Maternal health in Namibia: Lessons learned from obstetric surveillance

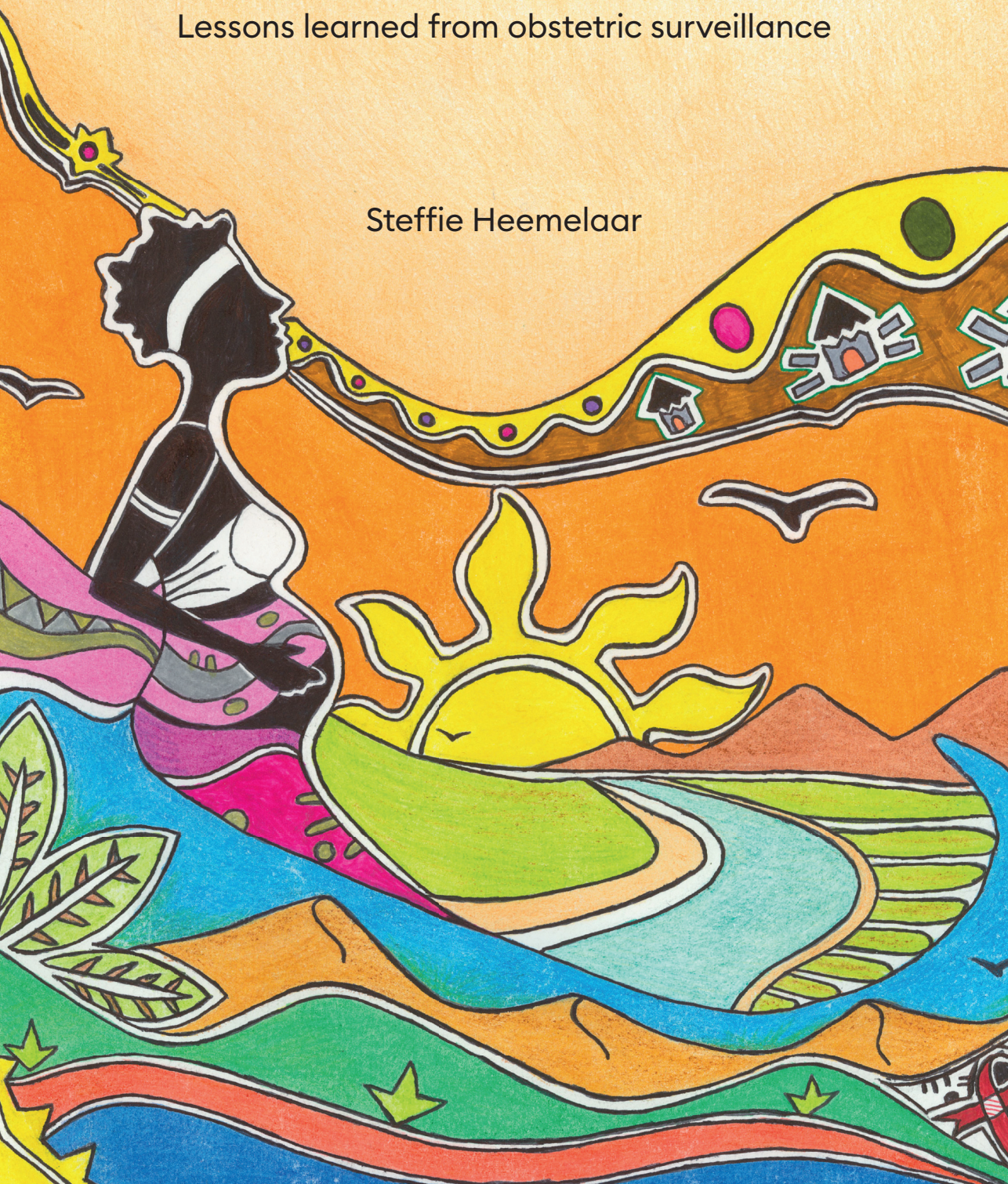
Heemelaar, S.

Safe motherhood

Maternal health in Namibia

Lessons learned from obstetric surveillance

Steffie Heemelaar



Maternal health in Namibia

Lessons learned from obstetric surveillance

Steffie Heemelaar

Artworks	Morgan Shali Elifas
Lay out	Tom Rutgers | www.tomrutgers.nl
Printing	Ridderprint
ISBN	978-94-6458-668-8

This thesis was partly funded by Stichting Oranjekliniek and the Catharine van Tussenbroek Fund. The funders had no role in study design, data collection and analyses, decisions to publish, preparations of manuscript or thesis

Financial support for printing of this thesis was kindly provided by the Department of Obstetrics and Gynaecology of Leiden University Medical Center, Walaeus University Library, Haaglanden Medical Center, Bayer, Titus Health Care, ChipSoft.

Maternal health in Namibia

Lessons learned from obstetric surveillance

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 18 april 2023
klokke 16.15 uur

door

Stéphanie Heemelaar

geboren te Amsterdam
in 1986

Promotores

Prof. dr. J.M.M. van Lith	
Prof. dr. T.H. van den Akker	VU University, Amsterdam
Prof. dr. J. Stekelenburg	University Medical Center Groningen, Groningen

Leden promotiecommissie

Prof. dr. M. Yazdanbakhsh	
Prof. dr. J.W. Roos-Hesselink	Erasmus University Medical Center, Rotterdam
Dr. T. Endjala	University of Namibia, Windhoek
Dr. J.J. Beltman	

To Marietjie de Klerk,
who has devoted her life to caring for vulnerable Namibians
and made Namibia my second home

Contents

Chapter 1.	General introduction	9
Part I.	**Maternal death and near-miss surveillance**	25
Chapter 2.	Confidential enquiry into maternal deaths in Namibia, 2018-2019: findings and lessons learned from implementation	27
Chapter 3.	Measuring maternal near-miss in a middle-income country: assessing the use of WHO and sub-Saharan Africa maternal near-miss criteria in Namibia	45
Chapter 4.	Maternal near-miss surveillance, Namibia	69
Part II.	**The impact of cardiac disease and acute Hepatitis E on maternal outcome**	89
Chapter 5.	Maternal mortality due to cardiac disease in low- and middle-income countries: a systematic review	91
Chapter 6.	Experiences of a dedicated Heart and Maternal Health Service providing multidisciplinary care to pregnant women with cardiac disease in a tertiary centre in Namibia	111
Chapter 7.	Maternal and fetal outcomes of pregnancies complicated by acute hepatitis E and the impact of HIV status: A cross-sectional study in Namibia	135
Part III.	**Discussion and summary**	153
Chapter 8.	General discussion	155
Chapter 9.	Summary / samenvatting	173
	Publications	182
	About the author	185
	Acknowledgements	186
	The Safe Motherhood Series	188

Chapter 1.

General introduction

Personal justification

The story of Selma

In 2017 Selma entered the labour ward of the Windhoek Hospital Complex around 4:00 AM. As the medical officer on call, I was responsible for her care. Selma was bleeding, had a high blood pressure and severe abdominal pain. On examination I felt that her womb was as hard as a rock. Her baby was still alive but the heartbeat very slow. I suspected that Selma had an abruption of the placenta, meaning that her baby was in immediate danger. Her cervix was dilated to one centimetre only, so to expedite birth we rushed her to the operating room for a caesarean section. I had a quick look on Selma's health passport and saw it was her fifth pregnancy: she had had four stillborn babies from pregnancies complicated by high blood pressure. I realized how long Selma had been hoping to become a mother of a live baby. Fortunately, the staff of the operating room was readily available and within a few minutes we could start the operation. Nevertheless, we were too late to save Selma's baby. Moreover, the operation was complicated by massive blood loss. After placing a B-lynch suture, a technique to compress the uterus, the bleeding finally stopped, just before we would have had to resort to the last option: removing her uterus. Selma is an example of a so-called 'maternal near-miss', meaning that she nearly died but survived a severe complication of pregnancy.

Selma's complication could possibly have been prevented with better care. In her current pregnancy, Selma was seen weekly by one of the doctors in the antenatal care clinic. Her blood pressure was carefully managed with medication. She reached a gestation of 32 weeks, already one month further than the term at which she lost her previous babies. During her most recent visit she had been seen by an intern, a medical doctor with limited clinical experience who had recently graduated from medical school. Interns are not supposed to work unsupervised, but an obstetrician-gynaecologist, or even a medical officer with basic clinical experience, had not been available that day due to staff shortages. The intern had not realized that the blood pressure of Selma had been too high and had sent her home.

After the operation, I had to tell Selma she had lost yet another baby. I was sad and angry. Sad that this death could potentially have been prevented and unlikely would have happened in a Dutch health facility. And angry at those in power. Why is there still so much inequity in this world in the 21st century? How can it be that in high-income settings there are so many resources that expensive robots can assist doctors with operations, whilst we cannot even ensure that in this part of the world a woman simply sees an appropriately trained health worker when she needs one?

It was during my final year of medical school that I had made up my mind that I wanted to work where there was a shortage of doctors. My final rotation was at the obstetric department in a Dutch hospital. On the labour ward, it happened more than once that, on a quiet day, the obstetrician, obstetrician-in-training, midwife, midwife-in-training, and one or two medical students were waiting for women in need of a skilled birth attendant. The contrast with my previous internship in a rural hospital in Zambia could not be more harrowing. There, I had been impressed by the overwhelming challenges confronting health workers, including lack of staff at all levels resulting in permanently overburdened personnel.

After my specialization as a medical doctor in Tropical Medicine & International Health, I had started as a medical officer in the department of obstetrics and gynaecology at the national referral hospital of Namibia. There was a shortage of doctors in the country, as only in 2010 the first medical school had opened its doors. Until then, doctors working in Namibia were either Namibians trained elsewhere, or foreigners. At the hospital, my colleagues and I were confronted with the death of one or two women every month. Many women probably would have survived with better care. Maternal near-misses occurred nearly every day. On the night Selma lost her baby and nearly lost her life, I realized that simply having more doctors, midwives and nurses is not the silver bullet. Only when health workers are working in a functioning system, they can deliver good care. I started questioning myself: what is needed to achieve a better functioning maternity care system in Namibia to ensure that women like Selma have a pregnancy without severe adverse outcomes?

If this were an easy question to answer, there would have been no need to raise it. One important realisation was that, in my quest for an answer, I was not alone. Many devoted colleagues were similarly looking for ways to make things better: in the department and the hospital at large, as well as in other public hospitals in Namibia. Motivated to improve maternal health, we started several initiatives and tried to improve existing ones, such as the confidential enquiry into maternal deaths. This thesis describes the outcomes of our joint efforts, and I feel grateful with this opportunity to share our journey. I am hopeful that some of the lessons learned along our journey may be helpful to colleagues who are seeking to develop similar initiatives elsewhere.

Background

Maternal health, the global numbers

It is rather confronting that still in 2023, I have to include in the introduction of my thesis, like many others before me, the following sentence: it is estimated that globally each year 295 000 women die from complications of pregnancy and childbirth.[1] More than two out of three deaths occur in sub-Saharan Africa and the overwhelming majority could have been prevented with better care.[2] It is estimated that for each maternal death there are five maternal near-misses.[2,3] This means that globally, every day, there are 5000 women like Selma with severe maternal outcome, which is the term applied for the combination of maternal near-miss and maternal death. So why is this tragedy still continuing? One would expect that focus and resources go where the need is highest. But the distribution of COVID-vaccines painfully illustrates how the real world works: rich countries first ensure their own health facilities are sufficiently stocked to be able to more than double vaccinate their entire population, before they share the left-overs of less effective vaccines with poor countries.[4,5] The rich come first and the poor last.

In the past decades there has been increasing attention to improve the health of pregnant women around the world, especially from the year 2000 onwards, when improving maternal health became one of the eight Millennium Development Goals. This may have contributed to the overall reduction in the number of maternal deaths globally: the maternal mortality ratio (MMR), a ratio commonly used to monitor maternal deaths, reduced from 385 deaths in 1990 to 216 per 100 000 live births in 2015.[6] Nevertheless, gross inequity persists: the regional MMR of sub-Saharan Africa is still 45 times higher compared to the average MMR of all high-income countries combined. It is obvious that further reductions are urgently needed, particularly among the poor and the vulnerable.

Learning from success stories

In several countries, the number of maternal deaths has been going down considerably in the course of centuries or decades. By analysing the progress in countries that went from high to low maternal mortality, a common pathway was identified. Based on this common pathway, the World Health Organization designed the five-stage 'obstetric transition' model.[7] Policymakers aiming to reduce maternal mortality are advised to first determine in which stage of the model their country is, since in each stage different strategies are recommended to further improve maternal outcome. In this model, countries that are in stage 1 hardly have a functioning health system and the MMR is above 1000 deaths per 100 000 live births. In countries in stage 2, women are trying to reach health facilities but lack of access still plays an

important role, as well as marked weaknesses within the health system. For countries in both stage 1 and 2, it is recommended by the World Health Organization to improve infrastructure to increase access to maternity care, and simultaneously invest in basic preventive measures, such as family planning, infection prevention and iron supplementation.[7] In stage 3 the MMR is still high, 50-299 deaths per 100 000 live births. Women are reaching the formal health system, often leading to overburdened facilities, and improving quality of care is the core determinant to further reduce mortality in this stage. As obstetric care is improving, some obstetric deaths are reduced and the impact of deaths due to pre-existing medical conditions starts to increase. In countries in stage 4, nearly all obstetric deaths are avoided and mainly deaths due to pre-existing medical conditions are seen. With an MMR below 50 deaths per 100 000 live births, the occurrence of maternal deaths will be rare in most health facilities and, as a result, in this stage health workers are predominantly confronted with maternal near-miss complications.[8] In stage 5 all avoidable maternal deaths are indeed avoided.

Namibia

Namibia had an MMR estimated at 195/100,000 live births in 2017.[9] In 2015, the commonest causes of maternal death were obstetric haemorrhage, hypertension-related complications, tuberculosis and cardiac disease.[10] Key indicators suggest high access to maternity care, with 97% of women having at least one antenatal visit and 88% giving birth in a health facility in 2013.[11] In line with the obstetric transition, Namibia can therefore be situated in stage 3, whereby many women are reaching health facilities and, as a result, improving quality of care at the facility level becomes key to further improve maternal outcome.

Although globally the MMR nearly halved between 1990 and 2015, in Namibia this reduction was less than 25%.[6] Such insufficient progress was seen in most countries in southern sub-Saharan Africa, the high burden of HIV in this region being an important determinant.[12] The high impact of HIV was a result of both the severe complications directly caused by the virus, such as the rise in opportunistic infections and severe anaemia, and the indirect mechanisms taking place at the health system level, such as resources being diverted away from maternity to HIV care.[12] The impact of HIV is compounded by a high prevalence of tuberculosis. Namibia has one of the highest tuberculosis/HIV co-infection rates in the world: in 2017, an estimated 36% of the newly diagnosed tuberculosis cases were also HIV positive. The HIV prevalence was estimated at 15.7% among women aged 15-64 years in 2017.[13] In comparison to neighbouring countries, Namibia performs well with regard to the implementation of HIV treatment services: in 2017, 97.1% of HIV-infected females were on treatment, of whom 92.2% were virally suppressed.[13]

Another important determinant of the poor progress in reducing maternal mortality in Namibia can be found in the presence of extreme socioeconomic inequalities.[14] At the end of apartheid, Namibia inherited these when it gained independence from South Africa in 1990.[15] Since independence, there has been peace and political stability and from 2008 Namibia has been classified by the World Bank as an upper middle-income country. Nevertheless, even in 2015, Namibia was one of the countries with the highest income disparities in the world, with over 60 percent of the population living of less than $5.5 per day, the poverty line for an upper middle-income country.[14]

Considering gender equity, there is a discrepancy between various indicators. The literacy rate is relatively high at 88.7% in 2016, with hardly any differences between men and women.[16] Completion of secondary school is comparable for both men and women.[16] After the elections in 2020, women took the seats of nearly half of the parliament.[17] At the same time, there is a high teenage pregnancy rate of nearly 20%. One in three married women has experienced gender-based domestic violence, and over 1000 cases of rape are reported to the police every year.[11] Namibia ranks 106th out of 189 countries based on the Gender Inequality Index.[18]

The Namibian health system consists of both private and public health facilities. Private facilities are well-equipped and staffed, employing 72% of the doctors in Namibia.[19] Nevertheless, access to private health facilities is limited to a small proportion of the population, with only 18% of the population covered by medical aid.[19] Moreover, a significant proportion of the people covered by medical aid also makes use of public health facilities, as most medical aid programs do not fully cover all care expenses provided in private health facilities, such as surgery or admission. Many cannot afford the additional fees. There are 35 public hospitals: the national referral hospital, four regional hospitals and 30 district hospitals, Figure 1. In public health facilities, patients pay a small fee (about US$ 0.65) for each health visit. No additional costs are paid for diagnostics or management options including clinical admissions and surgery. All reproductive health related services, including contraception, are provided free-of-charge. In 2017, there were about ten consultant obstetrician-gynaecologists working at public hospitals, of whom more than half were employed by the hospital in the capital. Nurses follow a four-year training, whereby they can specialize in midwifery in their final year, in order to qualify as nurse-midwives. Besides these specialized nurses, there is no post-graduate midwifery training within Namibia, such as there is in, for instance, neighbouring South Africa. There is a national midwifery association for those trained abroad. There is no national association for obstetricians and gynaecologists.

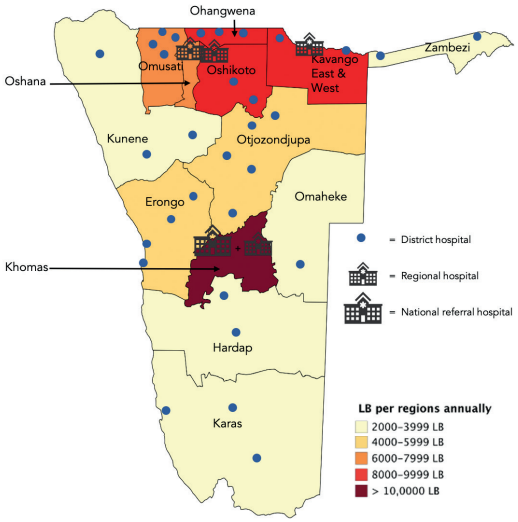


Figure 1. Map of Namibia with its 14 regions. Number of live births (LB) annually and location of public hospitals are shown. The distance between the three regional hospitals outside Khomas region and the national referral hospital are 678, 722 and 714 kilometre respectively. The longest distance between a district hospital and the national referral hospital is 1227 kilometre (this district hospital being located in Zambezi region).

The impact of cardiac disease and hepatitis E

During my employment as a medical officer in the capital of Namibia, both cardiac disease and hepatitis E were common causes of maternal death. Before coming to Namibia, I had not expected to be confronted with the considerable impact of particularly these two conditions in pregnancy, since these are relatively rarely discussed in reports on maternal health in low- and middle-income countries. Several challenges were encountered to provide good care to women affected by either condition.

For hepatitis E in pregnancy there was very limited data on outcome, so we did not know which women were at risk of severe maternal outcome. No curative treatment was available. For cardiac disease in pregnancy, quite some data was available on outcome, as well as clinical guidance for managing these high-risk pregnancies. However, data and guidance were mainly available from high-income settings. To give better insight into the complexity of caring for pregnant women with cardiac disease in a middle-income setting like Namibia, and explain why outcome data and guidelines from high-income settings may not be applicable to this setting, I present the story of two women.

The story of Esperance and Martha

On a regular antenatal care morning I met Esperance, a Congolese woman, pregnant for the third time. She had rheumatic heart disease complicated by mitral valve stenosis. This means that due to her cardiac condition she was at high risk of a complicated course of pregnancy. Her previous two pregnancies had been complicated by severe heart failure, early in the third trimester. As a result, she had to give birth by emergency caesarean section twice. Nevertheless, both of her babies had died soon after birth due neonatal asphyxia caused by her own poor condition. Esperance herself also nearly died during the last pregnancy. When I met her she was twelve weeks pregnant and determined to keep this pregnancy, despite being well aware of its risks. She explained that she wanted to have a large family or rather die if she would not be able to have living children.

On the same day I met Martha. Martha had been admitted into the cardiology department and was in poor condition. Two years ago, after her first pregnancy, she had developed heart failure due to peripartum cardiomyopathy. Her heart never fully recovered and she had been started on chronic heart medication. She was told she should not become pregnant due to her condition and while using heart failure medication, since these posed markedly increased risks for the baby. Interrupted supplies of contraceptives at the local clinic contributed to her becoming pregnant unintentionally. When she realized she was pregnant, she stopped taking all pills, being under the impression that this would be better for her baby. She decided not to go back to the hospital, out of fear for the doctor's opinion about her getting pregnant. When she was six months into the pregnancy, she developed severe heart failure and was brought to the hospital by her relatives.

For both women, doctors of the obstetric and cardiology departments worked closely together to prevent and manage any cardiac, maternal or fetal complications. Both women gave birth to healthy boys and after birth, both women were observed in the ICU department for two days. They recovered without any complications. After counselling, they both received long-acting reversible contraceptives before being discharged.

These stories show that management of these high-risk pregnancies requires a multidisciplinary approach, with involvement of -at the very least- doctors of the cardiac and obstetric departments, ideally starting before pregnancy with preconception counselling. However, for accurate counselling, more data on maternal

and perinatal outcomes were needed, specified to the Namibian setting. Also, given the differences in diagnostic and therapeutic options between high- and middle-income countries, it was unclear whether it was possible to implement the available guidelines in the Namibian setting.

Hepatitis E only started having an impact on maternal outcome in Namibia in 2017, when the first case was reported. The number of infections rapidly increased among the entire population. As it is transmitted via contaminated drinking water, the infection was mainly seen in areas with poor sanitation. Usually, hepatitis E infection is self-limiting with a low mortality rate. However, during pregnancy, a severe clinical course is frequently seen, the pathogenesis of which being poorly understood. The nationwide outbreak, therefore, had a devastating impact on maternal and fetal health, and in 2018-2019 hepatitis E even became the leading cause of maternal death.

Several barriers to good care were encountered. First, it was unclear which women were at risk of severe maternal outcome. The outbreak in Namibia concerned hepatitis E genotype 2. Adverse outcomes had previously been described in areas where genotype 1 is endemic, and, although these previously appeared to be confirmed in reports from genotype 2 endemic areas, the latter type is far less prevalent leading to paucity of data. Another concern was the high HIV prevalence in Namibia. As with most infections among HIV-infected individuals, a more severe outcome of the course of hepatitis E was anticipated. However, there were no reports available reporting outcomes of pregnant women co-infected with HIV and acute hepatitis E. Second, most health workers were not familiar with diagnosis and management of hepatitis E, since the most recent previous outbreak in Namibia had taken place in 1995. Many women presented in a confused state caused by hepatic encephalopathy, and especially in the beginning of the outbreak, women were misdiagnosed to have alcohol intoxication. Third, no curative treatment was available. In case of liver failure, only supportive care could be provided.

