness graft, trimmed to 2.5 cm and preserved in wet gauze until the end of the mastectomy. The mammary pocket was cleaned, and hemostasis was checked. The excess skin was removed, and the inframammary fold was closed in layers over a drain. Finally, the NAC was placed and fixed onto a de-epithelialized bed previously marked symmetrically on the chest so the new nipple–sternal notch distance was 15 cm bilaterally.

The removed specimens weighed 1.5 kg (right) and 1.7 kg (left).

Postoperative antibiotics and analgesics (amoxicillin and clavulanic acid 1000 mg every 8 h and ibuprofen 600 mg every 8 h) were administered, and a moulage compressive dressing with non-stick gauze was maintained on the wounds for 3 days. The drain was then removed, and the patient was discharged on the fifth postoperative day without any complication. Compressive dressing of the wounds for 2 weeks was recommended. The patient continued with the same ART drugs and dosage. Although all instructions were given to the patient with a recommendation to return for follow-up, he never did so.

Histopathological examination confirmed the clinical diagnosis of gynecomastia, reporting epithelial and ductal cells and myxoid stroma.

Discussion

In low-income settings, it is common to be faced with extreme and late-stage diseases, with consequent management difficulties and negative outcomes. In fact, in these contexts, healthcare must deal with many sociocultural aspects such as superstitions and (often misinformed) traditional healers turning patients away from conventional medicine. Moreover, people are often reluctant to refer to conventional doctors because of the risk of stigma and marginalization in doing so.

We reported a case of gynecomastia in a patient receiving ART for HIV. The weak healthcare system, poor-quality infrastructure and equipment, and limited tests and diagnostic procedures available to us meant an accurate diagnosis was impossible. However, given the clinical features and histopathological examination, we excluded other causes and, based on the literature, we concluded this case was ART related.

The management of this patient represented a challenge, most of all due to the delay before treatment, which led to physical, social, and psychological disability, reducing the chance of optimal results. For our patient, surgery represented the only therapeutic possibility, so we performed a bilateral mastectomy. We did not perform a reductive mastoplasty, even though it would have been aesthetically more suitable, because of the risk of glandular residue that with therapy would have again hypertrophied. The procedure we performed has already been reported in the literature as treatment for gynecomastia, with satisfactory results [9]. In this case, the mastectomy procedure was not difficult because of the well-delineated surgical plans and well-defined glandular tissue, which did not trespass into the pectoral regions or beyond the anterior axillary line.

The other big challenge in this case was the follow-up. In fact, the patient did not return for regular follow-up, which is common behavior in low-income settings, particularly when there are no complications. On the other hand, it was not possible to perform appropriate biochemical evaluation, including sex hormones, for adequate post-operative follow-up from an endocrine point of view.

Conclusion

Our approach to this case of gynecomastia was successful and effective, resulting in a satisfied patient, despite the extreme condition of the disease presentation. However, in low-income settings, it is crucial that the health system be strengthened in terms of both healthcare and prevention. In fact, if further studies confirm the frequent association between ART and gynecomastia, given the high prevalence of patients with HIV worldwide, it is crucial that prevention and early diagnosis strategies are developed to improve treatment and patient health and reduce health costs.

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Complaince with Ethical Standards

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Conflict of interest Mario Antunes, Marcella Schiavone, Damiano Pizzol, Francesco Di Gennaro, Rossana Ludovico, and Angela De Palma have no conflicts of interest.

Informed consent The patient provided written informed consent to publish this case report and any accompanying images. A copy of the written consent may be requested for review from the corresponding author.

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Characteristics, prevalence, and outcomes of diabetic foot ulcers in Africa. A systemic review and meta-analysis

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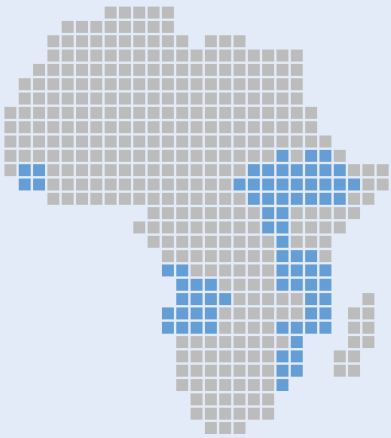

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Abstract

A chronic disease, diabetes is a fast-growing health problem throughout Africa, with prevention and treatment needs such as those associated with diabetic foot conditions being left largely unmet.

This study reviewed the literature on diabetic foot ulcer patients in Africa, focusing on the clinical characteristics of the disease, limb amputation rates and mortality rates associated with the latter.