Problem statement and aims of thesis

It has been obvious for a considerable time that Namibia's high burden of severe maternal outcome must be addressed. However, it was unclear how a significant reduction could be achieved. The double burden of both direct obstetric causes as well as medical conditions suggested to our group of researchers that a set of diverse interventions would be needed. Improved basic obstetric care was needed for women like Selma, whereas more complex care was needed for women with medical

conditions like Esperance and Martha. Even though indicators suggested that women were reaching the health facilities, this did not mean that women had *timely* access, or access to high-quality care.

For the development of applicable and effective interventions, a better understanding was needed of the drivers of severe maternal outcome and current challenges present in the maternity care system. These insights can be obtained through obstetric surveillance.[20] Until 2017, assessment of the maternity care system was mainly done through review of maternal deaths, using the confidential enquiry into maternal deaths methodology. However, successful implementation was hampered by a blame culture that allegedly made clinicians refrain from reporting cases to the enquiry committee.[21] Committee members of the national confidential enquiry gradually became aware that not all deaths were reported or found that, in case a death was reported, not all medical notes were submitted for review. Moreover, review of maternal deaths mainly provided insight into functioning of the larger hospitals. Due to Namibia's small population of 2.5 million there were about 70 000 births per annum and the absolute number of maternal deaths was low. Maternal deaths seldom occurred in district hospitals, as the majority of these facilities had less than 1500 births per annum and the most critically ill women were transferred to higher level facilities. There was no system in place to monitor other severe complications such as maternal near-misses, which are more frequent, also at lower level facilities.

The first aim of this thesis was to enhance implementation of a national obstetric surveillance system to enable a better understanding of the underlying causes of the high burden of severe maternal outcome and the second aim was to come up with recommendations on how to improve maternal health in Namibia.

Research questions

- What are facilitators and barriers of successful implementation of obstetric surveillance in Namibia?
- What are the main maternal health problems in Namibia?
- What are recommended interventions to improve maternal outcome given the Namibian context?

Obstetric surveillance

The enhanced implementation of obstetric surveillance in Namibia was based on three components. The first was improved implementation of the confidential enquiry into maternal deaths. Secondly, a maternal near-miss approach was added

to the national obstetric surveillance system. This approach was chosen as, besides maternal near-misses occurring in larger numbers, review of these complications is probably less threatening to health workers as the focus is on women who survived rather than those who were lost.[22,23] Although the maternal near-miss approach is recommended by the World Health Organization, implementation in low-and middle-income countries has been hampered by several challenges.[24] For example, the near-miss identification criteria appeared to be less suitable for lower-income settings, due to limited availability of diagnostics and therapeutic options, leading to underreporting.[25-28] Before implementation, suitable near-miss criteria were identified for the Namibian setting. And third, two facility-based studies were performed in the national referral hospital to assess in greater detail the outcomes of pregnant women with cardiac disease and hepatitis E and explore options to reduce the risk of severe maternal outcome in these women.

Conceptual framework

A conceptual framework was developed, to place into perspective the requirements to reduce severe maternal outcome in Namibia (Figure 2). In general, to achieve favourable maternal outcome and avoid and manage severe complications women should have access to health workers who are providing good care. For a functioning health system, each element has to function. This means that women need to have timely access to the health system, as good care can only be 'delivered' to a woman when she is there and when she is there in time. This requires a supportive system around the woman to ensure that she is only pregnant when she chooses to be (**choice**), is able to access care when she needs it (**ability**) and is in good health (**women's health status**) when she becomes pregnant to reduce the risk of severe maternal outcome. On the other hand, health workers must be enabled to 'deliver' good care: they need to have **knowledge and skills**, have access to sufficient **supplies**, such as medication or medical equipment, and they need to be with enough (**human resources**).

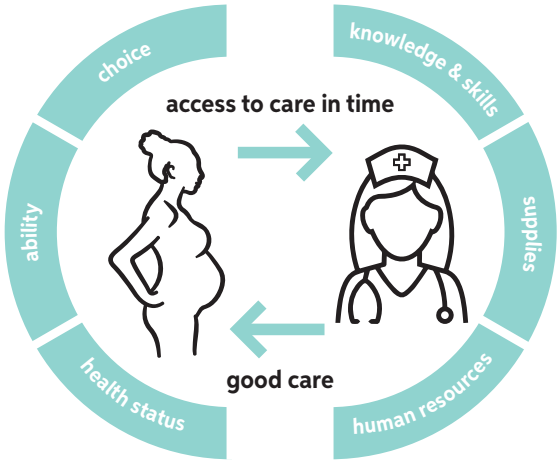


Figure 2. Framework used for this thesis to map the requirements identified through obstetric surveillance to improve maternal health in Namibia.

Thesis outline

Part I of this thesis describes both the implementation and findings of maternal death and near-miss surveillance. Chapter 2 describes the process of improving implementation of the confidential enquiry into maternal deaths by focussing on attempts to increase trust among health workers in the enquiry process. Chapter 3 presents the findings of a pilot study to identify suitable maternal near-miss criteria for a middle-income country like Namibia. Chapter 2 assesses why women die during pregnancy, birth or the postpartum period in Namibia, and chapter 4 shows why women nearly die. Lastly, based on findings of the national maternal death and near-miss surveillance studies, chapters 2 and 4 present recommendations for improvement of the maternity care system in Namibia.

Part II focuses on the impact of cardiac disease and hepatitis E. Chapter 5 explores the burden of maternal mortality due to cardiac disease in low- and middle-income countries. Chapter 6 assesses the maternal and fetal outcomes of women with cardiac disease in Namibia. A multidisciplinary approach providing care from preconception up to postpartum for women with cardiac disease was implemented in the national referral hospital of Namibia, and chapter 6 describes the challenges and benefits of such approach. Chapter 7 describes the maternal and fetal outcomes of pregnancies complicated by acute hepatitis E and whether or not the HIV status of the woman had an impact on outcome.

References

1. World Health Organization. Trends in maternal mortality 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. World Health Organization: Geneva, 2019.
2. Graham W, Woodd S, Byass P, et al. Diversity and divergence: the dynamic burden of poor maternal health. Lancet. 2016;388(10056):2164-2175.
3. Souza JP, Gulmezoglu AM, Vogel J, et al. Moving beyond essential interventions for reduction of maternal mortality (the WHO Multicountry Survey on Maternal and Newborn Health): a cross-sectional study. Lancet. 2013;381(9879):1747-1755.
4. Reuters. African Union drops AstraZeneca vaccine, which COVAX will supply; 2021. (Available from: https://www.reuters.com/article/uk-health-coronavirus-africa-idUSKBN2BV19H) [25-06-2022]
5. BBC News Peter Mwai. Covid-19 vaccines: Why some African states can't use their vaccines; 2021. (Available from: https://www.bbc.com/news/56940657) [25-06-2022]
6. Alkema L, Chou D, Hogan D, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet. 2016;387(10017):462-474.
7. Souza JP, Tuncalp O, Vogel JP, et al. Obstetric transition: the pathway towards ending preventable maternal deaths. BJOG. 2014;121(Suppl 1):1-4.
8. Heitkamp A, Meulenbroek A, van Roosmalen J, et al. Maternal mortality: near-miss events in middle-income countries, a systematic review. Bull World Health Organ. 2021;99(10):693-707F.
9. Maternal Mortality Estimation Inter-Agency Group. Maternal mortality in 2000-2017. Internationally comparable MMR estimates by the Maternal Mortality Estimation Inter-Agency Group (MMEIG), Namibia. World Health Organisation: Geneva, 2017.
10. Stillbirth and Neonatal Death Review National Committee for Maternal Death. Maternal and perinatal death review, 2012-2015: Second Report. Namibia Ministry of Health and Social Services: Unpublished.
11. Ministry of Health and Social Services. Demographic and Health Survey Namibia 2013. Ministry of Health and Social Services: Windhoek, 2014.
12. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9947):980-1004.
13. Ministry of Health and Social Services. Namibia Population-Based HIV impact assessment NAMPHIA 2017. Ministry of Health and Social Services: WIndhoek, 2019.
14. World Bank Data. Country statistics Namibia; 2017. (Available from: https://data.worldbank.org/country/NA) [1-4-2019]
15. TRP Associates. 1995 Residents Survey. Municipality of Windhoek: Windhoek, 1996.
16. Namibia Statistics Agency. Namibia Inter-censal Demographic Survey 2016. Namibia Statistics Agency: Windhoek, 2017.
17. Sampaya F. Namibia narrowly misses 50% women in parliament; 2020. (Available from: https://genderlinks.org.za/news/namibia-narrowly-misses-50-mark-after-special-appointments/) [12-08-2021]
18. Human Development Reports United Nations Development Programme. Gender Inequality Index; 2019. (Available from: http://hdr.undp.org/en/content/gender-inequality-index-gii) [26-10-2021]
19. Ministry of Health and Social Services. Namibia 2014/15 Health Accounts Report. Ministry of Health and Social Services: Windhoek, 2017.
20. World Health Organization. Beyond the Numbers. Reviewing maternal deaths and complications to make pregnancy safer. World Health Organization: Geneva, 2004.
21. Ministry of Health and Social Services. Report of the Prevalence and Contributing Factors of Facility-Based Maternal and Neonatal Deaths in Five Regions of Namibia (Erongo, Hardap, //Karas, Khomas, Omaheke) during 2010–2012. Hardap Regional Health Directorate: Mariental, 2014.
22. Bakker W, van den Akker T, Mwagomba B, Khukulu R, van Elteren M, van Roosmalen J. Health workers' perceptions of obstetric critical incident audit in Thyolo District, Malawi. Trop Med Int Health. 2011;16(10):1243-1250.
23. Cecatti JG, Souza JP, Parpinelli MA, de Sousa MH, Amaral E. Research on severe maternal morbidities and near-misses in Brazil: what we have learned. Reprod Health Matters. 2007;15(30):125-133.
24. World Health Organization. Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. World Health Organization: Geneva, 2011.

25. Nelissen E, Mduma E, Broerse J, et al. Applicability of the WHO maternal near miss criteria in a low-resource setting. PLoS One. 2013;8(4):e61248.
26. van den Akker T, Beltman J, Leyten J, et al. The WHO maternal near miss approach: consequences at Malawian District level. PLoS One. 2013;8(1):e54805.
27. Tura AK, Trang TL, van den Akker T, et al. Applicability of the WHO maternal near miss tool in sub-Saharan Africa: a systematic review. BMC Pregnancy Childbirth. 2019;19(1):79.
28. Verschueren KJ, Kodan LR, Paidin RR, et al. Applicability of the WHO maternal near-miss tool: A nationwide surveillance study in Suriname. J Glob Health. 2020;10(2):020429.

Part I.

Maternal death and near-miss surveillance

Chapter 2.

Confidential enquiry into maternal deaths in Namibia, 2018-2019: findings and lessons learned from implementation

Steffie Heemelaar, Beatrix Callard, Hilma Shikwambi, Jana Ellmies, Wilhelmina Kafitha, Jelle Stekelenburg, Thomas van den Akker, Shonag Mackenzie

Submitted

Abstract

Objective

Successful implementation of a national maternal death review was hampered by several challenges, including fear of blame among healthcare providers. First objective was to improve implementation by focussing on gaining trust of healthcare providers. Second objective was to describe findings of the review.

Methods

Confidential Enquiry into Maternal Deaths methodology was used to review maternal deaths. Reported maternal deaths, that occurred between 1 April 2018 and 31st of March 2019 in Namibia, were included. To improve implementation there was a focus on addressing fear of blame, dissemination of findings, and acting on recommendations.

Results

Seventy maternal deaths were reported; for 69 (98.6%) medical records were available, compared to 80/119 (67.2%) in 2012-2015. Reported maternal mortality ratio was 92/100 000 live births compared to 62/100 000 in 2012-2015 (OR 1.5, 95% CI 1.1-2.0). Obstetric haemorrhage and hepatitis E were leading causes of death. The “no name, no blame” policy, aiming to identify health system failures, rather than mistakes of individuals, was repeatedly explained to healthcare providers during facility visits. Recommendations based on findings of the review, such as retaining experienced staff, continuous in-service training and guidance, were shared with decision makers at regional and national levels. Healthcare providers received training based on lessons learned, which resulted in improved management of similar cases.

Conclusion

Nationwide implementation of Confidential Enquiry into Maternal Deaths was possible in a middle-income country. Focussing on obtaining trust of healthcare providers and feeding back findings, resulted in better reporting and prevention of potential maternal deaths.

Introduction

Namibia, an upper-middle income country in sub-Saharan Africa, has a high maternal mortality ratio (MMR) of an estimated 385/100,000 live births in 2013.[1] The Namibian government has been committed to reducing this MMR and reaching the target of 70/100,000 livebirths in 2030, as set by the sustainable development goals (SDG3).[2] Namibia is one of the least densely populated countries in the world with 2.8 people per square kilometre.[3] Key indicators suggest high access to maternity care, with 96.6% of women having at least one antenatal visit and 87.4% giving birth in a health facility in 2013.[1] However, these figures do not indicate whether women reached the facility in time, nor do they provide information about quality of care.

To analyse and improve the quality of care, a national maternal death review committee has analysed all maternal deaths since 2010, using the Confidential Enquiry into Maternal Deaths (CEMD) methodology.[4,5] There have been several challenges with successful implementation. With the confidential enquiry of 2012-2015 members of the national committee were informed by their clinical colleagues that they feared being blamed for the woman's death. This contributed to deaths not being reported and medical notes not being submitted for the review. This fear was exacerbated by media reports, accusing healthcare providers of bad attitudes, providing poor quality care or even holding them responsible for the death of a woman or baby.[6-9]

Around the world, healthcare providers are frequently blamed by leaders or decision makers when a woman dies.[10-12] When a healthcare provider does make a mistake, the challenging working conditions and failures of the health system are often not taken into consideration, nor addressed in order to prevent similar incidents in the future.[11,13] The unsupportive environment can result in lack of trust by healthcare providers, leading to a counterproductive effect on the performance of confidential enquires.[10-14]

During the review period of 1st of April 2018 up to the 31st of March 2019 the national committee focused on increasing trust of healthcare providers to improve the implementation of CEMD in Namibia. Here are described findings of the review, underlying causes of maternal death and lessons learned, as well as the process of gaining the trust of healthcare providers in Namibia.

Methods

The division of Quality Assurance of the Ministry of Health and Social Services (MoHSS) was responsible for the CEMD process.[15] Committee members did not receive any remuneration as improving quality of care is seen as one of the responsibilities of all staff. Members were appointed by the MoHSS.

It is a legal requirement to notify every maternal death to MoHSS.[15] Relatives of deceased women in Namibia reported home deaths either to a health facility or police station. For each home death, community health workers performed a verbal autopsy. The findings of this autopsy, and if available, medical records and the woman's health passport were reviewed at the nearest health facility.

Facility deaths were initially reviewed at facility level by the midwifery and medical staff working in obstetrics to identify and address lessons learned without delay. From facility level, matrons reported to the regional CEMD committee, which consisted of the regional medical director, an obstetrician when available or otherwise at least one experienced medical officer, and one or more nurse-midwives. At regional level, all documents were anonymized by administrative staff. All deaths were reviewed, and a summary report was written for each mortality meeting describing causes of death, identified lessons learned and proposed interventions. These reports were sent to national level, including copies of all medical records.

At national level, all deaths were reviewed by an expert committee. For this review, the national committee consisted of four obstetricians working in both the national referral hospital, the medical school and/or a private hospital, a medical doctor working in an Obstetrics and Gynaecology department in a public hospital, senior nurses and midwives from both public and private facilities, representatives of the Independent Midwives Association of Namibia and senior lecturers of all nursing-midwifery training institutions. A quorate meeting was when at least two medical doctors of which one was an obstetrician and at least two nurse/midwives were present.

A single underlying cause of death was identified by the national committee, defined as the cause which initiated the chain of events leading to death. Direct and indirect causes were defined according to the ICD-MM definitions.[16] Factors related to quality of care were categorized into either patient, administrative (e.g. lack of equipment, medical supplies, transport or supervision) or healthcare provider related. In conclusion, the received care by the woman was assessed as either 'good care', 'improvements to care would not have prevented the death', or 'improvements to care which may have prevented the death'.

To increase trust of healthcare providers in the review process the committee focussed on; addressing fear of being blamed, dissemination of findings at all levels and acting on the recommendations forthcoming from the enquiry. Whenever a committee member visited a facility, e.g. for data collection, provision of feedback or other quality improvement projects, the anonymous and confidential aspect of the review was explained. The staffing, working conditions, hospital facilities and equipment were noted. The importance of MD reporting and the CEMD as a tool to address these issues was emphasized.

Findings and recommendations were shared with all relevant stakeholders to improve implementation of the recommendations and the committee acted upon several recommendations themselves. All recommendations were shared with decision makers at Ministry level in a meeting with all relevant divisions present. Management staff and healthcare providers were visited in all 14 regions to discuss that regions' specific cases as well as to feedback important lessons learned at national level, and to follow up on implementation of previous recommendations. For healthcare providers, feedback was provided through a video conference and a two-day conference, which was attended by over 200 doctors and nurses, representing nearly all hospitals. Lastly, instantaneous feedback was provided throughout the review, meaning that if a review at national level identified findings of educational value, these findings were shared in a blame-free manner with healthcare providers at the facility where the death had occurred. Representatives of the medical and nursing/ midwifery training institutions were part of the national committee. These members were tasked with the incorporation of adequate training in the identification and management of the commonest conditions contributing to maternal deaths into the respective nursing and medical curricula to prepare future staff appropriately. Lastly, the most recent CEMD guidelines included a paragraph stating that the findings of CEMD could not be used for any medico-legal or disciplinary procedure and, if needed, MoHSS would provide legal support to ensure this.[15]

For each maternal death, data were extracted from medical records using a structured data collection tool, including socio-demographic characteristics, general and obstetric history, antenatal care history, laboratory and bacteriological results, pathology and autopsy reports.[15] Data were entered electronically, using Excel and Epidata v4.6.

Background data for number of live births (LB), maternal age, mode of birth, and HIV status were collected through the National Health Information Systems of Namibia. Findings were compared with the review of 2008-2012, of which the report was published, and the review of 2012-2015.[5] Possible associated factors for maternal

deaths were compared to the general pregnant population of Namibia and odds ratio (OR) and 95% confidence interval (CI) calculated. There were no national background data available to perform these calculations for potential risk factors such as parity, ANC attendance, or previous birth by caesarean section. Data analysis was performed with SPSS version 22 (IBM, Armonk, NY, USA).

Results

There were 76498 live births and 70 maternal deaths reported between 1 April 2018 and 31st of March 2019 giving an MMR of 92/100000 live births (LB). This is a statistically significant rise compared with the MMR of 62/100 000 LB in 2012-2015 (OR 1.5, 95% CI 1.1-2.0). There was no MMR available for the review of 2008-2012.[5] For 69/70 (98.6%) deaths medical records and reporting forms, filled in at facility level, were available and reviewed by the national committee, compared to 80/119 (67.2%) reviewed MD in the previous review. The current review included eight MD which occurred at home, compared to none in the previous reports.

Table 1 presents baseline characteristics of the reviewed deaths and Table 2 causes of maternal deaths. Most maternal deaths were from direct causes, 35/70 (50%), compared to 28/70 (40%) deaths from indirect causes. Obstetric haemorrhage and hepatitis E were the leading causes of death (both 11/70, 15.7%), followed by hypertensive disorders (9/70, 12.9%). There were no maternal deaths due to hepatitis E in previous reviews.

Table 1. Characteristics of all maternal deaths		
Characteristics	**(N = 70)**	**%**
Age		
< 20	5	7.1%
20-34	48	68.6%
≥ 35	16	22.9%
Unknown	1	1.4%
Parity		
Para 0	10	14.3%
Para 1-3	42	60.0%
≥ 4	13	18.6%
Unknown	5	7.1%
ANC attendance		
Yes	49	70.0%
No ANC	12	17.1%
Not applicable. pregnancy < 20 weeks	4	5.7%
Unknown	5	7.1%
Previous birth by caesarean section		
Yes	10	14.3%
No	58	82.9%
Unknown	2	2.9%
HIV status		
Positive	22	31.4%
Negative	38	54.3%
Unknown	10	14.3%
Mode of birth[a]		
Normal vaginal birth	31	62.0%
Instrumental birth	1	2.0%
Caesarean section	17	34.0%
Laparotomy uterine rupture	1	2.0%
Facility for birth		
Home	8	11.4%
Health centre	2	2.9%
Hospital	45	64.3%
Unknown	2	2.9%
Pregnant at time of death	13	18.6%
ANC. antenatal care.		

[a] Percentages given for 50 MD as 7 women had a miscarriage 13 women died antepartum.

Table 2. Causes of maternal deaths		
Causes of maternal death	**(N = 70)**	**%**
Direct deaths	**35**	**50.0%**
Obstetric haemorrhage	11	15.7%
Uterine atony	5	7.1%
Retained placenta	2	2.9%
Uterine rupture with previous scar	1	1.4%
Uterine rupture without previous scar	1	1.4%
Placental abruption with hypertension	1	1.4%
Abruptio without hypertension	1	1.4%
Hypertensive disorder	9	12.9%
Eclampsia	3	4.3%
Stroke	3	4.3%
HELLP	1	1.4%
Pre-eclampsia	1	1.4%
Pulmonary oedema	1	1.4%
Pregnancy with abortive outcome	6	8.6%
Septic miscarriage	4	5.7%
Ectopic pregnancy	1	1.4%
Abortion related haemorrhage	1	1.4%
Pregnancy related infection	5	7.1%
Puerperal sepsis after NVB	2	2.9%
Puerperal sepsis after caesarean section	2	2.9%
Puerperal sepsis due to bladder injury with caesarean section	1	1.4%
Other obstetric complications	2	2.9%
Pulmonary embolism	2	2.9%
Anaesthetic death	2	2.9%
Indirect deaths	**28**	**40.0%**
Hepatitis E	11	15.7%
Tuberculosis	7	10.0%
Cardiac disease	7	10.0%
Other infection	2	2.9%
Pneumonia	1	1.4%
Multi-organ failure, unclear cause	1	1.4%
Gastro-intestinal tract	1	1.4%
Unknown cause of death	**7**	**10.0%**
Lack of information	6	8.6%
Died at home	1	1.4%

HELLP, haemolysis elevated liver enzymes and low platelets; NVB, normal vaginal birth.

Table 3. Avoidable factors classified according to patient. health system and healthcare provider related and conclusion national committee		
Patient related factors	**(N = 69)**	**%**
No antenatal care	16	23.2%
Infrequent antenatal care	5	7.2%
Delay in woman seeking care	20	29.0%
Refusal of treatment or admission	8	11.6%
Unsafe abortion	4	5.8%
Health system related factors	**(N = 69)**	**%**
Lack of transport from home to health care facility	2	2.9%
Lack of transport between health care facilities	9	13.0%
Lack of accessibility	3	4.3%
Delay initiating critical care (overburdened facility)	37	53.6%
Communication breakdown between healthcare providers	13	18.8%
Lack of facilities. equipment or consumables	22	31.9%
Lack of human resources (doctors/nurses)	29	42.0%
Lack of expertise. training or education	43	62.3%
Lack of specialist	8	11.6%
Healthcare provider related factor	**(N = 69)**	**%**
Problem with recognition/diagnosis	40	58.0%
Delay in referring patient	38	55.1%
Managed at inappropriate level	34	49.3%
Incorrect management (incorrect diagnosis)	30	43.5%
Sub-standard management (correct diagnosis)	33	47.8%
Not monitored / infrequently monitored	30	43.5%
Prolonged abnormal monitoring with no action taken	33	47.8%
Conclusion substandard care	**(N = 70)**	**%**
Yes. it was a preventable death. improvements to care may have made a difference to outcome	40	57.1%
Substandard care. but improvements to care would have made no difference to outcome	17	24.3%
No. good care	10	14.3%
Unknown. lack of information	3	4.3%

For 69/70 maternal deaths. the file was available for assessment of avoidable factors by the national committee.

Most avoidable factors were related to healthcare providers and administrative factors, Table 3. The commonest avoidable factors were 'lack of expertise, training or education' (62.3%), 'problems with recognition and/or diagnosis' (58.0%), 'delay in referring the patient' (55.1%) and 'delay in initiating critical care due to overburdened facility' (53.6%). For example, for several maternal deaths, the healthcare providers did not recognize the woman had signs of hypovolemic or septic shock. Some critically ill women could not be admitted to an intensive care unit because no intensive care beds were available. For 22 cases, it was noted that there was lack of access to basic but essential services such as emergency blood or magnesium sulphate. There were patient related factors in some cases, of which delay in seeking care was most common (20/69, 29.0%). There were eight women who defaulted their tuberculosis or antiretroviral treatment for HIV. The committee concluded that in 40 (57.1%) of cases, maternal death may have been prevented if improved care had been provided, Table 3. For three deaths the committee could not determine whether the death could have been prevented: for two deaths the medical records were incomplete and for one death no records were available.

Possible associated factors for maternal death are presented in Table 4. Home birth (OR 7.48, 95% CI 3.18-17.58), birth by caesarean section (OR 3.17, 95% CI 1.76-5.68), and being HIV positive (OR 2.56 95% CI 1.55-4.24) were associated with maternal death, whereas age <20 years appeared to be protective against maternal death (OR 0.34, 95% CI 0.14-0.85). There were 22 HIV-positive women, of whom seven died of an AIDS-defining illness; five due to tuberculosis, two had stage 4 HIV-related illness and died of a lower respiratory tract infection and complications of a septic miscarriage respectively. Five women defaulted antiretroviral treatment. None of the HIV-positive women were given isoniazid preventive therapy as recommended in the Namibian HIV guidelines.[17]

Table 4. Possible associated factors for maternal death

Risk factor	**MD**	**Namibia**	**OR (95% CI)**
	(N=70)	**(N = 76 428)**	
Age <20 years	7,1%	18,4%	0.34 (0.14-0.85)
Age ≥ 35 years	22,9%	15,1%	1.67 (0.95-2.91)
Home birth	12,0%	1,8%	7.48 (3.18-17.58)
Instrumental birth	2,0%	0,4%	5.57 (0.77-40.50)
Birth by caesarean section	34,0%	14,0%	3.17 (1.76-5.68)
HIV-positive	31,4%	15,2%	2.56 (1.55-4.24)

MD, maternal death; OR, odds ratio; CI, confidence interval.

On several occasions instantaneous feedback was provided. For example, after review of a maternal death related to failed intubation, in-service anaesthetic refresher training was provided. A similar event occurred one week later in the same facility and both the woman and her baby were saved. On another occasion, training was provided to a facility where poor management of hypertension was observed. The following month a similar case was observed to be appropriately managed.

During a writing meeting, key findings and recommendations for the annual report were identified. Most of the key findings and recommendations were similar to those of previous reviews, and mainly related to healthcare providers and administrative factors. After the previous review, one of the most important interventions had been to provide Emergency Obstetric Care training to several doctors and nurses in each hospital, including an instructor course to facilitate continuous training of local colleagues. The continued provision of training locally was compromised by rotation of trained staff to other departments.

During facility visits it also appeared that several deaths were not reported to national level. Cases were expected to be reported after completion of the complete review cycle, and reporting documents had to include notes of an audit meeting and an autopsy report. Due to a variety of reasons, such as high workload of staff or missing documents, the review cycle was not always completed and, subsequently, the death not reported. To improve reporting the national committee amended the reporting system.[15] A brief rapid notification form was introduced, whereby the attending healthcare provider, involved in the care for a woman who died, was expected to report the death within 24 hours to national level, even if very scarce details pertaining to the death were available at that time.

During the meeting with decision makers at Ministry level, several issues, such as lack of experienced staff, continuous in-service training and guidance and the availability of essential medication and equipment were discussed. The MoHSS human resources department took immediate steps to retain experienced staff in obstetric departments.

Discussion

The national committee aimed to further improve implementation of the CEMD in Namibia, by increasing trust of healthcare providers in the review process, which appears to have resulted in improved reporting and availability of nearly all medical records. Obstetric haemorrhage and hepatitis E were the leading causes of death and most avoidable factors were related to the healthcare providers and administrative factors.
The national CEMD committee of Namibia used several interventions that are not part of standard CEMD methods applied elsewhere.[4] For instance, instead of waiting for the annual report, the national committee addressed important issues immediately after review of a maternal death. Using such timely feedback to facilities, potential deaths were avoided in the short term.

Secondly, during the review period members of the national committee visited nearly all hospitals at least once to enhance implementation of the CEMD. Also, these visits provided useful information for the establishment of key findings and recommendations, in addition to review of medical records only. Common challenges such as shortages of staff or equipment were often not mentioned in a woman's file as staff consider this the normal situation at the facility. For example, in one district hospital there happened to be only one blood pressure machine, which had to be shared between several wards. In this hospital there was a maternal death, with lack of blood pressure monitoring being a contributing factor.

Furthermore, due to these visits and the personal contact, committee members became more approachable to staff of the facilities. Availability of supervision and guidance by experienced doctors and nurse-midwives was previously limited in most health centers and smaller district hospitals. During improved CEMD implementation, committee members were contacted more frequently for clinical advice, which resulted in more timely referrals of critically ill women, which directly improved quality of care for individual women.

Lastly, in order to increase emphasis on the achievements of healthcare providers, the national committee also implemented 'Maternal Near-Miss' surveillance; a nationwide registry collecting quantitative data regarding such severe maternal morbidity, since this provided acknowledgement to the number of women that had been saved, rather than putting emphasis on maternal deaths only.[18]

Several challenges remained. All data pertaining to maternal deaths had to be entered manually in an electronic database at national level. This was done by

administrative staff, who were supported by several committee members. Such a system is difficult to sustain. Possibilities for electronic data collection at facility or regional level are currently being explored.

The committee has not yet addressed the media and their negative reporting on healthcare providers. During the meeting at ministry level, it was attempted to increase recognition of achievements of healthcare providers by politicians and high government officials. Recognition by supervisors and higher-level officials is important for several reasons. It has a positive effect on the performance of CEMD and the provided quality of care.[11,13] Furthermore, a study performed in Namibia indicated that lack of recognition was associated with the provision of disrespectful maternity care.[19]

Currently, due to severe staff shortages, junior staff are forced to make decisions and perform procedures above their level of competency and senior staff are unable to provide enough supportive supervision. In several cases this affected the quality of provided care, which may have contributed to the death of the woman. These experiences may be demotivating, may cause psychological distress or even make healthcare providers leave their jobs.[20-22] One of the key recommendations was therefore employment of more staff and retaining experienced staff. The MoHSS has an active programme of training Namibian specialists and it is anticipated that the number of Specialist obstetricians employed in public hospitals will increase over the next few years.

A reliable MMR is crucial for monitoring progress over time. However, the identified MMR in the current review is still far lower than estimated by the demographic health survey or WHO, suggesting underreporting is still present.[1,23] Half of the reported home deaths occurred within the same region whereas other regions with rural communities reported no home deaths. A survey performed in the five southern regions identified an underreporting of more than 70 percent through national reporting in 2010-2012.[9] The identified rise in the current review may suggest better reporting. However, there may have been an actual rise due to the nationwide hepatitis E outbreak since December 2017. Hepatitis E during pregnancy has an estimated case fatality rate of 20% and it was one of the leading causes of death in the current review.[24,25] Large discrepancies between MMRs based on national reporting and vital statistics, as identified in Namibia, were also found in other low and- middle-income countries such as South Africa, Ethiopia and Malawi.[12,26,27] Enhanced implementation of CEMD will enable Namibia to produce a more accurate MMR, as in the United Kingdom, France and the Netherlands, countries with a low MMR and well-functioning surveillance system, CEMD is the most accurate method for maternal mortality surveillance in comparison to vital statistics.[28]

Namibia has a high teenage pregnancy rate of 18.0%. Surprisingly, we found that teenagers are less likely to have a maternal death compared to all other ages. Possibly, the risk for poor outcome of teenagers differs per complication. Due to our small numbers we cannot analyse this finding in further detail. The CEMD in South Africa showed that teenagers are at higher risk of death from anaesthetic complications, hypertension and pregnancy-related infections but less likely from other causes.[29]

The high proportion of preventable deaths, challenges with reporting and failed implementation of recommendations from previous reviews were discouraging findings. But looking at other countries, these experiences are not unique. South Africa, which started with CEMD in 1998, had similar recommendations until 2007 and only started to see a reduction in maternal deaths from 2011.[27] In 2014, 57% of the reviewed deaths in South Africa were classified as preventable.[30] But also countries with a low MMR, such as the United Kingdom or the Netherlands identified substandard care in more than half of their reviewed deaths.[31,32]

Conclusion

This Namibian CEMD review of 2018-2019 indicates that 'in-facility' delays contribute most to substandard care in Namibia. Within the five-step 'obstetric transition' as described by the World Health Organization, Namibia is now in stage III, where women are reaching the health facility, and improving quality of maternity care becomes the critical step to achieve a reduction of maternal mortality.[33] CEMD is designed to assess and improve quality of care, but successful implementation is key. In Namibia several challenges with implementation were overcome by focussing on gaining trust of healthcare providers and the provision of guidance and support. However, MD reporting needs to improve, as only with a reliable MMR can the impact of interventions be monitored. We recommend other countries performing CEMD to implement instantaneous feedback before the end of the review period to avoid preventable deaths as soon as possible.

References

1. Ministry of Health and Social Services. Demographic and Health Survey Namibia 2013. Ministry of Health and Social Services: Windhoek, 2014.
2. Geingob H. Harambee Prosperity Plan; 2016. (Available from: http://www.nied.edu.na/assets/documents/08Governments/13HPP_page_70-71.pdf) [19-01-2020]
3. Namibia Statistics Agency. Namibia Inter-censal Demographic Survey 2016. Namibia Statistics Agency: Windhoek, 2017.
4. World Health Organization. Beyond the Numbers. Reviewing maternal deaths and complications to make pregnancy safer. World Health Organization: Geneva, 2004.
5. Lihongeni M, Indongo N. Causes and risk factors of maternal deaths in Namibia. University of Namibia: Journal for Studies in Humanities and Social Sciences. 2012;3):239-252.
6. Kangootui N. Nurses guilty of Kleopas' death. The Namibian, 22-05-2014.
7. Kooper L. Woman dies after nurses refuse to help. The Namibian, 08-12-2016.
8. Shinana K. No care, no empathy. Namibian Sun, 22-08-2015.
9. Ministry of Health and Social Services. Report of the Prevalence and Contributing Factors of Facility-Based Maternal and Neonatal Deaths in Five Regions of Namibia (Erongo, Hardap, //Karas, Khomas, Omaheke) during 2010–2012. Hardap Regional Health Directorate: Mariental, 2014.
10. Hodorogea S, Friptu V. The Moldovan experience of maternal death reviews. Br J Obstet Gynaecol. 2014;121 Suppl 4):81-85.
11. Lewis G. The cultural environment behind successful maternal death and morbidity reviews. BJOG. 2014;121 Suppl 4):24-31.
12. Melberg A, Mirkuzie AH, Sisay TA, Sisay MM, Moland KM. 'Maternal deaths should simply be 0': politicization of maternal death reporting and review processes in Ethiopia. Health Policy Plan. 2019;34(7):492-498.
13. Rousseva C, Kammath V, Tancred T, Smith H. Health workers' views on audit in maternal and newborn healthcare in LMICs: a qualitative evidence synthesis. Trop Med Int Health. 2020;25(5):525-539.
14. Smith H, Ameh C, Roos N, Mathai M, Broek NVD. Implementing maternal death surveillance and response: a review of lessons from country case studies. BMC Pregnancy Childbirth. 2017;17(1):233.
15. Ministry of Health and Social Services Division Quality Assurance. National Guidelines for Review and Response to Maternal Deaths, Near Misses, Stillbirths and Neonatal Deaths. Windhoek, 2019.
16. World Health Organization. The WHO Application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM. Geneva, 2012.
17. Directorate of Special Programmes Ministry of Health and Social Services. Namibian HIV Guidelines Fifth Edition. Ministry of Health and Social Services: Windhoek, 2016.
18. Heemelaar S, Josef M, Diener Z, et al. Maternal near-miss surveillance, Namibia. Bull World Health Organ. 2020;98(8):548-557.
19. Wesson J, Hamunime N, Viadro C, et al. Provider and client perspectives on maternity care in Namibia: results from two cross-sectional studies. BMC Pregnancy Childbirth. 2018;18(1):363.
20. Chimwaza W, Chipeta E, Ngwira A, et al. What makes staff consider leaving the health service in Malawi? Hum Resour Health. 2014;12):17.
21. Muliira RS, Bezuidenhout MC. Occupational exposure to maternal death: psychological outcomes and coping methods used by midwives working in rural areas. Midwifery. 2015;31(1):184-190.
22. Pezaro S, Clyne W, Fulton EA. A systematic mixed-methods review of interventions, outcomes and experiences for midwives and student midwives in work-related psychological distress. Midwifery. 2017;50):163-173.
23. Maternal Mortality Estimation Inter-Agency Group. Maternal mortality in 2000-2017. Internationally comparable MMR estimates by the Maternal Mortality Estimation Inter-Agency Group (MMEIG), Namibia. World Health Organisation: Geneva, 2017.
24. Jin H, Zhao Y, Zhang X, Wang B, Liu P. Case-fatality risk of pregnant women with acute viral hepatitis type E: a systematic review and meta-analysis. Epidemiol Infect. 2016;144(10):2098-2106.
25. Outbreak of Hepatitis E Virus (HEV) in Namibia, Situation Report (SITREP No. 64); 2019. (Available from: https://www.afro.who.int/sites/default/files/2019-08/National%20SITREP%2064%20on%20Hepatitis%20E%20%20%20outbreak%20Final.pdf) [19-01-2020]
26. Mataya R, Kachale F, Chiudzu G, Kwaitaine, Oyeyipo C, Dube Q, et al. Report on the Confidential Enquiry into Maternal Deaths in Malawi (2008-2012). Ministry of Health Republic of Malawi: Blantyre, 2014.

27. Moodley J, Pattinson RC, Fawcus S, et al. The Confidential Enquiry into Maternal Deaths in South Africa: a case study. BJOG. 2014;121(Suppl 4):53-60.
28. Creanga A. Maternal mortality in the developed world: a review of surveillance methods, levels and causes of maternal deaths during 2006-2010. Minerva Ginecol. 2017;69(6):608-617.
29. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2011-2013: Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa. Department Health: Republic of South Africa: Pretoria, 2015.
30. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2014, Annual report and detailed analysis of maternal deaths due to non-pregnancy related infections. Department Health: Republic of South Africa: Pretoria, 2015.
31. Schutte JM, Steegers EA, Schuitemaker NW, et al. Rise in maternal mortality in the Netherlands. BJOG. 2010;117(4):399-406.
32. M. Knight, K. Bunch, D. Tuffnell, J. Shakespeare, R. Kotnis, S. Kenyon, et al. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2015-17. University of Oxford National Perinatal Epidemiology Unit: Oxford 2019.
33. Souza JP, Tuncalp O, Vogel JP, et al. Obstetric transition: the pathway towards ending preventable maternal deaths. BJOG. 2014;121(Suppl 1):1-4.

Chapter 3.

Measuring maternal near-miss in a middle-income country: assessing the use of WHO and sub-Saharan Africa maternal near-miss criteria in Namibia

Steffie Heemelaar, Leonard Kabongo, Taati Ithindi, Christian Luboya, Fidelis Munetsi, Ann-Kathrin Bauer, Amelie Dammann, Anna Drewes, Jelle Stekelenburg, Thomas van den Akker, Shonag Mackenzie

Glob Health Action. 2019;12(1):1646036

Abstract

Background

Namibia, a middle-income country in sub-Saharan Africa (SSA), plans to use the Maternal Near-Miss (MNM) approach. Adaptations of the World Health Organization (WHO) MNM defining criteria ('WHO MNM criteria') were previously proposed for low-income settings in sub-Saharan Africa ('SSA MNM criteria'), but whether these adaptations are required in middle-income settings is unknown.

Objective

To establish MNM criteria suitable for use in Namibia, a middle-income country in SSA.

Methods

Cross-sectional study from 1 March 2018 to 31 May 2018 in four Namibian hospitals. Pregnant women or within 42 days of termination of pregnancy or birth, fulfilling at least one WHO or SSA MNM criterion were included. Records of women identified by either only WHO criteria or only SSA criteria were assessed in detail.

Results

194 Women fulfilled any MNM criterion. WHO criteria identified 61 MNM, the SSA criteria 184 MNM. Of women who only fulfilled any of the unique SSA MNM criteria, 18 fulfilled the criterion 'eclampsia', one 'uterine rupture' and five 'laparotomy'. These women were assessed to be MNM. Thresholds for blood transfusion to define MNM due to haemorrhage were two units in the SSA and five in WHO set. Two or three units were given to 95 women for mild/moderate haemorrhage or chronic anaemia who did not fulfil any WHO criterion and were not considered MNM. Fourteen women who were assessed to be MNM from severe haemorrhage received four units.

Conclusion

WHO MNM criteria may underestimate and SSA MNM criteria overestimate the prevalence of MNM in a middle-income country such as Namibia, where MNM criteria 'in between' may be more appropriate. Namibia opts to apply a modification of the WHO criteria, including eclampsia, uterine rupture, laparotomy and a lower threshold of four units of blood to define MNM. We recommend that other middle-income countries validate our criteria for their setting.

Introduction

Maternal mortality has been reduced but remains high in sub-Saharan Africa (SSA).[1] Even though sub-Saharan African countries aim for zero avoidable maternal deaths, many struggle to achieve substantial progress.[1-5] To further improve quality of maternity care, the World Health Organization (WHO) has promoted the Maternal Near-Miss (MNM) approach since 2004.[6] An MNM is 'a woman who nearly died but survived a pregnancy-related complication during pregnancy, birth or within 42 days after termination or birth'.[6] Women with an MNM event often share the same characteristics and risk factors as women who died, such as underlying medical or pregnancy-related conditions and delays in reaching and obtaining adequate health care. Much can be learned with regard to the functioning of the health system, and failing of the system, by analysing MNM and maternal deaths. However, MNM occurs in larger numbers and may be less threatening for health-care workers to discuss since these can be regarded as great saves.[7,8]

Namibia has a high maternal mortality ratio of an estimated 385/100,000 livebirths in 2013.[9] Even though it has a very large surface area, it is one of the least densely populated countries in the world with 2.8 people per square kilometre.[10] Annually, there are around 75,000 births.[10] To analyse and improve maternity care, Namibia is planning to apply the MNM approach. Adoption of a recognized set of MNM criteria will allow comparison across settings and is therefore preferred. Reports from other SSA countries indicated that the WHO MNM criteria (Appendix 1) may not be suitable for use in district hospitals in low-income settings, due to limited availability of laboratory tests, blood products and management options leading to under-registration of MNM.[11,12] Recently, a Delphi study was published proposing MNM criteria deemed suitable for hospitals in low-income settings in SSA.[13] The SSA criteria added several clinical criteria such as eclampsia, sepsis and uterine rupture and lowered the threshold for blood transfusion from five to two units of red cells (Appendix 1). For Namibia, classified by the World Bank as a sub-Saharan upper middle-income country, it is unclear which set of MNM criteria would be appropriate to use.[14] The national referral hospital in Windhoek, the capital of Namibia, has all the facilities to apply the WHO MNM criteria, but in district hospitals, several laboratory tests to identify organ failure or management options are not available. Nevertheless, Namibian district hospitals are generally better supplied compared to most district hospitals in low-income settings in SSA. The aim of this study was to establish MNM criteria suitable for use in all Namibian hospitals by applying both the WHO and the adapted SSA MNM criteria to a cohort of women in four Namibian hospitals.

Methods

Study setting and design

Participating facilities were the national referral hospital, Windhoek Hospital Complex (Hospital A), a large regional hospital, Rundu Intermediate Hospital (Hospital B), and two smaller district hospitals, Gobabis and Okahandja State Hospital (Hospital C and D). The hospitals were selected based on their characteristics, to obtain a representative sample of Namibian hospitals. Namibia has only three regional hospitals of which one is part of the hospital complex in the capital (Hospital A). Hospital B and the third regional hospital (not included) are similar in terms of number of births, available resources and catchment area. Of the 31 district hospitals, approximately half have more than 2000 births annually. Staff and resources are allocated accordingly. We selected two district hospitals representing a higher and lower burden facility. Since Namibia is a large but sparsely populated country with long distances between health-care facilities, Hospital C was chosen since this facility is located in one of the least densely populated districts.

Hospital A is located in the capital, has almost 14,000 births annually, and is the only tertiary facility in Namibia for the entire population of 2.3 million.[10] There are three consultant obstetrician and gynaecologists. The Intensive Care Unit (ICU) has advanced equipment including ventilators and a dialysis machine. Sophisticated laboratory tests including pH and lactate measurements are available to identify and manage organ failure. Hospital B is located near the Angolan border, has just over 6,000 births annually and serves a population of approximately 350,000.[10] There is one consultant gynaecologist, an ICU with mechanical ventilation and a well-supplied blood bank. The district hospitals have around 2500 and 1200 births, respectively, and there are no ICU facilities or consultants. Hospital C has basic haematology and chemistry laboratory tests available on site. Hospital D has no laboratory tests on site. Both district hospitals have a reliable supply of red cells for blood transfusion but no other blood products.