Our data analysis showed a diabetic foot ulcer prevalence of 13% in the 56,173 cases taken into consideration by the study. Approximately 15% of the patients underwent a foot amputation and 14.2% died during hospitalization.

However, both the number of amputations and the mortality rate appear to have decreased over the years, probably due to the recent implementation of diabetes screening programs in Africa.

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Characteristics, prevalence, and outcomes of diabetic foot ulcers in Africa. A systemic review and meta-analysis

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ABSTRACT

Background: Among non-communicable diseases, diabetes represents a growing public health problem in Africa, where diabetes-related needs remain mostly unmet and the disabling features of foot are worsened by hygienic, cultural, and healthcare issues. We aimed to review clinical characteristics, prevalence, and outcomes of patients with diabetic foot ulcer in Africa.

Methods: We searched the literature for cross-sectional and longitudinal studies reporting the characteristics of patients with diabetic foot in African countries, with a particular focus on ulcer prevalence, amputation rate, and mortality.

Findings: Fifty-five full-text papers and ten abstracts were retrieved, reporting data from 19 African countries on 56,173 diabetic patients. According to the data collected, the overall prevalence of foot ulcers was 13% and increased over time, especially since 2001. Approximately 15% of patients with foot lesions underwent major amputation and 14.2% died during hospitalization. In patients with diabetic ulcers, insulin therapy was uncommon and neuropathy was the most common predisposing factor, but the prevalence of peripheral arterial disease correlated with amputation rates. Amputation and mortality decreased over time, probably as result of the implementation of screening programs in the last ten years. Mortality was directly related to previous amputation.

Interpretation: The diabetic foot disease in Africa is a growing problem and is burden by high rate of in-hospital mortality. Educational interventions and screening programs including evaluation of the vascular status may play a crucial role to counter diabetic foot disease in Africa.

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01 → Mozambique
X Conferência Científica UEM,
Maputo – Mozambique, September 26th – 28th 2018 Maputo
- De Meneghi G., Cebola R.B., Llapur Figueredo R., Mazive S.A., De Vivo E., Praticò L., *Pattern of domestic violence from 2011 to 2015 in Beira, Mozambique*

02 → Mozambique
X Conferência Científica UEM,
Maputo – Mozambique, September 26th – 28th 2018 Maputo
- De Meneghi G., Cebola R.B., Pizzol D., De Vivo E., Praticò L., Figueredo Lapur R., Mazive S.A., P*hysical injury and depression in six low-middle income countries*

03 → Sierra Leone
XVII Italian Conference of the SIMIT (National Society of Infectious and Tropical Diseases),
Turin – Italy, December 2nd – 5th 2018
- Di Gennaro F., Marotta C., Kamara V., Pizzol D., Putoto G., Pellizzer G., Mazzucco W., Monno L., Saracino A., *Maternal caesarian section infection (MACSI) in Sierra Leone: a case control study. Preliminary data of the first 5 months of the study*

04 → Uganda
5th Annual National Healthcare Quality Improvement Conference,
Kampala – Uganda, December 4th – 6th 2018
- Wangubo A., Anguzu J., Nandutu H., Ictho J., Ogwang D., Ndungutse A., Katungi A., Lochoro P., *Improving reporting on nutrition indicators into the health management information system using the continuous quality improvement approach: A case of Nakapiripirit District*

05 → Uganda
5th Annual National Healthcare Quality Improvement Conference,
Kampala – Uganda, December 4th – 6th 2018
- Ariko A.I., Kisembo G., Mindraa P., Katungi A., Ictho J., Ndungutse A., Piriyo P., Ochero J., Lochoro P., *Strengthening Neonatal Intensive Care Unit to improve on the quality of care for Sick Newborns: A case of Kiryandongo Hospital, Kiryandongo District*

06 → Uganda
5th Annual National Healthcare Quality Improvement Conference,
Kampala – Uganda, December 4th – 6th 2018
- Wamboya D., Pacutho M., Katungi A., Ictho J., Ndungutse A., Ochero J., Pirio P., Lochro P., *Improving partograph use to reduce perinatal mortality: a case of Anyiribu Health Centre III, Arua District, Uganda*

07 → Mozambique
I International Conference on Social Determinants of Health – Medicus Mundi International,
Maputo – Mozambique, December 5th – 7th 2018
- Fogliati P, Monforte L.P., Aly M.M., *Inequitable access to antenatal services in rural primary health care facilities in northern Mozambique. Findings from a community and health facility assessment in Cabo Delgado Province*

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