For this prospective cross-sectional study we included all pregnant women or within 42 days after termination of pregnancy or birth, regardless of gestational age, fulfilling at least one WHO or SSA MNM criterion. Furthermore, they had to present between 1 March 2018 and 31st of May 2018 to the participating facilities.[6,13] Maternal deaths, defined as death of a woman while pregnant or within 42 days of termination of pregnancy or birth, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes, were excluded.[6]

MNM identification criteria and sample size

The WHO and SSA criteria are presented in Appendix 1. The SSA criterion 'Laparotomy other than caesarean section' was modified to 'Laparotomy other than caesarean section (CS) or ectopic pregnancy', since we anticipated an over-reporting of ectopic pregnancies that were not necessarily an MNM. The threshold of transfusion of two units of blood was adopted from the SSA MNM criteria. The WHO MNM criterion defining MNM from haemorrhage has a threshold of five units of blood, so inclusion from two units of blood and above would allow further analysis of the women who received two, three or four units of blood to identify which threshold would most accurately define severe haemorrhage without over-reporting mild or moderate haemorrhage. In the proposed SSA criterion 'severe pre-eclampsia with ICU admission', ICU was not clearly defined. For our study, we decided to regard the ICU as a ward where mechanical ventilation and administration of continuous vasoactive drugs were possible, together with the continuous presence of a medical doctor.

At the time of design of the study, the performance of the SSA criteria was not yet assessed in clinical setting, rendering sample size calculations difficult. A large global study performed by the WHO found a prevalence of approximately 15 MNM per 1000 live births in countries with a maternal mortality ratio similar to that of Namibia.[6,15] Considering the lower threshold for transfusion and the addition of clinical criteria, we expected the SSA criteria to identify approximately twice as many MNM. To identify at least five MNM in the district hospitals, we set our study period at 3 months, with the possibility to extend it with another 3 months in case of insufficient inclusions in hospital C and D.

Data collection and analysis

Doctors and nurses working in participating facilities, involved in the care of pregnant and/or postpartum women were trained in MNM identification and data collection prior to the study by members of the research team. A manual with information on data collection was present in each participating facility. MNM identification and data collection were supported in hospital A through daily visits to the maternity wards, gynaecology wards, acute care and ICU by AB, AD, AD, SH. On the respective wards, the admission books were screened for possible missed MNM. The register of the blood bank was screened for missed MNM by screening blood units delivered to the above-mentioned wards. Daily rounds and screening of blood bank registers were not feasible in the other hospitals due to budget and logistical restrictions. In hospitals B, C and D a doctor and two nurses were in charge of the project. These staff members were supervising MNM identification and data collection and were in close contact with the research team for support.

For the identified MNM, data were collected anonymously from medical records using a structured data collection tool, including socio-demographic characteristics, contributing factors, maternal and neonatal outcome, the main cause of MNM and long-term complications. All collected data were verified with medical records by either SH, LK, CL, FM, SM, who are medical doctors with at least 3 years of experience providing obstetric care in Namibia. We collected the total number of live births and maternal deaths that occurred within the facility during the study period. Data were double entered and crosschecked in Epidata version 4.2. Data analysis consisted of frequencies of demographic and clinical variables. Data analysis was performed with SPSS version 22. All results are reported as numbers (n) and frequencies. Confidence intervals (CI) were calculated using the Clopper-Pearson exact test.

Severe maternal outcome (SMO) was defined as the number of MNM and maternal deaths combined. The MNM ratio was defined as the number of maternal near-miss per 1000 live births and the SMO ratio by the number of women with SMO per 1000 live births.[6] The confidence interval was calculated using Poisson distribution.

In order to establish MNM criteria which will identify all MNM in Namibian hospitals without over-reporting minor morbidities we did the following: for the women identified as an MNM by one of the unique criteria, medical records were reviewed by SH, LK, CL, FM, SM. Based on their clinical judgement it was decided for each unique criterion if it should be used for MNM identification in Namibia.

This study was reviewed and approved by the research unit of the Namibian Ministry of Health and Social Services. We followed the STROBE reporting guidelines.

Results

In the three-month study period, 194 women were identified to be MNM according to the WHO and/or SSA criteria. Of these 194 MNM, 31 were identified through the blood bank register and ward registers of hospital A. Nine women were included by staff, but upon verification with medical records, it appeared these did not fulfil any MNM criterion and were excluded. Four of these nine women were included for ‘severe pre-eclampsia with ICU admission’, however these women were not admitted to an ICU department. Two women received one unit of blood for transfusion, whereas the threshold of the MNM criterion was at least two units of blood. Two women were included for sepsis but did not reach any of the clinical thresholds in the definition of the SSA criterion, Appendix 1. One woman was included for uterine rupture. However, only a pending uterine rupture was found with the lower uterine segment thin but intact.

Table 1. Characteristics of all maternal near-miss women		
Characteristics	**(N = 194)**	**%**
Age		
< 20	32	16.5%
21-34	130	67.0%
≥ 35	32	16.5%
Parity		
Para 0	60	30.9%
Para 1-3	114	58.8%
≥ 4	18	9.3%
Unknown	2	1.0%
Gestational age[a]		
≤ 12 weeks	32	16.5%
13 - 26 weeks	25	12.9%
27 - 36 weeks	46	23.7%
≥ 37 weeks	80	41.2%
Unknown	11	5.7%
Previous CS		
No	155	79.9%
Yes	32	16.5%
Unknown	7	3.6%
HIV status		
Positive	18	9.3%
Negative	144	74.2%
Unknown	32	16.5%
Chronic anaemia		
No	118	60.8%
Yes	32	16.5%
Unknown	44	22.7%
Other comorbidities		
Astma	1	0.5%
GDM	2	1.0%
Chronic hypertension	3	1.5%
TB	1	0.5%
Nephrotic syndrome	1	0.5%
Unknown	6	3.1%
Pregnancy outcome		
NVB	57	29.4%
Vacuum	3	1.5%
CS	71	36.6%
Laparotomy uterine rupture	2	1.0%
Miscarriage	31	16.0%
Ectopic	15	7.7%
Pregnant at time of discharge	14	7.2%
TOP	1	0.5%

NVB, normal vaginal birth; CS, caesarean section; TOP, termination of pregnancy; GDM, gestational diabetes mellitus.

[a] Number of completed weeks at the end of pregnancy or on admission if still pregnant at time of discharge.

Characteristics of the identified MNM are presented in Table 1. There were 32 (16.5%) teenage pregnancies and 60 (30.9%) women were primiparous. Chronic anaemia was present in 32 (16.5%) women. Obstructed labour was present in 18 (9.3%) women and 71 (36.6%) women gave birth by caesarean section. Miscarriage was present in 31 women, of whom 28 needed surgical evacuation, one women received medical treatment and two women had a spontaneous complete abortion.

Table 2. For each hospital number of live births, maternal near-miss, maternal deaths, MNM ratio and the SMO ratio.

Facilities	Livebirths	MNM	MD	MNM / 1000 LB	95% CI	SMO/ 1000 LB	95% CI
Hospital A	3515	150	6	43	36 - 50	44	37 - 51
Hospital B	1326	30	3	23	15 - 31	25	16 - 33
Hospital C	664	12[a]	0	18	8 - 28	18	8 - 28
Hospital D	267	6[a]	0	22	4 - 40	22	4 - 40
Total	5772	194	9	34	29 - 38	35	30 - 40

MNM, maternal near-miss; MD, maternal death; LB, livebirths; CI, confidence Interval; SMO, severe maternal outcome.

[a] Three MNM women from hospital C and one MNM woman from Hospital D were referred to hospital A and part of the total number of these hospitals.

Table 2 shows the number of live births, MNM, MD, MNM ratio and SMO ratio for each hospital. Hospital A had the most live births (3515) in the three-month study period, most MNM (150) and the highest MNM ratio (43/1000 live births). The six maternal deaths in hospital A were due to tuberculosis (2), hepatitis E (2), ruptured uterus (1) and septic miscarriage (1). The three maternal deaths in hospital B were due to complicated malaria (2) and a woman who died upon arrival due to an unclear cause. The SMO ratio for all hospitals was 35/1000 live births, 95% CI 30–40.

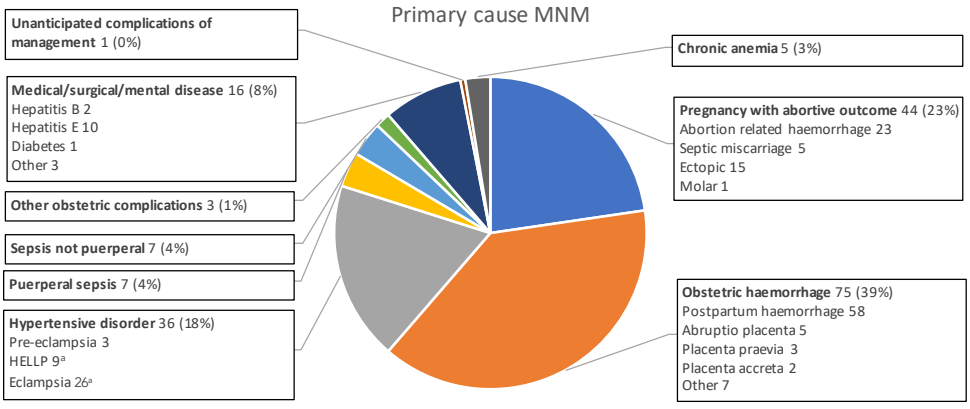


Figure 1. Primary cause of maternal near-miss. N = 194
[a] Two women with eclampsia also had HELLP syndrome and are counted twice.

Underlying causes of MNM and MNM criteria

The underlying cause of the MNM is presented in Figure 1. The commonest causes were obstetric haemorrhage (75, 38.7%, 95% CI 31.8–45.9), abortion-related complications (44, 22.7%, 95% CI 17.0–29.2) and hypertensive disorders (36, 18.6%, 95% CI 13.3–24.8).

Table 3 compares the two sets of MNM criteria and the frequency of each criterion present among the 194 MNM. The frequencies of each criterion separated for the four hospitals are presented in Appendix 2. Of the unique SSA criteria, eclampsia and sepsis were most frequently present with 26 women fulfilling each of these criteria. Eighteen women with eclampsia and 16 women with sepsis did not fulfil any WHO criterion and would have been missed by this set of criteria. Sepsis was caused by endometritis (6), septic miscarriage (3), pyelonephritis (2), wound sepsis (2), abdominal sepsis (2) and pneumonia (1). For these women, sepsis resolved within 24 h after starting antibiotics, wound treatment or evacuation of retained products of conception and therefore were assessed as not severe morbidity. There were two women with uterine rupture of whom one did not fulfil any other WHO criterion. All women with eclampsia and uterine rupture were assessed as severe morbidity. Four women with severe malaria had also either renal, hepatic or neurological dysfunction and this criterion did not contribute to the identification of MNM. The five women who fulfilled the criterion of 'laparotomy other than caesarean section or ectopic pregnancy' but no other (WHO) criteria were due to septic cervical ectopic pregnancy not suitable for vaginal approach (Text box 1 case 3), laparotomy after caesarean section to perform B-lynch suture, perforated appendix, septic abdominal pregnancy and transabdominal approach to remove missed miscarriage in second trimester after failed medical induction. All five were assessed as having sustained severe morbidity. Of the unique WHO criteria, 'bilirubin > 100 mmol/L' was most frequently present, in 13 women. At the time of study, a hepatitis E outbreak was ongoing and became the underlying disease in ten MNM and two maternal deaths.

Table 3. Frequencies of maternal near-miss by type of organ system dysfunction			
MNM identification criteria	**Total per MNM criterion (n=194)**	**MNM by SSA only (n=133)**	**MNM by WHO only (n=10)**
	N, % (95% CI)		
Severe maternal complications	72, 37.3% (30.3 – 44.3)		
Eclampsia	26	18	
Sepsis or severe systemic infection	26	16	
Uterine rupture	2	1	
Pulmonary oedema	7	2	
Severe abortion complications	8	3	
Severe malaria	4	0	
Severe pre-eclampsia with ICU admission	4	1	
Laparotomy other than caesarean section or ectopic pregnancy	12	5	
Cardiovascular dysfunction	21, 10.8% (6.8 – 16.1)		
Shock	20		
Cardiac arrest	0		
Use of continuous vasoactive drugs	3		0
CPR	0		
pH < 7.1	1		1
Lactate >5 mEq/mL	0		0
Respiratory function	16, 8.2% (4.8 – 13.0)		
Acute cyanosis	0		
Gasping	0		
Respiratory rate >40 or <6/min	5		
Intubation and ventilation for ≥60 minutes not related to anaesthesia	11		
Oxygen saturation <90% for ≥60 minutes	4		
Renal dysfunction	4, 2.1% (0.6 – 5.2)		
Oliguria non-responsive to fluids or diuretics	4		
Creatinine ≥300µmol/l or ≥3.5mg/dL	1		
Dialysis for acute renal failure	1		0
Coagulation/hematologic dysfunction	147, 75.8% (69.1 – 81.6)		
Failure to form clots	6		
Transfusion of ≥ 2 units of red blood cells	140	103	
Acute thrombocytopenia (<50,000 platelets/ml)	12		
Hepatic dysfunction	13, 6.7% (3.6 – 11.2)		
Jaundice in the presence of pre-eclampsia	0		
Bilirubin >100mmol/l or >6.0 mg/dL	13		9
Neurological dysfunction	8, 4.1% (1.8 – 8.0)		
Loss of consciousness lasting 12 hours (GCS < 10)	6		
Stroke	0		
Loss of consciousness and ketoacids in urine	0		
Uncontrollable fit	1		
New onset of paralysis	1		
Uterine dysfunction	6, 3.1% (1.1 – 6.6)		
Hysterectomy following infection or haemorrhage	6		

In italics unique SSA criteria and underlined unique WHO criteria. A woman could fulfil more than one MNM criterion. At the top of each section the total number of women with each organ dysfunction, followed by the proportion, calculated by the total divided by 194 MNM women and presented as percentage. The second and third column presents the number of women that only fulfilled criteria of either the WHO or SSA set and would have been missed if the other set was applied.

MNM, maternal near-miss; CI, confidence interval; SSA, sub-Saharan Africa; WHO, World Health Organization, ICU, intensive care unit; CPR, cardiopulmonary resuscitation; GCS, Glasgow coma scale.

Severe morbidity

Eclampsia

1. A 17-year old primigravida fitted eight times due to eclampsia at home and in a small district hospital 119 km away from hospital B. She was referred to hospital B were a CS was done. She recovered well.

Uterine rupture

2. A 28-year old G3P2 with one previous CS was admitted in active labour in hospital A. An emergency CS was done and a uterine rupture found. A fresh stillborn baby was delivered. The woman developed a vesicovaginal fistula and received 1 unit of blood during admission.

Laparotomy other than CS or ectopic

3. A 33-year old G3P2 presented to Hospital A with a septic cervical pregnancy. A hysterotomy, abdominal approach, was done to remove the pregnancy since a vaginal approach was deemed not to be feasible. To control the bleeding a bilateral ligation of the uterine arteries was done. The woman did not fulfil the criteria of shock. She received four units of blood and two units fresh frozen plasma.

Transfusion of 2 or more units of blood

4. A 21-year old primigravida presented to hospital D with severe bleeding due to an incomplete miscarriage. Her Hb was 5.2 g/dL, she received four units of blood and the retained products of conception were removed.

No severe morbidity

Sepsis

1. A 27-year old woman developed fever 1 day after her normal birth in hospital A. She had a heart rate of 100/min, WBC of 9. She was not acutely ill, endometritis was suspected and she recovered well on intravenous antibiotics.

Transfusion of 2 or more units of blood

2. A 28-year old G5P4 presented to hospital A with symptomatic anaemia at 32 weeks of gestation. Her Hb was 6.8 g/dL and she was transfused 2 RCCs.
3. A 17-year old primigravida gave birth in Hospital B with minimal blood loss. During antenatal care an Hb of 5.9 g/dl was found. Three units of blood were transfused postpartum.

Text box 1. Summary of cases missed by WHO criteria sorted by assessment of research team as severe or not severe morbidity case
CS, caesarean section; G, gravida; P, parity; Hb, haemoglobin; WBC, white blood cells x 10^9/L; RCC, red cell concentrate.

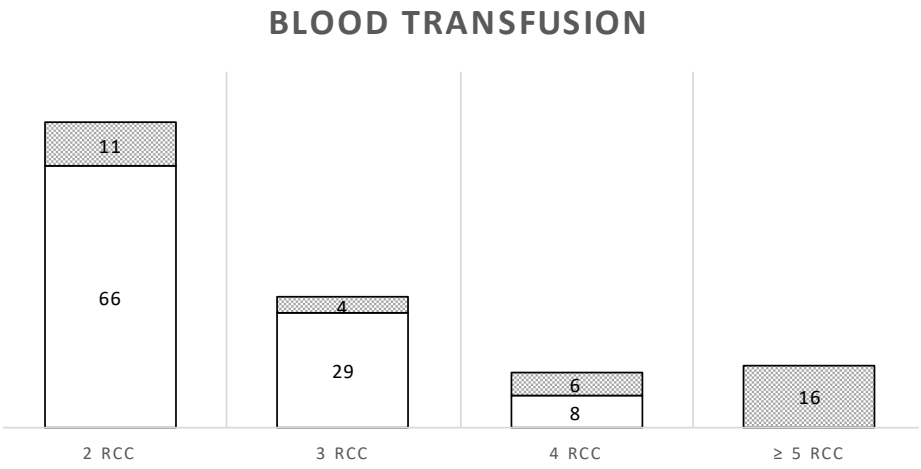


Figure 2. Summary of number of women who received two or more units of blood transfusion.
In white the women that did not fulfil another criterion of the WHO set and would have been missed by the WHO MNM criteria.
In grey the number of women that did fulfil another criteria of the WHO MNM criteria.
RCC, red cell concentrate.

Figure 2 summarizes the number of units of blood given to MNM. SSA MNM criterion of at least two units of blood was fulfilled by 140 women. An estimation of the amount of blood loss was not available in medical records. Assessment of severity of haemorrhage was based on the vitals of the patients and interventions performed to stop the bleeding. Two or three units of red cells were given to 95 women for mild/moderate haemorrhage or chronic anaemia who did not fulfil any WHO criterion and were not considered to be MNM. Fourteen women received four units and were assessed to be MNM from severe haemorrhage. Even though these women did not reach the clinical thresholds of shock, they often had tachycardia and needed several interventions to stop the bleeding and to restore these clinical parameters (Text box 1 case 3 and 4). Of the women identified through the register of blood bank, 20 women received two units of blood and eight women three.

If only the WHO criteria would have been applied to our cohort 61 MNM would have been identified and if the SSA criteria were applied 184 MNM. In Textbox 1, several summaries are presented of MNM that would have been missed if the WHO MNM criteria were applied.

Long-term outcome

Although 194 women survived the pregnancy-related complication, 15 (7.7%) women sustained a long-term complication. Six (3.1%) women underwent hysterectomy of whom five were haemorrhage and one infection related. Three (1.5%) women

developed cardiomyopathy and three needed a colostomy: one woman had iatrogenic bowel perforation during caesarean section, one had an abdominal pregnancy with placental invasion into the sigmoid and one woman with a previous caesarean section had an obstructed bowel due to adhesions during her current pregnancy. Two (1.0%) women had a ruptured uterus due to obstructed labour of whom one developed a vesicovaginal fistula. One women with known chronic renal failure developed acute on chronic renal failure secondary to pre-eclampsia and was still in need of dialysis after discharge. The two women with a uterine rupture, two women who needed a colostomy and one woman with a haemorrhage-related hysterectomy had had one or more previous caesarean sections.

Discussion

In the middle-income setting of Namibia, both the WHO and SSA MNM criteria cannot be applied without amendments. Even though the WHO developed the criteria to be applied across settings, our findings suggest it would result in an underestimation of MNM in Namibia, which corresponds with experiences from low-income settings.[11,12,16] The SSA criteria were proposed for use in low-income settings. Application of the SSA criteria to our cohort resulted in an overestimation of MNM which suggests that both sets are less feasible to be applied to a middle-income setting such as Namibia. There are several other middle-income countries which used the MNM approach. However, they applied the WHO criteria or locally established criteria without validating them, and most of these studies only included referral or tertiary hospitals.[16–22] For example, a large national study from Brazil included 27 referral hospitals and used the WHO criteria.[18] India developed its own MNM criteria and performed a pilot in six tertiary facilities.[22] A recently published systematic review assessed the applicability of WHO criteria in sub-Saharan Africa and included 15 reports of which four reported findings from middle-income countries.[16,17,23–25] These four reports were all from tertiary facilities with availability of resources to apply the WHO criteria.[17,23–25]

For MNM registration in all Namibian hospitals of all levels, we decided to adopt the WHO criteria with the addition of the criteria eclampsia, uterine rupture, laparotomy other than caesarean section or ectopic pregnancy' and a lower threshold of four units of blood. Even though eclampsia and uterine rupture are not part of the WHO criteria, high case fatality rates are reported for both conditions across settings.[26–28] Furthermore, these are commonly used in both high and low-income countries to define MNM for local and national registrations and recently suggested as a standard outcome to define severe morbidity in maternal health-related research.[11,29–32] To our knowledge, the criterion 'Laparotomy other than caesarean section or ectopic

pregnancy' is not commonly used to define MNM. However, in our cohort, several women would have been missed and this criterion, therefore, turned out to be a useful addition. We opted to change the threshold for blood transfusion to four units of red cells. The threshold of two or three units resulted in inclusion of many women with minor to moderate haemorrhage-related complications, as well as inclusion of women with chronic anaemia. At a threshold of five units of blood, women with severe haemorrhage would have been missed.

The criterion sepsis led to overinclusion in our cohort of women who were not critically ill. The SSA set used a definition of sepsis developed for the non-obstetric population.[33] Amendment of the definition of sepsis, with higher thresholds of clinical signs, might lead to better MNM identification. The remaining SSA criteria (pulmonary oedema, severe abortion complications, severe malaria and severe pre-eclampsia with ICU admission), appeared not to be essential to identify MNM, resulted in inclusion of women with minor morbidity or were unclear leading to incorrect inclusion.

The prevalence of SMO is expected to correlate with the MMR of a country.[6] The WHO multi country survey showed an SMO ratio of 15.9/1000 livebirths in countries with a comparable MMR.[15] By applying the SSA criteria we found a more than double SMO ratio, whereas by applying the above-suggested amendments we would have identified 93 MNM, which leads to an SMO ratio of 17.5/1000 live births.

We recommend other middle-income countries to validate our criteria in their setting. A country's income level does not necessarily correlate with maternal outcome.[34] For example, Namibia has a relatively high prevalence of severe maternal outcome. The income level is based on national income per person and does not take into account income inequities.[14] However, a country's income level will, in most cases, affect the availability of resources. This poses the most important restriction in use of the WHO MNM criteria.

Access to care does not seem to be a major issue contributing to poor maternal outcome in Namibia. The country has one of the best road networks in Africa and an effective referral system appears to be in place. This is reflected by the high antenatal care attendance rate of 96% and the fact that 87% of women give birth in health facilities, attended by a skilled health-care worker.[9] A recent national maternal death review, of which the report is expected to be published next year, indicates that most deaths occur whilst the woman is in the health facility. Namibian health facilities, like most state funded facilities in sub-Saharan Africa, have high turnover of staff, and are staffed mainly by junior staff with limited experience and supervision. Within the five-

step ‘obstetric transition’ as described by the World Health Organization, Namibia is now in stage III, the typical state of a middle-income country that has largely overcome barriers for women to access care, where women are now indeed reaching health facilities, and hence where improved quality of care becomes the critical step to achieve a reduction of maternal mortality.[35]

Over 80% of the underlying causes of the MNM were direct pregnancy-related causes. We feel that this might be an overrepresentation, caused by the over-reporting of haemorrhage. A better representation of the underlying causes is expected to be found in the planned national MNM observational study with the amended criteria. Abortion-related complications were the second most common underlying cause of the MNM. In Namibia, women only have limited access to abortion and only for significant maternal or fetal indications. A high incidence of abortion-related MNM events is seen in other countries where women have limited access to safe abortion as well.[36]

A considerable proportion of our women had a previous caesarean section and over half of our women gave birth by caesarean section which correlates with other reports.[15] A possible explanation for this high proportion could be our sick population. However, even in an MNM population, there are reports available indicating a high number of caesarean sections without medical indication and for some women, the MNM event was the direct result rather than the indication for caesarean section.[37] In our cohort, a woman sustained iatrogenic bowel injury during birth by caesarean section and needed several laparotomies and went home with a colostomy.

Our study has several limitations. We used a relatively small cohort and were unable to perform a sample size calculation. Possibly larger studies, such as the planned national MNM observational study, may permit additional conclusions with statistical significance. Availability of background data was very limited regarding maternal morbidity and mortality in Namibia. Objective data such as case fatality rate would have been useful to further support our decisions to amend the WHO criteria.

Data were collected by local staff who already had a high workload and MNM might have been missed. Even though data collection done by full-time research staff might have been more accurate, we aimed for data collection mainly done by local staff as this would enable us to identify barriers and challenges for a planned routine national MNM data collection in all Namibian hospitals. The project was overall well received by staff members as they felt they could finally report ‘the other side of the story, rather than only reporting maternal deaths’. The research team identified an additional 31 women, of whom the majority appeared to not be critically ill. This

further supports the experience that our staff were motivated to report MNM. We found a higher prevalence of MNM in the capital. As the national referral centre, this was expected. However, this is most likely also caused by reporting bias since this was the only facility where data collection was supported by the research team. We suggest the assessment of long-term complications should become part of all MNM projects. Even though these women nearly died but survived a pregnancy-related complication, a considerable proportion left the hospital with significant disability.

Conclusion

This report validated MNM criteria to be applied nationwide in hospitals of all levels in a sub-Saharan African country. Our findings suggest that a middle-income country such as Namibia needs MNM criteria 'in between' the WHO and SSA criteria. Context specific MNM criteria are vital to help Namibia and other middle-income countries to identify MNM. Only with accurate MNM criteria can this tool be used for what it is designed for; to improve maternity care and to stop women dying of avoidable causes. We recommend other middle-income countries to validate our criteria in their setting when the WHO criteria are not feasible, rather than developing new criteria, as this will allow comparison of findings.

References

1. Alkema L, Chou D, Hogan D, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet. 2016;387(10017):462-474.
2. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2011-2013: Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa, short report. Department Health: Pretoria, 2015.
3. Sayinzoga F, Bijlmakers L, van Dillen J, Mivumbi V, Ngabo F, van der Velden K. Maternal death audit in Rwanda 2009-2013: a nationwide facility-based retrospective cohort study. BMJ Open. 2016;6(1):e009734.
4. Bekele A, Hassen A, Abebe S, Usmael A, Dagnew F, Hadush A, et al. Second Ethiopian national Maternal Death Surveillance and Response (MDSR) report EFY 2008. Ethiopian Public Health Institute: Addis Abeba, 2017.
5. Mataya R, on behalf of Malawi National Confidential Committee on Enquiry into Maternal Death. Report on the Confidential Enquiry into Maternal Deaths in Malawi (2008-2012). Ministry of Health: Lilongwe, 2014.
6. World Health Organization. Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. World Health Organization: Geneva, 2011.
7. Bakker W, van den Akker T, Mwagomba B, Khukulu R, van Elteren M, van Roosmalen J. Health workers' perceptions of obstetric critical incident audit in Thyolo District, Malawi. Trop Med Int Health. 2011;16(10):1243-1250.
8. Cecatti JG, Souza JP, Parpinelli MA, de Sousa MH, Amaral E. Research on severe maternal morbidities and near-misses in Brazil: what we have learned. Reprod Health Matters. 2007;15(30):125-133.
9. Ministry of Health and Social Services. Demographic and Health Survey of Namibia 2013. Ministry of Health and Social Services: Windhoek, 2014.
10. Namibia Statistics Agency. Namibia Inter-censal Demographic Survey 2016 Report. Namibia Statistics Agency: Windhoek, 2017.
11. Nelissen E, Mduma E, Broerse J, et al. Applicability of the WHO maternal near miss criteria in a low-resource setting. PLoS One. 2013;8(4):e61248.
12. van den Akker T, Beltman J, Leyten J, et al. The WHO maternal near miss approach: consequences at Malawian District level. PLoS One. 2013;8(1):e54805.
13. Tura AK, Stekelenburg J, Scherjon SA, et al. Adaptation of the WHO maternal near miss tool for use in sub-Saharan Africa: an International Delphi study. BMC Pregnancy Childbirth. 2017;17(1):445.
14. World bank. Country statistics Namibia; 2017. (Available from https://data.worldbank.org/country/NA) [1-4-2015]
15. Souza JP, Gulmezoglu AM, Vogel J, et al. Moving beyond essential interventions for reduction of maternal mortality (the WHO Multicountry Survey on Maternal and Newborn Health): a cross-sectional study. Lancet. 2013;381(9879):1747-1755.
16. Tura AK, Trang TL, van den Akker T, et al. Applicability of the WHO maternal near miss tool in sub-Saharan Africa: a systematic review. BMC Pregnancy Childbirth. 2019;19(1):79.
17. Tuncalp O, Hindin MJ, Adu-Bonsaffoh K, Adanu RM. Assessment of maternal near-miss and quality of care in a hospital-based study in Accra, Ghana. Int J Gynaecol Obstet. 2013;123(1):58-63.
18. Cecatti JG, Costa ML, Haddad SM, et al. Network for Surveillance of Severe Maternal Morbidity: a powerful national collaboration generating data on maternal health outcomes and care. BJOG. 2016;123(6):946-953.
19. Zhu J, Liang J, Mu Y, et al. Sociodemographic and obstetric characteristics of stillbirths in China: a census of nearly 4 million health facility births between 2012 and 2014. Lancet Glob Health. 2016;4(2):e109-118.
20. Norhayati MN, Nik Hazlina NH, Sulaiman Z, Azman MY. Severe maternal morbidity and near misses in tertiary hospitals, Kelantan, Malaysia: a cross-sectional study. BMC Public Health. 2016;16):229.
21. Bolnga JW, Morris M, Totona C, Laman M. Maternal near-misses at a provincial hospital in Papua New Guinea: A prospective observational study. Aust N Z J Obstet Gynaecol. 2017;57(6):624-629.
22. Purandare C, Bhardwaj A, Malhotra M, Bhushan H, Chhabra S, Shivkumar P. Maternal near-miss reviews: lessons from a pilot programme in India. BJOG. 2014;121 Suppl 4):105-111.
23. Mbachu, II, Ezeama C, Osuagwu K, Umeononihu OS, Obiannika C, Ezeama N. A cross sectional study of maternal near miss and mortality at a rural tertiary centre in southern nigeria. BMC Pregnancy Childbirth. 2017;17(1):251.

24. Soma-Pillay P, Pattinson RC, Langa-Mlambo L, Nkosi BS, Macdonald AP. Maternal near miss and maternal death in the Pretoria Academic Complex, South Africa: A population-based study. S Afr Med J. 2015;105(7):578-563.
25. Peprah N. Severe maternal morbidity and associated factors in Suntreso and Kumasi south government hospitals, Ashanti region. University of Ghana: Accra, 2015.
26. Vandenberghe G, Bloemenkamp K, Berlage S, et al. The International Network of Obstetric Survey Systems study of uterine rupture: a descriptive multi-country population-based study. BJOG. 2019;126(3):370-381.
27. Woldeyes WS, Asefa D, Muleta G. Incidence and determinants of severe maternal outcome in Jimma University teaching hospital, south-West Ethiopia: a prospective cross-sectional study. BMC Pregnancy Childbirth. 2018;18(1):255.
28. Schaap TP, Knight M, Zwart JJ, et al. Eclampsia, a comparison within the International Network of Obstetric Survey Systems. BJOG. 2014;121(12):1521-1528.
29. Zwart JJ, Richters JM, Ory F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies. BJOG. 2008;115(7):842-850.
30. Knight M, Acosta C, Brocklehurst P, Cheshire A, Fitzpatrick K, Hinton, L et al. Beyond maternal death:improving the quality of maternal care through national studies of 'near-miss' maternal morbidity. Programme Grants Appl Res 2016;4(9).
31. Kalisa R, Rulisa S, van den Akker T, van Roosmalen J. Maternal Near Miss and quality of care in a rural Rwandan hospital. BMC Pregnancy Childbirth. 2016;16(1):324.
32. Schaap T, Bloemenkamp K, Deneux-Tharaux C, et al. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG. 2019 Feb;126(3):394-401.
33. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest. 1992;101(6):1644-1655.
34. Mujica OJ, Vazquez E, Duarte EC, Cortez-Escalante JJ, Molina J, Barbosa da Silva Junior J. Socioeconomic inequalities and mortality trends in BRICS, 1990-2010. Bull World Health Organ. 2014;92(6):405-412.
35. Souza JP, Tuncalp O, Vogel JP, et al. Obstetric transition: the pathway towards ending preventable maternal deaths. BJOG. 2014;121 Suppl 1):1-4.
36. Calvert C, Owolabi OO, Yeung F, et al. The magnitude and severity of abortion-related morbidity in settings with limited access to abortion services: a systematic review and meta-regression. BMJ Glob Health. 2018;3(3):e000692.
37. Heemelaar S, Nelissen E, Mdoe P, Kidanto H, van Roosmalen J, Stekelenburg J. Criteria-based audit of caesarean section in a referral hospital in rural Tanzania. Trop Med Int Health. 2016;21(4):525-534.

Appendix 1. Comparison of WHO MNM criteria and SSA MNM criteria

MNM, Maternal near-miss; SSA, sub-Saharan Africa; WHO, World Health organisation, ICU, intensive care unit; CPR, cardio pulmonary resuscitation; GCS, Glasgow coma scale.
[a] persistent systolic blood pressure <80 mmHg or a persistent systolic blood pressure <90 mmHg with a pulse rate at least 120 bpm
[b] urinary output <30 ml/hour over 4 hours or <400 ml/24 hr
[c] presence of fever (Temp >38°C) AND confirmed or suspected infection AND at least one of the following: heart rate >90, respiratory rate >20, WBC > 12 or < 4 x 109/L
[d] complete rupture of uterus during labour confirmed by laparotomy
[e] septic incomplete abortion, complicated gestational trophoblastic disease with anaemia
[f] major signs of organ dysfunction and/or high level parasitaemia or cerebral malaria

Appendix 1. Comparison of WHO MNM criteria and SSA MNM criteria	
WHO near-miss criteria	**Sub-Saharan Africa near-miss criteria**
Clinical criteria	**Clinical criteria**
Acute cyanosis	Acute cyanosis
Gasping	Gasping
Respiratory rate >40 or <6/min	Respiratory rate >40 or <6/min
Shock [a]	Shock
Oliguria non-responsive to fluids or diuretics [b]	Oliguria non-responsive to fluids or diuretics
Failure to form clots	Failure to form clots
Loss of consciousness lasting >12 h	Loss of consciousness lasting 12 hours
Cardiac arrest	Cardiac arrest
Stroke	Stroke
Uncontrollable fit / total paralysis	Uncontrollable fit / total paralysis
Jaundice in the presence of pre-eclampsia	Jaundice in the presence of pre-eclampsia
Laboratory-based criteria	**Laboratory-based criteria**
Oxygen saturation <90% for ≥60 minutes	Oxygen saturation <90% for ≥60 minutes
PaO2/FiO2 <200 mmHg	
Creatinine ≥300µmol/l or ≥3.5mg/dL	Creatinine ≥300µmol/l or ≥3.5mg/dL
Bilirubin >100mmol/l or >6.0 mg/dL	
pH < 7.1	
Lactate >5 mEq/mL	
Acute thrombocytopenia (<50,000 platelets/ml)	Acute thrombocytopenia (<50,000 platelets/ml)
Loss of consciousness and ketoacids in urine	Loss of consciousness and ketoacids in urine
Management-based criteria	**Management-based criteria**
Use of continuous vasoactive drugs	
Hysterectomy following infection or haemorrhage	Hysterectomy following infection or haemorrhage
Transfusion of ≥5 units of red cells	Transfusion of ≥ 2 units of red cells
Intubation and ventilation for ≥60 minutes not related to anaesthesia	Intubation and ventilation for ≥60 minutes not related to anaesthesia
Dialysis for acute renal failure	
Cardio-pulmonary resuscitation	Cardio-pulmonary resuscitation
	Laparotomy other than caesarean section or ectopic pregnancy
Severe maternal complications	**Severe maternal complications**
	Eclampsia
	Sepsis or severe systemic infection[c]
	Uterine rupture[d]
	Pulmonary oedema
	Severe abortion complications[e]
	Severe malaria[f]
	Severe pre-eclampsia with ICU admission

Appendix 2. Frequencies of maternal near-miss by type of organ system dysfunction in the four hospitals

In *italic* unique SSA criteria and <u>underlined</u> unique WHO criteria. A woman could fulfil more than one MNM criterion. At the top of each section the total number of women with each organ dysfunction, followed by the proportion, calculated by this total divided by 194 MNM women and presented as percentage.
MNM, Maternal near-miss; SSA, sub-Saharan Africa; WHO, World Health organization; ICU, intensive care unit; CPR, cardio pulmonary resuscitation; GCS, Glasgow coma scale.
[a] presence of fever (Temp >38°C) AND confirmed or suspected infection AND at least one of the following: heart rate >90, respiratory rate >20, WBC > 12 or < 4 x 10^9/L
[b] complete rupture of uterus during labour confirmed by laparotomy
[c] septic incomplete abortion, complicated gestational trophoblastic disease with anaemia
[d] major signs of organ dysfunction and/or high level parasitaemia or cerebral malaria
[e] persistent systolic blood pressure <80 mmHg or a persistent systolic blood pressure <90 mmHg with a pulse rate at least 120 bpm
[f] urinary output <30 ml/hour over 4 hours or <400 ml/24 hr

Appendix 2. Frequencies of maternal near-miss by type of organ system dysfunction in the four hospitals					
	Facilities				
	A	**B**	**C**	**D**	**Total**
Severe maternal complications	**52**	**16**	**4**	**0**	**72, 37.3%**
Eclampsia	17	7	2	0	26
Sepsis or severe systemic infection[a]	22	2	2	0	26
Uterine rupture[b]	1	1	0	0	2
Pulmonary oedema	5	2	0	0	7
Severe abortion complications[c]	7	1	0	0	8
Severe malaria[d]	0	4	0	0	4
Severe pre-eclampsia with ICU admission	1	3	0	0	4
Laparotomy other than caesarean section or ectopic pregnancy	12	0	0	0	12
Cardiovascular dysfunction	**17**	**2**	**2**	**0**	**21, 10.8%**
Shock[e]	16	2	2	0	20
Cardiac arrest	0	0	0	0	0
Use of continuous vasoactive drugs	3	0	0	0	3
CPR	0	0	0	0	0
pH < 7.1	1	0	0	0	1
Lactate >5 mEq/mL	0	0	0	0	0
Respiratory function	**14**	**2**	**0**	**0**	**16, 8.3%**
Acute cyanosis	0	0	0	0	0
Gasping	0	0	0	0	0
Respiratory rate >40 or <6/min	4	1	0	0	5
Intubation and ventilation for ≥60 minutes not related to anaesthesia	10	1	0	0	11
Oxygen saturation <90% for ≥60 minutes	4	0	0	0	4
Renal dysfunction	**3**	**1**	**0**	**0**	**4, 2.0%**
Oliguria non-responsive to fluids or diuretics[f]	3	1	0	0	4
Creatinine ≥300µmol/l or ≥3.5mg/dL	1	0	0	0	1
Dialysis for acute renal failure	1	0	0	0	1
Coagulation/hematologic dysfunction	**112**	**24**	**6**	**5**	**147, 75.8%**
Failure to form clots	4	2	0	0	6
Transfusion of ≥ 2 units of red blood cells	108	21	6	5	140
Acute thrombocytopenia (<50,000 platelets/ml)	8	4	0	0	12
Hepatic dysfunction	12	1	0	0	13, 6.7%
Jaundice in the presence of pre-eclampsia	0	0	0	0	0
Bilirubin >100mmol/l or >6.0 mg/dL	12	1	0	0	13
Neurological dysfunction	**6**	**2**	**0**	**0**	**8, 4.2%**
Loss of consciousness lasting 12 hours (GCS < 10)	4	2	0	0	6
Stroke	0	0	0	0	0
Loss of consciousness and ketoacids in urine	0	0	0	0	0
Uncontrollable fit	1	0	0	0	1
New onset of paralysis	1	0	0	0	1
Uterine dysfunction	**5**	**1**	**0**	**0**	**6, 3.0%**
Hysterectomy following infection or haemorrhage	5	1	0	0	6
Total	**150**	**30**	**9**	**5**	**194**

Chapter 4.

Maternal near-miss surveillance, Namibia

Steffie Heemelaar, Mirjam Josef, Zoe Diener, Melody Chipeio, Jelle Stekelenburg, Thomas van den Akker, Shonag Mackenzie

Bull World Health Organ. 2020 Aug 1;98(8):548-557

Abstract

Objective

To analyse and improve the Namibian maternity care system by implementing maternal near-miss surveillance during 1 October 2018 to 31 March 2019, and identifying the challenges and benefits of such data collection.

Methods

From the results of an initial feasibility study, we adapted the World Health Organization criteria defining a maternal near-miss to the Namibian health-care system. We visited most (27 out of 35) participating facilities before implementation and provided training on maternal near-miss identification and data collection. We visited all facilities at the end of the surveillance period to verify recorded data and to give staff the opportunity to provide feedback.

Results

During the 6-month period, we recorded 37106 live births, 298 maternal near-misses (8.0 per 1000 live births) and 23 maternal deaths (62.0 per 100 000 live births). We observed that obstetric haemorrhage and hypertensive disorders were the most common causes of maternal near-misses (each 92/298; 30.9%). Of the 49 maternal near-misses due to pregnancies with abortive outcomes, ectopic pregnancy was the most common cause (36/298; 12.1%). Fetal or neonatal outcomes were poor; only 50.3% (157/312) of the infants born to maternal near-miss mothers went home with their discharged mother.

Conclusion

Maternal near-miss surveillance is a useful intervention to identify within-country challenges, such as lack of access to caesarean section or hysterectomy. Knowledge of these challenges can be used by policy-makers and programme managers in the development of locally tailored targeted interventions to improve maternal outcome in their setting.

Introduction

A target within the third sustainable development goal (SDG 3: ensure healthy lives and promote well-being for all at all ages)[1] is to reduce the maternal mortality ratio to 70 per 100 000 live births globally by 2030. Even though the global maternal mortality ratio was reduced by nearly half in 2015 compared with 1990, large discrepancies remain between regions; the highest maternal mortality ratio of 546 was recorded in sub-Saharan Africa, compared with 12 deaths per 100 000 live births in high-income countries.[2] Namibia, a middle-income country in sub-Saharan Africa, is one of the least densely populated countries in the world (2.8 people per km^2) and has around 70 000 births per annum.[3,4] Although Namibia had an estimated maternal mortality ratio of 385 per 100 000 live births in 2013, the government is committed to achieving SDG 3.[5,6]

To analyse and improve the maternity care system, the World Health Organization (WHO) recommends including maternal near-misses, that is, severe maternal morbidity, defined by a specific set of criteria, within national obstetric surveillance systems.[7] National surveillance of maternal near-misses, or other specifically defined maternal morbidities, is conducted in several high-income countries, but such data collection occurs infrequently in low- or middle-income countries.[8,9]

The low absolute numbers of maternal deaths in Namibia present a challenge to the monitoring of the performance of the maternity care system. After an initial feasibility study, the National Maternal Death Review Committee of the Ministry of Health and Social Services agreed to include surveillance of maternal near-misses within the national obstetric surveillance system for a 6-month period. The aim of this surveillance was to obtain more robust data on pregnancy outcomes and assess the benefits of such surveillance in comparison with maternal death surveillance only.

We describe the implementation of maternal near-miss surveillance from 1 October 2018 to 31 March 2019 in Namibia, and discuss the challenges and benefits of such data collection. Using a cross-sectional study design, we provide nationwide incidence data and discuss the underlying causes of maternal near-misses, while also examining neonatal outcomes.

Methods

Study setting

All Namibian public hospitals – 1 tertiary, 4 regional and 30 district – participated in the surveillance of maternal near-misses. The largest hospital complex, located in the capital of Windhoek and comprising the tertiary and a regional hospital, has around 12 000 births per annum. This hospital employs three consultant obstetrician-gynaecologists. The intensive care unit has advanced equipment including ventilators and dialysis. The other three regional hospitals (6500 births per year each) have high-dependency units with mechanical ventilation, and renal dialysis can be performed at two of these hospitals. District hospitals have two to eight general medical doctors who provide care across all specialities. District hospitals have basic haematology and chemistry laboratory tests available, such as blood count, renal function and basic liver function tests. Most district hospital blood banks only have access to 2 units of packed red cells. All hospitals are expected to have functioning operating theatres for basic surgical procedures, such as caesarean section or laparotomy for ruptured ectopic pregnancy.

Feasibility study and preparation

Because of the limited availability of laboratory tests and management options resulting in the underreporting of maternal near-miss cases, other sub-Saharan African countries have indicated that the WHO maternal near-miss criteria may not be suitable for use in district hospitals in low-income settings.[10,11] As 30 of the 35 Namibian hospitals are district hospitals, four of the authors of this study, together with several other clinicians working in Namibian public facilities, conducted a feasibility study in 2018 in four hospitals to compare WHO maternal near-miss criteria with a set of criteria proposed for low-income settings.[12] This study was performed in the hospital complex in the capital and in a regional and two district hospitals. The authors of the feasibility study reported that the WHO criteria resulted in the underreporting of maternal near-misses in Namibia; we therefore adapted the WHO maternal near-miss identification criteria to the Namibian healthcare system (Text box 1).[13] Within management-based criteria, we adopted the lower threshold of 4 units of blood transfused and included laparotomy; we also included eclampsia and uterine rupture within the category of severe maternal complications.

Before national implementation of maternal near-miss surveillance, most participating facilities were visited; due to a lack of funding, eight smaller district hospitals could not be visited. Medical staff involved in the care of pregnant and/or postpartum women were trained in the identification of maternal near-misses and relevant data collection. Staff at the eight hospitals that could not be visited received

Clinical criteria

WHO: Acute cyanosis; gasping; respiratory rate >40 or <6/min; shock;[a] oliguria non-responsive to fluids or diuretics;[b] failure to form clots; loss of consciousness lasting >12 hours (Glasgow coma scale <10); cardiac arrest; stroke; uncontrollable fit/total paralysis; and jaundice in the presence of pre-eclampsia.

Namibia: the same as WHO.

Laboratory-based criteria

WHO: Oxygen saturation <90% for 60 minutes; PaO2/FiO2 <200 mmHg; creatinine 300 µmol/L or 3.5 mg/dL; bilirubin >100 mmol/L or >6.0 mg/dL; pH <7.1; lactate >5 mq/mL; acute thrombocytopenia (<50 000 platelets/mL); and loss of consciousness and ketoacids in urine.

Namibia: the same as WHO.

Management-based criteria

WHO: Use of continuous vasoactive drugs; hysterectomy following infection or haemorrhage; transfusion of 5 units of red blood cells; intubation and ventilation for 60 minutes not related to anaesthesia; dialysis for acute renal failure; cardio–pulmonary resuscitation.

Namibia: As for WHO with the exception of transfusion of 4 units of blood products, and inclusion of laparotomy other than caesarean section or ectopic pregnancy of <12 weeks gestation

Severe maternal complications

WHO: No criteria.

Namibia: Eclampsia and uterine rupture.[c]

Text box 1. Maternal near-miss criteria as defined by the World Health Organization and as locally amended for Namibia
FiO2: fraction of inspired oxygen; min: minute(s); Pao2: arterial oxygen partial pressure; WHO: World Health Organization.
[a] Persistent systolic blood pressure of <80 mmHg, or a persistent systolic blood pressure <90 mmHg with a pulse rate of >120 bpm.
[b] Urinary output <30 mL/hour over 4 hours or <400 mL per 24 hours.
[c] Complete rupture of uterus during labour confirmed by laparotomy.

training when presenting at one of the referral hospitals (either a regional hospital or a larger, better-equipped district hospital) for other training courses. At all 35 hospitals, a maternal near-miss doctor and nurse were nominated to supervise data collection and provide the research team with verbal monthly updates during pre-arranged telephone calls.

Data collection

A case of a maternal near-miss was defined as a woman either pregnant (independent of gestational age), or within 42 days of termination of pregnancy or birth, fulfilling at least one of the criteria listed in Text box 1. Using a structured data collection tool (Maternal Near-Miss Form, available in the data repository),[14] nominated staff collected anonymous data from medical records on maternal sociodemographic characteristics, maternal outcome, the main underlying cause of the maternal near-miss and the neonatal outcome. Stillbirths were defined as deaths before birth after 28 weeks of gestation, and documented as either fresh or macerated in the medical file. Neonatal death was defined as the death of an infant within the first 28 days of life. Because we aimed to assess maternal outcome, neonatal outcome was assessed upon discharge of the mother even if the infant was still being cared for in the intensive care unit.

We identified possible missed cases in the Windhoek hospital complex during weekly ward visits or through personal communication with nominated medical staff. Although we had planned to visit all facilities 2 months after the onset of the surveillance, we had to cancel these visits because of a lack of resources. At the request of staff at two of the hospitals, we made an extra visit to provide additional training on data collection. After 6 months, we visited all hospitals to verify the recorded surveillance data against medical records. We screened the ward registers of maternity, female, high-dependency and intensive care units, theatre registers and referral registers for missed cases. During this visit, at least one member of the National Maternal Death Review Committee met with the local hospital staff, including the nominated doctor and nurse, the doctor and nurse in-charge, and all available doctors and nurses involved in the care of pregnant women. During these meetings, staff were given the opportunity to describe their experience with data collection and the challenges encountered related to clinical duties. We obtained the total number of live births in Namibia from the National Health Information Systems. We collected data on maternal deaths from the national reporting and audit system.[15]

Data analysis

Direct and indirect causes of maternal near-misses were defined according to the International Statistical Classification of Diseases-Maternal Mortality definitions.[16] We defined the number of severe maternal outcomes as the total of maternal near-misses and maternal deaths. We calculated the incidence of the most common causes of, and other conditions contributing to, maternal near-misses, namely major obstetric haemorrhage, eclampsia, uterine rupture and hysterectomy, per 1000 live births during the study period. We defined mortality index as the number of maternal deaths as a percentage of the number of severe maternal outcomes.

As a result of poor documentation of blood loss, we diagnosed major obstetric haemorrhage as a woman with obstetric haemorrhage who needed either: 4 units of blood; fulfilled the criteria of shock;[17] a laparotomy (to perform a B-lynch) or a hysterectomy; or had disseminated intravascular coagulopathy, requiring fresh frozen plasma. To diagnose eclampsia, uterine rupture and hysterectomy, we used definitions proposed by the International Network of Obstetric Survey Systems.[18]

Finally, because an outbreak of hepatitis E had been causing significant maternal mortality since December 2017, we also calculated the incidence and mortality index of severe maternal outcomes for women with acute hepatitis E with a bilirubin concentration of more than 100 mmol/L.[19]

Dissemination of findings

We shared all findings with the executive management committee of the Ministry of Health and Social Services during a meeting in July 2019, attended by representatives of the departments of human resources, clinical support services and quality assurance division, responsible for training clinical staff. We addressed several issues and set priorities for the following year, namely: (i) the human resources department to focus on recruiting and retaining doctors and nurses with obstetric experience and/or essential surgical skills; and (ii) the clinical support services department to ensure functionality of operating theatres in district hospitals. We also discussed the possibility of launching a debate within parliament to legalize abortion, using data describing abortion-related complications.

In the same month we also shared all findings with all participating facilities through video conferencing and during a 2-day national conference organised by the Ministry of Health and Social Services and the University of Namibia, funded by several Namibian companies, the WHO, United Nations Population Funds and the European Union. A doctor and nurse from each facility were invited to attend the conference, where we provided staff training and issued relevant guidelines according to the most

common issues identified in the maternal near-miss and death reviews. The guidelines were written by doctors working in maternity departments of the regional hospitals, and reviewed by members of the National Maternal Death Review Committee.

Budget

Costs were kept as low as possible. When feasible, facility visits for maternal near-miss surveillance were combined with visits for other training courses. Most of the available budget was spent on travel and accommodation; the costs for two committee members to travel 9600 km to visit participating hospitals before and after completion of data collection were approximately 8000 United States dollars (US$). A further US$ 700 was spent on stationary, such as the printing of case reporting forms and guidelines. External advisors from outside Namibia were not remunerated.

Ethics

This study was reviewed and approved by the research unit of the Ministry of Health and Social Services. After stabilizing and treating the women, data were collected from medical records without identification of the patient; inclusion in the study had no effect on clinical management. The need for individual informed consent was therefore waived.

Results

Over the 6-month surveillance period, we recorded 37106 live births, 298 maternal near-misses and 23 maternal deaths. We calculated the incidence of maternal near-misses in Namibia as 8.0 per 1000 live births, the maternal mortality ratio as 62.0 per 100000 live births and the ratio of maternal near-misses to maternal deaths as 13:1.

Table 1. Characteristics of all women who experienced a maternal near-miss or maternal death, Namibia, 1 October 2018 - 31 March 2019

Characteristics	No. (%)		
	Maternal near-misses (n = 298)	Maternal deaths (n = 23)	Severe maternal outcomes (n = 321)
Age (years)			
≤ 20	54 (18.1)	4 (17.4)	58 (18.1)
21–34	174 (58.4)	15 (65.2)	189 (58.9)
≥ 35	69 (23.2)	4 (17.4)	73 (22.7)
Unknown	1 (0.3)	0 (0.0)	1 (0.3)
Parity			
0	96 (32.2)	3 (13.0)	99 (30.8)
1–3	149 (50.0)	15 (65.2)	164 (51.1)
4	38 (12.8)	5 (21.7)	43 (13.4)
Unknown	15 (5.0)	0 (0.0)	15 (4.7)
Antenatal care attendance			
Yes	199 (66.8)	21 (91.3)	220 (68.5)
No	20 (6.7)	2 (8.7)	22 (6.9)
NA[a]	51 (17.1)	0 (0.0)	51 (15.9)
Unknown	28 (9.4)	0 (0.0)	28 (8.7)
Gestational age (weeks)			
≤ 12	36 (12.1)	0 (0.0)	36 (11.2)
13–25	20 (6.7)	4 (17.4)	24 (7.5)
26–36	104 (34.9)	9 (39.1)	113 (35.2)
≥ 37	108 (36.2)	9 (39.1)	117 (36.4)
Unknown	30 (10.1)	1 (4.3)	31 (9.7)
Previous caesarean section			
Yes	66 (22.1)	6 (26.1)	72 (22.4)
No	212 (71.1)	17 (73.9)	229 (71.3)
Unknown	20 (6.7)	0 (0.0)	20 (6.2)
HIV status			
Positive	36 (12.1)	6 (26.1)	42 (13.1)
Negative	222 (74.5)	15 (65.2)	237 (73.8)
Unknown	40 (13.4)	2 (8.7)	42 (13.1)
Pregnancy outcome			
Normal vaginal birth	73 (24.5)	11 (47.8)	84 (26.2)
Instrumental birth	2 (0.7)	1 (4.3)	3 (0.9)
Caesarean section	137 (46.0)	5 (21.7)	142 (44.2)
Laparotomy uterine rupture	15 (5.0)	0 (0.0)	15 (4.7)
Miscarriage	15 (5.0)	1 (4.3)	16 (5.0)
Ectopic	38 (12.8)	0 (0.0)	38 (11.8)
Still pregnant at discharge	15 (5.0)	5 (21.7)	20 (6.2)
Termination of pregnancy	2 (0.7)	0 (0.0)	2 (0.6)
Unknown	1 (0.3)	0 (0.0)	1 (0.3)

HIV: human immunodeficiency virus; NA: not applicable.
[a] Gestation < 20 weeks

We list the characteristics of the women identified as having experienced a maternal near-miss or death in Table 1. Among the women who experienced a severe maternal outcome, 18.1% (58/321) were teenagers and 30.8% (99/321) were primiparous.

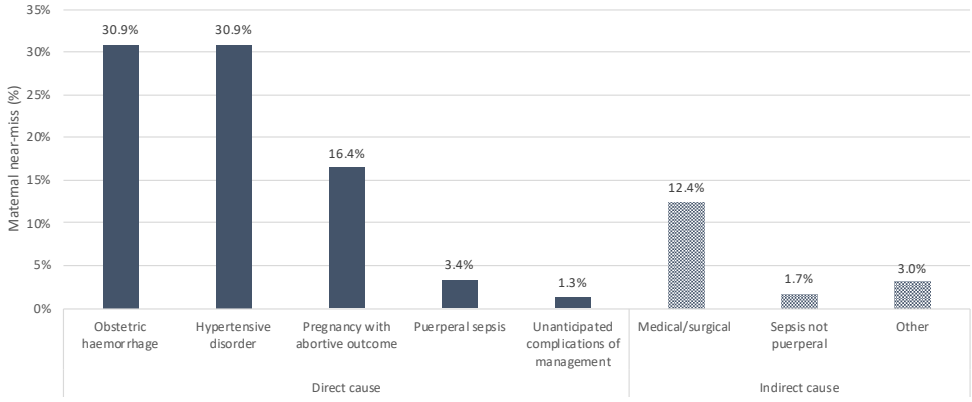


Figure 1. Direct and indirect causes of maternal near-misses, Namibia, 1 October 2018–31 March 2019

Table 2. Direct and indirect causes of maternal near misses, Namibia, 1 October 2018–31 March 2019

Cause of maternal near miss (n = 298)	**No. of maternal near misses (%)**
Direct cause	
Obstetric haemorrhage	92 (30.9)
Postpartum haemorrhage	34 (11.4)
Abruptio placentae	27 (9.1)
Uterine rupture	15 (5.0)
Placenta praevia	7 (2.3)
Placenta accreta[a]	5 (1.7)
Bleeding related to caesarean section[b]	12 (4.0)
Hypertensive disorder	92 (30.9)
Eclampsia[c]	71 (23.8)
HELLP syndrome	20 (6.7)
Pre-eclampsia	3 (1.0)
Pulmonary oedema	5 (1.7)
Stroke	1 (0.3)
Pregnancy with abortive outcome	49 (16.4)
Ectopic	36 (12.1)
Septic miscarriage[d]	10 (3.4)
Abortion-related haemorrhage	1 (0.3)
Ruptured uterus	1 (0.3)
Heterotopic pregnancy	1 (0.3)
Puerperal sepsis	10 (3.4)
Post emergency caesarean section	5 (1.7)
Post elective caesarean section	3 (1.0)
Post vaginal birth	2 (0.7)

Unanticipated complications of management	4 (1.3)
Aspiration pneumonia	1 (0.3)
Laryngospasm post intubation	1 (0.3)
Massive intra-abdominal haematoma post caesarean section	1 (0.3)
Pubic diastasis post normal vaginal birth, needing open reduction and internal fixation	1 (0.3)
Indirect cause	
Medical or surgical	37 (12.4)
Hepatitis E	23 (7.7)
Cardiac disorder	5 (1.7)
Acute abdomen needing laparotomy	4 (1.3)
Pancytopaenia	1 (0.3)
Epilepsy	1 (0.3)
Guillain-Barré Syndrome	1 (0.3)
Bowel gangrene post herbal intoxication	1 (0.3)
Stab wound	1 (0.3)
Non-puerperal sepsis	5 (1.7)
Liver abscess	1 (0.3)
Tuberculosis	1 (0.3)
Pneumonia	1 (0.3)
Pelvic inflammatory disease, grade IV	1 (0.3)
Meningitis	1 (0.3)
Other	9 (3.0)
Chronic anaemia	5 (1.7)
Pulmonary oedema, cause unclear	2 (0.7)
Domestic violence	1 (0.3)
Morbidly obese	1 (0.3)

HELLP: haemolysis, elevated liver enzymes and low platelet count.
[a] Two of these women also had placenta praevia.
[b] Five of these women also had postpartum haemorrhage and one had placental abruption.
[c] Eight of these women also had HELLP syndrome.
[d] Two of these women also had a ruptured uterus after self-induced abortion, and one after induction with misoprostol for missed miscarriage. One woman arrived in septic shock with a perforated uterus after self-induced abortion using a branch.

The main underlying causes of maternal near-misses are summarized in Fig. 1 and reported in detail in Table 2. We observed that the most common causes were obstetric haemorrhage (92/298; 30.9%) and hypertensive disorders (92/298; 30.9%). Of the 49 maternal near-misses due to pregnancies with abortive outcomes, ectopic pregnancy was the most common underlying cause (36/298; 12.1%). Ten women experienced a septic miscarriage, recorded in the medical file to be the result of self-induced abortion in five women. Of these self-induced abortions, two were complicated by ruptured uterus and one of these needed a hysterectomy. One woman had a perforated uterus after self-induced abortion using a branch.
Direct causes of maternal deaths were haemorrhage (three), hypertension (two), puerperal sepsis after caesarean section (two) and anaesthesia-related complications (two). Indirect causes were hepatitis E (five), cardiac disorder (four), tuberculosis (two)

Table 3. Number of maternal near-misses and deaths plus incidence and mortality index for the most common direct and indirect causes, Namibia, 1 October 2018–31 March 2019

Variable	Massive obstetric haemorrhage	Eclampsia	Uterine rupture	Hysterectomy	Hepatitis E, bilirubin >100 mmol/L
No. maternal near-misses (n = 298)	83	73	18	23	23
No. maternal deaths (n = 23)	3	1	1	1	5
Incidence of severe maternal outcomes per 1000 live births[a]	2.3	2	0.5	0.6	0.8
Mortality index (%)[b]	3.5	1.4	5.3	4.2	17.9

[a] Total number of live births during the study period was 37 106.
[b] Number of maternal deaths as a percentage of number of severe maternal outcomes (i.e. number of maternal near-misses plus number maternal deaths).

and gastric perforation (one). The cause of death remained unclear for two women. We present incidence calculations and mortality indices in Table 3. We observed the highest incidence of a severe maternal outcome for massive obstetric haemorrhage (2.3 per 1000 live births). We calculated the highest mortality index for women with hepatitis E (5/28; 17.9%).

Table 4. Regional birth numbers and types of births, Namibia, 1 October 2018–31 March 2019

Region	No. of live births	No. (%) of normal vaginal births	No. (%) of assisted vaginal births	No. (%) of caesarean sections	Total no. of births
Erongo	2 451	2 086 (84.1)	1 (0.0)	393 (15.8)	2 480
Hardap	1 140	924 (83.9)	3 (0.3)	174 (15.8)	1 101
Karas	1 085	901 (82.4)	11 (1.0)	182 (16.6)	1 094
Kavango (east and west)	4 052	3 585 (86.6)	35 (0.8)	520 (12.6)	4 140
Khomas	6 211	4 777 (78.4)	49 (0.8)	1 269 (20.8)	6 095
Kunene	1 327	1 276 (94.9)	0 (0.0)	69 (5.1)	1 345
Ohangwena	4 147	4 086 (97.2)	3 (0.1)	114 (2.7)	4 203
Omaheke	1 206	1 051 (86.8)	3 (0.2)	157 (13.0)	1 211
Omusati	3 820	3 640 (94.3)	18 (0.5)	200 (5.2)	3 858
Oshana	3 386	2 357 (69.5)	2 (0.1)	1 033 (30.5)	3 392
Oshikoto	4 285	3 599 (84.0)	0 (0.0)	687 (16.0)	4 286
Otjozondjupa	2 353	2 129 (89.0)	6 (0.3)	258 (10.8)	2 393
Zambezi	1 643	1 527 (94.6)	0 (0.0)	87 (5.4)	1 614
Total	37 106	31 938 (85.8)	131 (0.4)	5 143 (13.8)	37 212

The proportion of births by caesarean section varied across the regions from 2.7% (114/4203) in Ohangwena to 30.5% (1033/3392) in Oshana (Table 4). For five women in need of a caesarean section, their uterus ruptured on the way from district to referral hospital. Hysterectomy was performed in 24 women (0.6 per 1000 live births), of which five were as a result of sepsis and 19 as a result of haemorrhage; 45.8% (11/24) of these women had received at least one caesarean section previously. A B-lynch suture to

prevent haemorrhage-related hysterectomy was placed in only one of the 19 women. For six other women who experienced a massive obstetric haemorrhage, a B-lynch suture was placed and no hysterectomy was needed.

Table 5. Fetal or neonatal outcome of the 298 maternal near-misses, Namibia, 1 October 2018–31 March 2019

Fetal or neonatal outcome (n = 312)[a]	**No. (%)**
Alive upon discharge of mother	157 (50.3)
Admitted to neonatal intensive care unit	33 (10.6)
Fresh stillborn	33 (10.6)
Macerated stillborn	6 (1.9)
Neonatal death	5 (1.6)
Terminated pregnancy	2 (0.6)
Miscarriage/ectopic	54 (17.3)
Mother still pregnant at discharge	15 (4.8)
Unknown	7 (2.2)

[a] There were 14 twin pregnancies.

Fetal and neonatal outcomes were poor (Table 5). Only 50.3% (157/312) of the infants went home alive at the time of discharge of the mother. Two pregnancies were terminated before the fetus had reached a viable gestational age: one woman had early-onset severe pre-eclampsia at 21 weeks gestation and one woman had an acute abdomen caused by bowel strangulation at 22 weeks gestation.

The most common challenge reported by medical personnel was understaffing and lack of experience in the staff present. Basic equipment, including blood pressure machines, was often lacking or not functioning. In 13 of the 30 district hospitals, no or only a few uncomplicated caesarean sections or laparotomies for ectopic pregnancies were performed as a result of a lack of skills, staff or equipment.

Discussion

Our collection of maternal near-miss data, in addition to routine maternal death analysis, has proven to be useful for several reasons. First, these data provide insights into the functioning of the health-care system, and several issues were addressed immediately. With less than 1500 live births per annum, maternal deaths seldom occur in district hospitals. The challenges met by these smaller facilities, such as a lack of access to basic surgery, have been highlighted. For several women, this lack of access to surgery led to a maternal near-miss complication such as uterine rupture or shock during transport to a referral hospital. We observed a low prevalence (0.6 per 1000 live births) of the life-saving intervention of hysterectomy, one of the few management options for haemorrhage when medical treatment fails; the relevant surgical skills are only available in eight of Namibia's 35 hospitals. This prevalence is lower than the global estimate of 0.9 per 1000 live births or 1.4 per 1000 live births in a South African district.[20,21] Underreporting is not likely to be the cause of this low prevalence, as missed cases were easily identified through theatre registers.

Second, an unanticipated but important benefit of maternal near-miss data collection was the positive effect on the morale of staff. Medical personnel are working under difficult circumstances with a high workload and constrained resources. However, by participating in the maternal near-miss surveillance, staff could take pride in their jobs by acknowledging the number of women they had saved.

Third, as maternal near-misses are more frequent than maternal deaths, near-miss data may be more useful in advocacy, for instance in abortion-related complications. Using data on the extent and complications of unsafe abortions was key in the battle to legalize abortion in Rwanda.[22]

Our study had several limitations. First, we only aimed to describe the implementation of maternal near-miss surveillance, although it is the resulting improvement in maternal outcome that is important. As surveillance continues, we anticipate that an apparent increase in the incidence of near-misses will be observed as a result of improved data collection, rather than any change in maternal outcome; similarly, an apparent increase in maternal deaths was reported in South Africa as a result of the implementation of national maternal death reviews.[23] Any observed trends may also be affected by the simultaneous implementation of other quality-improving projects, such as the provision of maternal death review feedback from a national to facility level, and the provision of emergency obstetric care courses to clinical staff and final-year medical students.

Second, our calculated incidence of maternal near-misses must be interpreted with caution, as we amended criteria to the local situation. Although this approach may hamper international comparison, the use of WHO criteria led to severe underreporting of maternal near-misses in the feasibility study conducted previously because of the limited diagnostics and management options in smaller facilities.[13] Two other middle-income countries – Brazil and Nigeria – implemented national maternal near-miss surveillance while adhering strictly to WHO identification criteria.[24,25] However, only tertiary health facilities participated in the Brazil and Nigeria surveys, in which the applicability of WHO criteria may not have been problematic as such facilities are generally better equipped than smaller hospitals.

Third, our calculated maternal mortality ratio (62.0 per 100 000 live births) is much lower than that estimated by the Demographic Health Survey or WHO.[3,6] On analysis of the annual maternal death review findings, the National Maternal Death Review Committee assume this result is due to underreporting; the fact that the maternal mortality ratio varied widely between regions is most likely explained by differences in quality of reporting rather than differences in quality of care. Similar or even larger discrepancies between WHO estimates and national maternal death reviews were also found in Ethiopia, Malawi and South Africa.[26–28] Such large discrepancies need to be explored further, as progress in improving quality of care can only be monitored with a reliable maternal mortality ratio.

Fourth, our biggest challenge to successful implementation of the surveillance was a limited budget. We were not able to fund any administrative staff to support data collection or visit every participating facility before the onset of the surveillance. Cases may have been missed, affecting the quality of our data. However, as data collection depended on local staff, the approach gave them the opportunity to show leadership and take ownership of data collection. In general, it appeared staff were more likely to collect accurate data when trained personally and when aware of the aim of the project. Barriers to accurate data collection by local staff were lack of time due to a high workload and the fear of making mistakes in data collection.

The maternal near-miss surveillance identified several issues that need to be explored further before they can be addressed. First, over 80% of maternal near-misses were the result of direct causes compared with less than half of the maternal deaths, which corresponds with findings in Brazil and Nigeria.[24,29–33] This difference could be the result of high mortality indexes among several indirect causes, such as observed for hepatitis E and described for some cardiac disorders, human immunodeficiency virus and tuberculosis, common among young women in Namibia.[32,34–36] However, underreporting of maternal near-misses as a result of indirect causes is also likely;

such patients were more likely to have been on general wards, where maternal near-miss data collection was not being supervised.

Second, nearly half of the women who experienced a maternal near-miss during our 6-month survey gave birth by caesarean section; caesarean sections are used for varying proportions of births across the regions, by up to as many of 30% of births at a population level (Table 4). The highest proportions are partly explained by the fact that some regions (namely Karas, Khomas, Oshana and Oshikoto) contain referral and regional hospitals; however, overuse of caesarean section, despite the well-known complications of this procedure, is also likely.[37] Over one-fifth of our study population had experienced a caesarean section previously, and among the women who needed a hysterectomy this proportion was almost half. Importantly, an instrumental vaginal birth, which could potentially prevent birth by caesarean section, was rarely performed in both our maternal near-miss and the general pregnant population: a common finding in low- and middle-income settings.[38,39] The inadequate use of these two potential lifesaving interventions (the overuse of caesarean section and underuse of instrumental vaginal birth), a problem in many countries,[40] and its potential negative effect on maternal outcome needs to be urgently assessed in Namibia.

Third, overall fetal and neonatal outcomes were poor, which is commonly seen among women with severe morbidity.[41] To assess the role of quality of care, neonatal outcome must be assessed in correlation with maternal condition.[29,32] Poor neonatal outcome due to uterine rupture is seen even in high-income countries, although neonatal outcome is better after a spontaneous vaginal birth complicated by postpartum haemorrhage.[42]

Conclusion

We identified two potentially important facilitators that will support the continuation of maternal near-miss surveillance in Namibia: its independence of the availability of donor funding and the motivation of staff to continue collecting data. Causes of maternal death are similar for most countries, but individual countries experience local challenges. Maternal near-miss surveillance is a useful intervention to identify these challenges, the knowledge of which can be used by policy-makers and programme managers in the development of locally tailored targeted interventions to improve maternal outcome in their setting.

References

1. United Nations. Sustainable development goal 3. Ensure healthy lives and promote well-being for all at all ages. (Available from: https://sustainabledevelopment.un.org/sdg3) [07-06-2020].
2. Alkema L, Chou D, Hogan D, Zhang S, Moller AB, Gemmill A, et al.; United Nations Maternal Mortality Estimation Inter-Agency Group collaborators and technical advisory group. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet. 2016 Jan 30;387(10017):462–74.
3. Maternal Mortality Estimation Inter-Agency Group. Maternal mortality in 2000-2017. Internationally comparable MMR estimates by the Maternal Mortality Estimation Inter-Agency Group (MMEIG), Namibia. World Health Organisation: Geneva, 2017.
4. Namibia Statistics Agency. Namibia Inter-censal Demographic Survey 2016 report. Namibia Statistics Agency: Windhoek, 2017.
5. Geingob H. Harambee Prosperity Plan; 2016. (Available from: http://www.nied.edu.na/assets/documents/08Governments/13HPP_page_70-71.pdf) [19-01-2020]
6. Ministry of Health and Social Services. Demographic and Health Survey Namibia; 2013. Ministry of Health and Social Services: Windhoek, 2014.
7. World Health Organization. Beyond the numbers. Reviewing maternal deaths and complications to make pregnancy safer. World Health Organization: Geneva, 2004.
8. Knight M; INOSS. The International Network of Obstetric Survey Systems (INOSS): benefits of multi-country studies of severe and uncommon maternal morbidities. Acta Obstet Gynecol Scand. 2014 Feb;93(2):127–31.
9. Knight M, Kurinczuk J. Spotlight on … MBRRACE-UK. Obstet Gynaecol. 2018;20(1):5–6.
10. Nelissen E, Mduma E, Broerse J, Ersdal H, Evjen-Olsen B, van Roosmalen J, et al. Applicability of the WHO maternal near miss criteria in a low-resource setting. PLoS One. 2013 04 16;8(4):e61248.
11. van den Akker T, Beltman J, Leyten J, Mwagomba B, Meguid T, Stekelenburg J, et al. The WHO maternal near miss approach: consequences at Malawian district level. PLoS One. 2013;8(1):e54805.
12. Tura AK, Stekelenburg J, Scherjon SA, Zwart J, van den Akker T, van Roosmalen J, et al. Adaptation of the WHO maternal near miss tool for use in sub-Saharan Africa: an international Delphi study. BMC Pregnancy Childbirth. 2017 12 29;17(1):445.
13. Heemelaar S, Kabongo L, Ithindi T, Luboya C, Munetsi F, Bauer AK, et al. Measuring maternal near-miss in a middle-income country: assessing the use of WHO and sub-Saharan Africa maternal near-miss criteria in Namibia. Glob Health Action. 2019;12(1):1646036.
14. Heemelaar S, Josef M, Diener Z, Chipeio M, Stekelenburg J, van den Akker T, et al. Maternal Near Miss Form; 2020. (Available from: https://doi.org/10.6084/m9.figshare.12456200.v1) [23-06-2020]
15. Ministry of Health and Social Services Division Quality Assurance. National Guidelines for Review and Response to Maternal Deaths, Near Misses, Stillbirths and Neonatal Deaths. Windhoek, 2019.
16. World Health Organization. The WHO Application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM. World Health Organization: Geneva, 2012.
17. World Health Organization. Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. World Health Organization: Geneva, 2011.
18. Schaap T, Bloemenkamp K, Deneux-Tharaux C, Knight M, Langhoff-Roos J, Sullivan E, et al.; INOSS. Defining definitions: a Delphi study to develop a core outcome set for conditions of severe maternal morbidity. BJOG. 2019 Feb;126(3):394–401.
19. Ministry of Health and Social Services. Outbreak of Hepatitis E Virus (HEV) in Namibia, Situation Report (SITREP No. 64). Ministry of Health and Social Services: Windhoek, 2019.
20. Roosmalen J, et al. A district-wide population-based descriptive study of emergency peripartum hysterectomy in a middle-income country. Int J Gynaecol Obstet. 2019 Jul;146(1):103–9.
21. van den Akker T, Brobbel C, Dekkers OM, Bloemenkamp KW. Prevalence, indications, risk indicators, and outcomes of emergency peripartum hysterectomy worldwide: a systematic review and meta-analysis. Obstet Gynecol. 2016 12;128(6):1281–94.
22. Umuhoza C, Oosters B, van Reeuwijk M, Vanwesenbeeck I. Advocating for safe abortion in Rwanda: how young people and the personal stories of young women in prison brought about change. Reprod Health Matters. 2013 May;21(41):49–56.
23. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2011-2013: Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa, short report. Department Health: Pretoria, 2015.

24. Cecatti JG, Costa ML, Haddad SM, Parpinelli MA, Souza JP, Sousa MH, et al.; Brazilian Network for Surveillance of Severe Maternal Morbidity study Group. Network for Surveillance of Severe Maternal Morbidity: a powerful national collaboration generating data on maternal health outcomes and care. BJOG. 2016 May;123(6):946–53.
25. Okusanya BO, Adetoro OO, Aboyeji P, Ekele BA, Etuk SJ, Chama CM, et al.; Nigeria Near-miss and Maternal Death Surveillance Network. Establishing a nationwide maternal death and near-miss surveillance system in a low-income country: lessons, prospects and challenges. BJOG. 2019 Jun;126(S3) Suppl 3:7–11.
26. Mataya R, on behalf of Malawi National Confidential Committee on Enquiry into Maternal Death. Report on the Confidential Enquiry into Maternal Deaths in Malawi (2008-2012). Ministry of Health: Lilongwe, 2014.
27. Melberg A, Mirkuzie AH, Sisay TA, Sisay MM, Moland KM. 'Maternal deaths should simply be 0': politicization of maternal death reporting and review processes in Ethiopia. Health Policy Plan. 2019 Sep 1;34(7):492–8.
28. Moodley J, Pattinson RC, Fawcus S, Schoon MG, Moran N, Shweni PM; National Committee on Confidential Enquiries into Maternal Deaths in South Africa. The confidential enquiry into maternal deaths in South Africa: a case study. BJOG. 2014 Sep;121(4) Suppl 4:53–60.
29. Adamu AN, Okusanya BO, Tukur J, Ashimi AO, Oguntayo OA, Tunau KA, et al. Maternal near-miss and death among women with hypertensive disorders in pregnancy: a secondary analysis of the Nigeria Near-miss and Maternal Death Survey. BJOG. 2019 Jun;126(S3) Suppl 3:12–8.
30. Sotunsa JO, Adeniyi AA, Imaralu JO, Fawole B, Adegbola O, Aimakhu CO, et al. Maternal near-miss and death among women with postpartum haemorrhage: a secondary analysis of the Nigeria Near-miss and Maternal Death Survey. BJOG. 2019 Jun;126(S3) Suppl 3:19–25.
31. Adanikin AI, Umeora O, Nzeribe E, Agbata AT, Ezeama C, Ezugwu FO, et al. Maternal near-miss and death associated with abortive pregnancy outcome: a secondary analysis of the Nigeria Near-miss and Maternal Death Survey. BJOG. 2019 Jun;126(S3) Suppl 3:33–40.
32. Adeniran AS, Ocheke AN, Nwachukwu D, Adewole N, Ageda B, Onile T, et al.; Nigeria Near-miss and Maternal Death Surveillance Network. Non-obstetric causes of severe maternal complications: a secondary analysis of the Nigeria Near-miss and Maternal Death Survey. BJOG. 2019 Jun;126(S3) Suppl 3:41–8.
33. Etuk SJ, Abasiattai AM, Ande AB, Omo-Aghoja L, Bariweni AC, Abeshi SE, et al. Maternal near-miss and death among women with rupture of the gravid uterus: a secondary analysis of the Nigeria Near-miss and Maternal Death Survey. BJOG. 2019 Jun;126(S3) Suppl 3:26–32.
34. Mgori NK, Mash R. HIV and/or AIDS-related deaths and modifiable risk factors: a descriptive study of medical admissions at Oshakati Intermediate Hospital in Northern Namibia. Afr J Prim Health Care Fam Med. 2015;7(1):e1–7.
35. Zühlke L, Engel ME, Karthikeyan G, Rangarajan S, Mackie P, Cupido B, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). Eur Heart J. 2015 May 7;36(18):1115–1222a.
36. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, et al.; ESC Scientific Document Group. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018 Sep 7;39(34):3165–241.
37. Sobhy S, Arroyo-Manzano D, Murugesu N, Karthikeyan G, Kumar V, Kaur I, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. Lancet. 2019 05 11;393(10184):1973–82.
38. Bailey PE, van Roosmalen J, Mola G, Evans C, de Bernis L, Dao B. Assisted vaginal delivery in low and middle income countries: an overview. BJOG. 2017 Aug;124(9):1335–44.
39. Betrán AP, Temmerman M, Kingdon C, Mohiddin A, Opiyo N, Torloni MR, et al. Interventions to reduce unnecessary caesarean sections in healthy women and babies. Lancet. 2018 10 13;392(10155):1358–68.
40. Miller S, Abalos E, Chamillard M, Ciapponi A, Colaci D, Comandé D, et al. Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. Lancet. 2016 10 29;388(10056):2176–92.
41. Geller SE, Koch AR, Garland CE, MacDonald EJ, Storey F, Lawton B. A global view of severe maternal morbidity: moving beyond maternal mortality. Reprod Health. 2018 06 22;15(S1) Suppl 1:98.
42. Vandenberghe G, Bloemenkamp K, Berlage S, Colmorn L, Deneux-Tharaux C, Gissler M, et al.; INOSS (the International Network of Obstetric Survey Systems). The International Network of Obstetric Survey Systems study of uterine rupture: a descriptive multi-country population-based study. BJOG. 2019 Feb;126(3):370–81.

Part II.

The impact of cardiac disease and acute Hepatitis E on maternal outcome

Chapter 5.

Maternal mortality due to cardiac disease in low- and middle-income countries: a systematic review

Steffie Heemelaar, Annelieke Petrus, Marian Knight, Thomas van den Akker

Trop Med Int Health. 2020 Jun;25(6):673-686

Abstract

Objective

To assess the frequency of maternal death (MD) due to cardiac disease in low- and middle-income countries (LMIC).

Methods

Systematic review searching Medline, EMBASE, Web of Science, Cochrane Library, Emcare, LILACS, African Index Medicus, IMEMR, IndMED, WPRIM, IMSEAR up to 01/Nov/2017. Maternal mortality reports from LMIC reviewing all MD in a given geographical area were included. Hospital-based reports or those solely based on verbal autopsies were excluded. Numbers of MD and cardiac-related deaths were extracted. We calculated cardiac disease MMR (cMMR, cardiac-related MD/100 000 live births) and proportion of cardiac-related MDs among all MDs. Frequency of cardiac MD was compared with the MMR of the country.

Results

Forty-seven reports were included, which reported on 38,486 maternal deaths in LMIC. Reported cMMR ranged from 0/100 000 live births (Moldova, Ghana) to 31.9/100 000 (Zimbabwe). The proportion of cardiac-related MD ranged from 0% (Moldova, Ghana) to 24.8% (Sri Lanka). In countries with a higher MMR, cMMR was also higher. However, the proportion of cardiac-related MD was higher in countries with a lower MMR.

Conclusion

The burden of cardiac-related mortality is difficult to assess due limited availability of mortality reports. The proportion of cardiac deaths among all MD appeared to be higher in countries with a lower MMR. This is in line with what has been called 'obstetric transition': pre-existing medical diseases including cardiac disease are becoming relatively more important where the MMR falls.

Introduction

It is generally assumed that cardiac disease is rare in women of reproductive age. However, in high-income countries such as the United Kingdom, the United States of America or the Nordic countries, cardiac disease has become the commonest cause of maternal deaths (MD).[1-3] Data regarding the number of maternal deaths due to cardiac disease in low- and middle-income countries (LMIC) are scarce. Attention to cardiac disease as a cause of maternal mortality is rare compared with conditions such as hypertensive disorders, postpartum haemorrhage and HIV/AIDS, which are regarded as more important causes.[4,5] However, the prevalence of cardiac disease is most likely underreported in LMIC due to inadequate diagnostic means and poor registration.[6-8]

Global progress reports on maternal mortality have emphasised the increased importance of indirect maternal deaths due to pre-existing medical conditions in LMICs that have managed to reduce their maternal mortality ratio (MMR).[5,9] It is likely that the role of cardiac disease in maternal deaths could become increasingly important where other causes, primarily direct obstetric causes, become less prevalent.

This is the first systematic review to assess the frequency of maternal deaths due to cardiac disease based on national and regional maternal mortality reports from LMIC and to compare these findings with the MMR of that country.

Methods

Search strategy and selection criteria

Maternal mortality reports from LMIC were identified by a systematic review of literature. Medline (using Pubmed), EMBASE, Web of Science, Cochrane Library, Emcare, LILACS, African Index Medicus, IMEMR, IndMED, WPRIM and IMSEAR databases were searched from January 1 2000 to November 1 2017 with the assistance of a qualified librarian at the Leiden University Medical Centre (Appendix 1). We screened the website of the Maternal Death Surveillance and Response (MDSR) Action Network and references from the maternal mortality country profiles of the WHO for eligible publications.[10,11] If a publication mentioned a different or more recent report, this reference was searched, or, if it could not be retrieved, the first author of the referring publication was contacted to obtain the report. The systematic review was conducted following the PRISMA guidelines.[12]

Regional and national maternal death reviews (MDR) performed in a low- or middle-

income country were eligible if the aim of the study was to review all maternal deaths (MD) in a given geographical area, preferably including out-of-facility deaths. However, a facility-based approach, exclusively reviewing facility-based MDs, is commonly used in regions with high institutional birth rates and in several mortality reports of high quality such as the confidential enquiries into maternal deaths of South Africa, Moldova and Kerala region, India.[13-19] Therefore, we considered reports documenting MDs from all health facilities of all levels within the study area, including health posts and health centres. Reports from single or non-population-based groups of hospitals were excluded as the data were unlikely to be representative of the study area. The World Bank rating of 2017 was used to assess whether a country was considered an LMIC.[20]

Reports were included if maternal deaths met the WHO definition of 'deaths of women while pregnant or within 42 days of termination of pregnancy from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes', and if the total number of MD and the number of deaths specified per cause were provided.[21] To identify MD due to cardiac disease, one of the following identifiers had to be used: cardiac disease, heart disease or the specific cardiac condition such as rheumatic heart disease (RHD), any type of cardiomyopathy or congenital heart disease. Authors of reports using less specific definitions such as 'cardiovascular disorders' or 'cardiac failure' were contacted to provide the exact number of MD due to cardiac disease. If these data could not be retrieved, the report was excluded.

Studies exclusively based on verbal autopsy, sisterhood methods or household survey were excluded since these were considered insufficient to robustly identify MD due to cardiac disease. Studies with a sample size below twenty were excluded. Reports were screened for duplication. If one of the duplicate reports contained data from a larger study area or longer study period, this report was included. Full text had to be available in English, French, German, Spanish or Portuguese.

Study selection was done by two independent researchers (SH and AP). The opinion of a third researcher (TA) was sought if consensus was not reached. Data extraction was performed by one author (SH) and reviewed by a second (AP).

Data analysis

To assess the quality of the included reports, we evaluated the methods used for identification of MD in the study area, and those for establishing cause of death, as well as the level of expertise available for case review. For each item, the best available method is listed at the top in Table 1. First, we evaluated robustness of MD

identification in the study area and whether out-of-facility deaths were included. We considered MD identification of the highest quality if there was a system in place to trace maternal deaths in an enhanced manner, including identifying out-of-facility deaths, for example through a Reproductive Age Mortality Survey (RAMOS),

Table 1. Quality assessment of mortality reports

Identification of MD	Review at facility level	Review at central level	Cause of death established by
OFD included, systematically traced	Facility-based audit	Audit of complete file	Panel with O&G and non-O&G specialists
OFD included, but not systematically traced	MD notification form	Review of MD notification form	Panel with O&G specialist
Excluded women who died outside a facility		None	Staff at facility
			Other

Presented are the different methods used to identify maternal deaths in the study area, to review cases at facility and central level and which level of expertise was available to establish cause of death. The best available method is listed at the top of each section.
MD, maternal death; OFD, out-of-facility death; O&G, obstetrics and gynaecology.

involvement of communities and/or analysis of information from mortuaries. Secondly, the method used to establish the cause of maternal deaths was assessed. At facility level, establishment of the cause of death could range from a MD notification form, filled in by the attending healthcare worker, up to a facility-based audit. At central level, for example regional or national level, review of the cause of death could range from analysing information of the MD notification forms up to a complete review of medical records. Finally, level of expertise for case review was based on the presence of an obstetrician and additional medical specialists such as anaesthetists, physicians, pathologists or paediatricians.

We did not produce a summary quality measure since we considered the robustness of MD identification of equal importance to the methods and level of expertise used to establish cause of death. For some reports, a high level of expertise was available at central level to review all cases, but identification of MD and quality of data collection at facility level was poor. On the contrary, some reports used a well-functioning MD notification system but had limited expertise available for case review. The total number of MD, deaths from cardiac disease and the study period were extracted from each report. The proportion of cardiac MDs among all MDs (%cMD) was calculated by dividing the number of reported cardiac MD by the total number of MD and is presented as a percentage. The MMR was calculated as the number of reported MD per 100 000 live births and cardiac disease MMR (cMMR) as the number of reported cardiac-related MD per 100 000 live births. For population-based studies, the MMR was extracted from the report. Reports were defined as population-based when the aim of the study was to review all MD that occurred during the study period in the study area, including women who died outside a health facility. For facility-based reports or if the report did not provide data to calculate an MMR, the national MMR estimated by the WHO for the closest corresponding year of the study period was

extracted from the 'Maternal mortality country profiles'.[11] Reports mentioning zero cardiac deaths were assessed for possible missed cardiac deaths. If the report included deaths due to unknown causes or unclear diagnoses, for example death due to anaemia, sudden death or out-of-facility death and no autopsy was performed, this meant that MDs due to cardiac disease were possibly missed. In such cases, the number of cardiac deaths was reported as 'missing', and the report excluded from data analysis. The level of income of a country was categorised as either upper MIC, lower MIC or LIC based on the World Bank rating at the time of data collection of each country.[20]

For all reports, the relation of the frequency of cardiac-related MD with the MMR of its country was assessed using plots. For countries with multiple reports of different study periods, but reporting data of the same geographical area, progress over time was explored using detailed plots. Data regarding the total number of cardiac MD were plotted in a world map. When multiple reports were available for one country, the most recent report, covering the largest geographical area and/or of highest quality, was used for comparison. Selection process is detailed further in Appendix 2.

Considering the low number and heterogeneity of the included reports, frequency of cardiac MD in relation to the MMR or time was not compared statistically. Data were analysed using SPSS version 22 (IBM Corp., Armonk, NY). Plots were drafted with Prism version 8.1 (GraphPad Software). The review was registered with PROSPERO (CRD42018089452). All results are presented in the tables and figures and therefore not published in a separate online database.

Results

Forty-seven maternal mortality reports were included, reporting on a total of 38,486 maternal deaths in LMIC.[13-19,22-61] Study selection is summarised in Figure 1. Titles and abstracts of 2064 identified records were screened, which resulted in 132 eligible records. Full-text articles of these records were evaluated and 85 reports excluded. In 11 of 132 reports, it was unclear whether the definition used comprised maternal deaths due to cardiac disease alone. In four reports, the quality of the methods section was insufficient to assess the methods used to identify MD and establish the cause of death. Three hospital-based reports reviewed MD for one or multiple hospitals only but were not population-based. Two regional reports from South Africa were excluded as national reports were available for the same study period.

The 47 included reports included maternal mortality data from 29 countries. Characteristics of these reports are presented in Table 2. The included reports presented data from eight LIC, thirteen lower MIC and eight upper MIC. Twenty

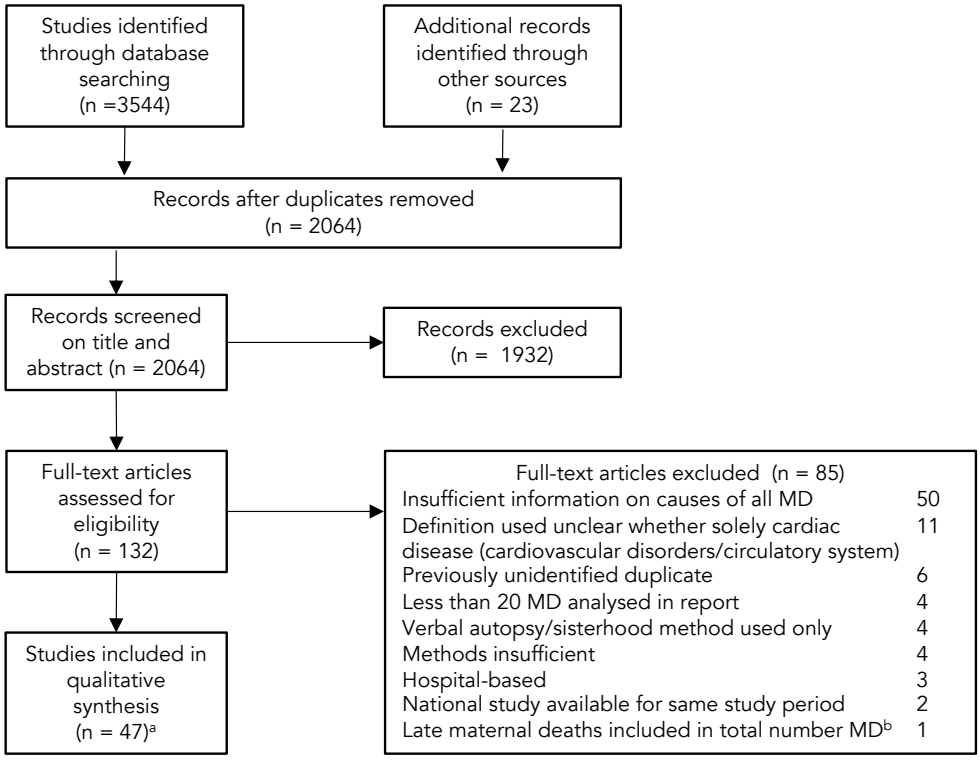


Figure 1. Flowchart showing selection of studies included in review.
MD, Maternal death
[a]The corresponding author of a report from Rwanda confirmed that MDs described as 'due to cardiac failure' were all MD due to cardiac disease. The report from Moldova for 2006–2008 only mentioned the total number of indirect deaths. The author of this report confirmed none of these deaths were caused by cardiac disease.
The same author provided us with the mortality data of the review of 2009–2013, of which the report in English is not yet available.
[b]Late maternal death is a death of a woman from direct or indirect causes more than 42 days but less than one year after termination of pregnancy.

reports presented regional maternal mortality data, and twenty-seven reported national data. The study period was clearly defined in all studies and ranged from 1992 until 2015. Twenty-seven studies were population-based. [23,26-28,31,33-34,37-38,40-41,43-44,46,55,57,59-61] Fourteen reports were facility-based.[13,19,22,32,35,42,45,56,58] The proportion of reviewed deaths outside facilities ranged from 1.8% (Botswana, 2010) to nearly half of the reviewed deaths in Zimbabwe (49.3%), Pakistan (50.0%), Bangladesh (51.6%) and Nepal (53.8%).[48,50,53,57] In 21 out of 27 population-based reports, an MMR was extracted directly from the report.[23,26-27,31,33-34,37-38,40-41,43,46-50,54,55,57,59,60] Five reports stated zero cardiac deaths of which data were reported as missing of the reports from Tanzania, Malawi and Sudan as possible deaths due to cardiac disease were missed (Appendix 2).[14,25,36,45,51] In these reports, cause of death was not known (330/1433 deaths in the report from Malawi), or unclear (75/898 deaths due to anaemia in the report from Sudan, 213/1433 deaths due to anaemia in the report from Malawi, 1/45 death due to anaemia and one sudden death in the report from Tanzania and in all three reports no autopsies were performed).

Table 2. Overview of 47 included maternal mortality reports

Country	LIC/l-MIC/u-Mic	MMR	Period	Cardiac MD/ total MD	Proportion cardiac MD (%)	cMMR
Bangladesh	LIC	479[b]	1996-1997	291/7086	4·1%	19·7
Ethiopia	LIC	523[b]	2008	14/633	2·2%	11·6
Ghana, Upper West reg.	LIC	325[b]	2009	0/47	0·0%	0·0
Ghana, Accra reg[a]	LIC	467[b]	2002	3/178	1·7%	7·9
Malawi	LIC	629[b]	2008-2012	XX[f]/1433	N/A	N/A
Malawi, Central reg.[a]	LIC	648[b]	2007	1/43	2·3%	15·1
Nepal, 8 reg.	LIC	229[c]	2008-2009	11/160	6·9%	15·7
Rwanda	LIC	381[b]	2009-2013	23/987	2·3%	8·9
Tanzania, Arusha reg.	LIC	961[b]	1995-1996	XX[f] /45	N/A	N/A
Zimbabwe	LIC	725[c]	2006	16/364	4·4%	31·9
Egypt, Dakahlia reg.	l-MIC	71[c]	2004-2005	15/171	8·8%	6·3
Egypt[a]	l-MIC	84[c]	2000	45/580	7·8%	6·5
El Salvador	l-MIC	50[c]	2011	4/64	6·3%	3·2
Guatemala, "dep. of Guatemala"	l-MIC	156[c]	1993-1996	2/435	0·5%	0·7
India, Kerala reg.	l-MIC	29[e]	2004-2009	32/501	6·4%	1·9
Jamaica[a]	l-MIC	95[c]	1998-2003	12/232	5·2%	4·9
Jamaica	l-MIC	96[c]	1993-1995	3/141	2·1%	2·1
Jordan	l-MIC	19[c]	2007-2008	8/76	10·5%	2·0
Moldova[a]	l-MIC	34[b]	2009-2013	2/49	4·1%	1·4
Moldova	l-MIC	39[b]	2006-2008	0/29	0·0%	0·0
Morocco, 6 priority reg.	l-MIC	121[c]	2015	7/152	4·6%	5·6
Morocco[a]	l-MIC	153[b]	2009	16/303	5·3%	8·1
Pakistan, Sindh reg.	l-MIC	279[c]	2006-2008	3/72	4·2%	11·6
Russia, St. Petersburg	l-MIC	43[c]	1992-2003	12/179	6·7%	2·9
Sri Lanka a	l-MIC	34[c]	2015	28/113	24·8%	8·4
Sri Lanka	l-MIC	32[c]	2014	16/112	14·3%	4·6
Sudan	l-MIC	349[b]	2010	XX[f]/898	N/A	N/A
Swaziland	l-MIC	586[b]	2000-2001	2/43	4·7%	27·3
Botswana	u-MIC	129[b]	2015	2/73	2·7%	3·5
Botswana[a]	u-MIC	169[b]	2010	7/55	12·7%	21·5
China, Wuhan reg.	u-MIC	15[c]	2001-2012	8/91	8·8%	1·3
China, Henan reg.	u-MIC	45[c]	1996-2009	90/1129	8·0%	3·6
China, Shanghai reg.	u-MIC	21[c]	2000-2009	24/262	9·2%	1·9
China, Zhejiang reg.	u-MIC	58[b]	1995-2008	95/901	10·5%	6·1
China combined[d]	u-MIC	35[d]	1995-2012	217/2383	9·1%	3·2
Fiji	u-MIC	34[b]	2008-2012	5/37	13·5%	4·6
Irak	u-MIC	27[c]	2010-2012	79/1039	7·6%	2·1
Iran, Yazd reg.	u-MIC	34[b]	2002-2011	8/40	20·0%	6·8
Malaysia[a]	u-MIC	29[c]	2009-2011	65/430	15·1%	4·3
Malaysia	u-MIC	27[c]	2006-2008	49/396	12·4%	3·4
South Africa[a]	u-MIC	138[b]	2014	49/1238	4·0%	5·5
South Africa	u-MIC	154[b]	2011-2013	169/4333	3·9%	6·0
South Africa	u-MIC	154[b]	2008-2010	157/4867	3·2%	5·0
South Africa	u-MIC	112[b]	2005-2007	97/3959	2·5%	2·7
South Africa	u-MIC	112[b]	2002-2004	85/3296	2·6%	2·9
South Africa	u-MIC	85[b]	1999	23/584	3·9%	3·3
South Africa	u-MIC	85[b]	1998	28/565	5·0%	4·2
Surinam	u-MIC	130[c]	2010-2014	2/65	3·1%	4·0

	OFD included	Review at facility level	Review central level	Case review by
	Yes	Research team	None	Recent medical graduates
	Yes	MD notification form	None	Staff at facility
	if reported	MD notification form	Audit of complete file	Panel, expertise unclear
	Yes	None	Audit of complete file	Panel with O&G specialist
	No	Facility audit	CEMD, audit of complete file	Panel with O&G specialist
	No	Facility audit	None	Staff at facility
	Yes	Facility audit	None	Staff at facility
	No	Facility audit	None	Staff at facility
	Yes	None	Audit of complete file	Panel with O&G specialist
	Yes	MD notification form	Review of MD notification forms	Staff at facility
	Yes	MD notification form	Audit of complete file	Panel, expertise unclear
	Yes	None	Audit of complete file	Panel with O&G and non O&G specialists
	Yes	MD notification form	Audit of complete file	Panel, expertise unclear
	Yes	None	Audit of complete file	Data clerk
	No	MD notification form	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	Yes	None	Audit of complete file	Panel, expertise unclear
	Yes	None	Audit of complete file	Panel, expertise unclear
	Yes	None	Audit of complete file	Panel, expertise unclear
	No	MD notification form	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	MD notification form	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	Yes	MD notification form	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	If reported	MD notification form	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	Yes	MD notification form	None	Staff at facility
	Yes	Facility audit	None	Research team with O&G specialist
	Yes	District audit	Audit of complete file	Panel with O&G and non O&G specialists
	Yes	District audit	Audit of complete file	Panel with O&G and non O&G specialists
	If reported	MD notification form	Review of MD notification forms	Panel, expertise unclear
	No	None	Audit of complete file	Panel, expertise unclear
	Unknown	Unclear	National statistics	Unknown
	Yes	MD notification form	Audit of complete file	Panel, expertise unclear
	Yes	MD notification form	Audit of complete file	Panel, expertise unclear
	Yes	MD notification form	Audit of complete file	Panel with O&G specialist
	Yes	MD notification form	Audit of complete file	Panel with O&G specialist
	Yes	MD notification form	Audit of complete file	Panel, expertise unclear
	If reported	MD notification form	None	Staff at facility
	Yes	MD notification form	Audit of complete file	Panel with O&G specialist
	Unknown	MD notification form	Unclear	Unclear
	Yes	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	Yes	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	No	Facility audit	CEMD, audit of complete file	Panel with O&G and non O&G specialists
	Yes	MD notification form	Audit of complete file	Panel with O&G and non O&G specialists

Table 2. Overview of 47 included maternal mortality reports. (*Table shown on previous page*)
LIC, low-income country; l-MIC, lower middle-income country; u-MIC, upper middle-income countries; MMR, maternal mortality ratio/100,000 live births; MD, maternal death; cMMR, cardiac related maternal mortality ratio/100,000 live births; N/A, not available; OFD, out of facility deaths; CEMD, Confidential enquiry into maternal deaths; O&G, obstetrics and gynaecology.
[a] Data report used for figure 3, as most representative data for country.
[b] MMR estimation of WHO, population-based study but no MMR available in report or not population-based study.
[c] MMR from report, population-based study.
[d] MMR based on average of 4 reports from China.
[e] MMR from report used even though facility based report. The region is known for a consistently lower MMR than the national MMR due better health indicators, more details available in appendix 2.
[f] Missing data.

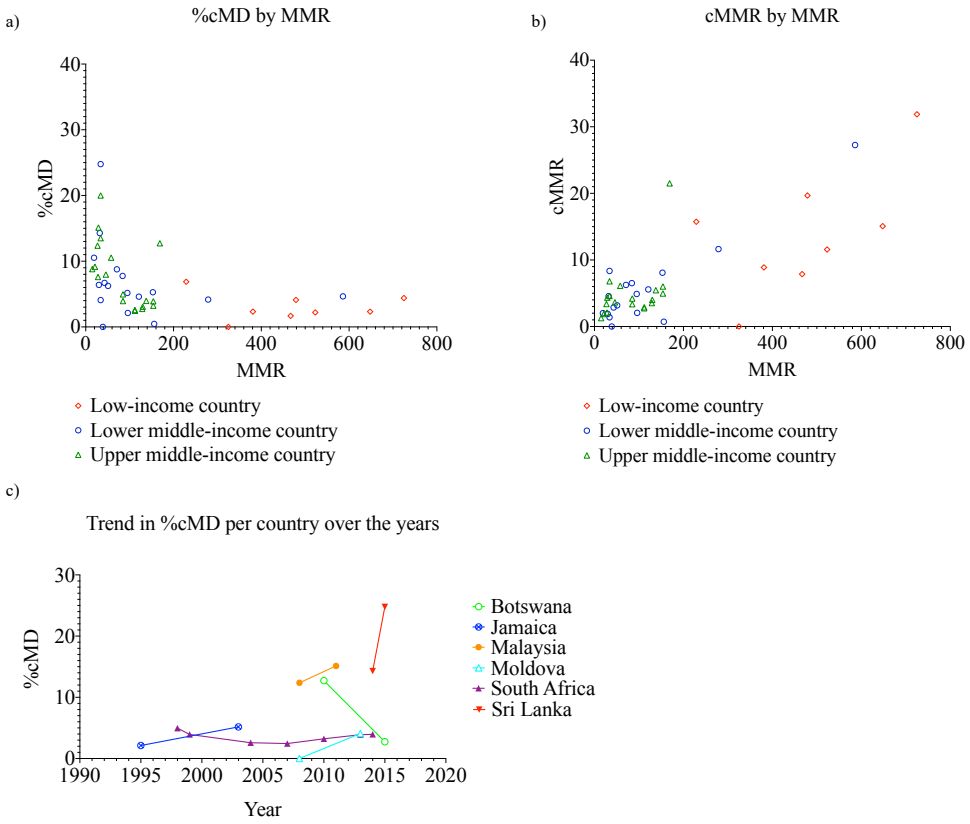


Figure 2. Three plots showing the trends of maternal deaths due to cardiac disease in relation to the MMR of it's country and over time.
a) The relation of the proportion of cardiac related maternal deaths with the MMR of it's country. All included studies are plotted.
b) The relation of cMMR with the MMR of it's country. All included studies are plotted.
c) For the available studies with multiple reports the proportion of cardiac related maternal deaths over time are plotted.
cMD, cardiac related maternal death.
MMR, maternal mortality ratio/100,000 live births; cMMR, cardiac related maternal mortality ratio/100,000 live births

Reported cMMR ranged from 0/100 000 live births in reports from Ghana and Moldova to 31.9/100 000 live births in Zimbabwe.[4,36,48] The proportion of reported cardiac-related MD among all MD ranged from 0% in reports from Ghana and Moldova to 24.8% in Sri Lanka.[14,36,38] Figure 2 shows the relation of the frequency of cardiac MD with the MMR of its country. Level of economy of the countries is indicated by colour. Reports from countries with a lower MMR appear to have a higher proportion of cardiac MD (Figure 2a), but the cardiac MMR is higher in countries with a higher MMR (Figure 2b). In reports from LIC, the proportion of cardiac MDs appeared to be lower compared with MIC; however, the cMMR is higher in LIC. For six countries, multiple reports of the same study area were available, and trends over time were plotted in Figure 2c. For five countries, the same methods were used to collect data over time, whereas two different methods were used for the two reports from Botswana.

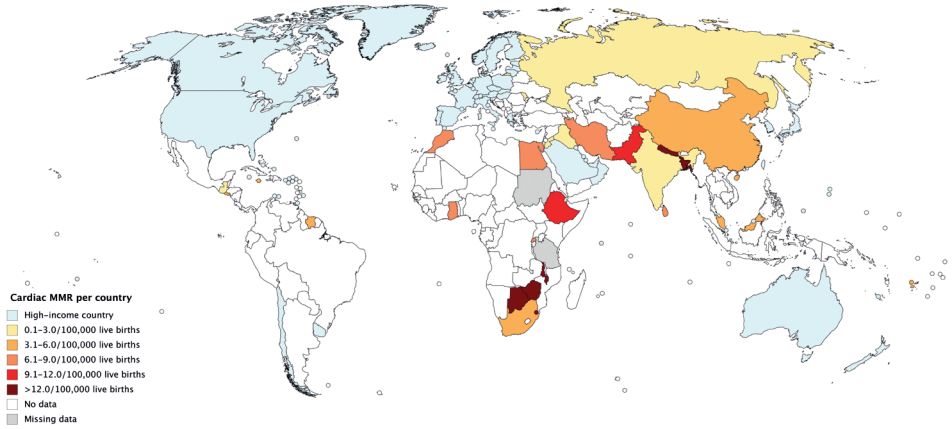


Figure 3. World map showing incidence of maternal deaths due to cardiac disease per country.
MMR, maternal mortality ratio.

Figure 3 shows the cardiac MMR for each country. For this figure, the national or most recent study was selected if multiple reports were available for these countries, Table 2. For Botswana, Ghana and Malawi, a regional or less recent report was considered to have more representative data and selected for country comparison (Appendix 2). For China, four regional reports with similar methods were available. The findings of these four reports were combined for country comparison in Figure 3.

The included reports used different methods to establish the cause of maternal deaths. In six reports, information regarding the cause of death was only based on maternal death notification forms, filled in at facility level (Table 2).[25,28,30,39,48,50] The report from Botswana in 2015 was a national statistics mortality report. In this report, it was unclear whether the cause of death was based on information from

death certificates, maternal death notification forms or audits.[29] Four reports were based on information from audits at facility level only.[34,42,56,57] For the 36 remaining reports, review of medical records was performed at regional or national level. Table 2 indicates the level of expertise available to establish cause of death. In the reports from Guatemala and Botswana (2015), the actual number of deaths due to cardiac disease may have been higher, but the definitions applied were unclear, thus we have reported the minimum number. In both reports, two maternal deaths due to cardiomyopathy were presented. In the report from Botswana, another eight MD due to 'diseases of the circulatory system' were documented and for Guatemala four maternal deaths due to 'cardiovascular problems'. We were unable to contact the authors, so we report the number of cardiac MD as two for both reports.[29,40]

Discussion

This review shows a substantial incidence of maternal deaths due to cardiac disease in LMIC. In the included reports, cardiac-related MMR was highest in countries with a high MMR, but the proportion of cardiac deaths among all maternal deaths appeared to be higher in countries with a lower MMR. Probably, we identified only 'the tip of the iceberg', and the number of MD due to cardiac disease is likely to be even be higher.

Health facilities are insufficiently equipped to identify cardiac deaths and cardiac MD might have been missed. In many LMIC, women do not have access to health facilities equipped with the diagnostic means or clinicians to diagnose cardiac disorders and it is not uncommon that a cardiac disorder is only identified during pregnancy when a woman presents in extremis with heart failure.[6-8] This might explain the finding of a lower proportion of cardiac deaths in countries with a lower level of income. A study undertaken in Eritrea identified rheumatic heart disease (RHD) in 2.3% of asymptomatic pregnant women during antenatal visits.[62] The Sudanese report included in our review suggested that there were no cardiac deaths although the country has a high prevalence of RHD among young women.[7,63,64] Underdiagnosis of cardiac disease in LMIC may explain the wide range of maternal mortality from 0 to 34% that has been reported among pregnant women with cardiac disease.[6,8,65-69.] It is likely that only the most severe cases are identified in settings with limited access to facilities where cardiac disease can be diagnosed. Lastly, many maternal deaths due to medical conditions including cardiac disease happen between six weeks and one year after the end of pregnancy and are therefore not included in the WHO definition of MD.[4,66]

Quality of the included reports varied and might have influenced the incidence

figures as well. For three reports, we had to report missing data due to the high likelihood of missed cardiac MD. The national report from Malawi noted a high level of missing data and although MD is notifiable by law, zero MDs were reported at central level.[45] The report from Ethiopia had information on only 6% of the expected number of MD.[28] No medical doctor was involved to confirm the cause of death for two reports.[40,53] Some reports used unclear definitions like cardiovascular disorder, which includes for example stroke. These were excluded since we could not establish the number of deaths due to cardiac disease. In four reports, half of the cases were out-of-facility deaths and no autopsies were performed.[48,50,53,57] Possible cardiac MDs were missed in these reports. Autopsy can assist in establishing the underlying cause of the MD, and several cardiac-related MDs were identified by autopsy in LMIC.[70,71]

Cardiac-related MMR was highest in countries with a high MMR, but the proportion of cardiac deaths among all maternal deaths appeared to be larger in countries with a lower MMR. This is an important finding since this is in line with what has been titled the 'obstetric transition model', a common pathway that has been identified among countries that were able to reduce their maternal mortality.[5] As the MMR falls, MDs from direct causes are of relative decreasing importance, while the opposite is true for maternal deaths due to pre-existing medical diseases. Since most LMIC are achieving progress in reducing maternal mortality, focus needs to shift from the prevention of deaths from the traditional 'big killers' such as hypertensive disorders, postpartum haemorrhage and HIV/AIDS to pre-existing medical diseases in these countries. Deaths from direct causes can be prevented by improving obstetric care. Different interventions will be needed to prevent deaths from cardiac disease. A multidisciplinary approach available for preconception counselling and during pregnancy, birth, and the postpartum period has been shown to improve maternal outcome, but remains unattainable in most LMIC.[16,19,54,72,73]

In LMIC, women of reproductive age with cardiac disease are facing challenges far different from those that women in high-income countries (HIC) face. Most management guidelines are based on research performed in HIC and not applicable or implementable in LMIC. Besides the differences in availability of resources, the most prevalent cardiac disorder among pregnant women in HIC is congenital heart disease, which needs a different approach than RHD, which is the most common cardiac condition among pregnant women in LMIC.[8,74] A global study on RHD, a cardiac condition preventable with timely administration of antibiotics, found that RHD patients were predominately young women of reproductive age. These women have limited access to family planning as is shown by the alarmingly low coverage of contraceptive use of 36%.[64] Surgical intervention for RHD patients with placement of mechanical valves is increasingly available for young girls and women in LMIC

and has increased survival in this group.[63-64,75,76] At the same time, these women might consider becoming pregnant in the future. With the need for lifelong anticoagulation therapy, the risks of maternal morbidity and mortality and fetal complications are high, based on findings mainly from HIC.[77,78] As previously mentioned, the limited available data from LMIC show a wide range of maternal mortality among cardiac patients. There is an adapted WHO risk classification available that classifies risk of maternal complications based on various cardiac conditions.[79] However, a global study showed that this risk classification does not perform as well in LMICs as compared with HICs.[74] Given all these limitations in LMIC, it is highly problematic to provide adequate risk assessment and treatment for a young woman with a cardiac condition, who is considering a pregnancy.

Despite the extensive search in several databases, we could only identify reports from 29 LMIC countries. It is possible that mortality reports from other countries have been missed. MDRs may not have been published in our searched databases or in any other online database. We attempted to overcome this by searching the publications of the MDSR Action Network website and references of the maternal mortality country profiles of the WHO, since both of these organisations are well-informed regarding the presence of MDRs globally.[9,10] An additional 23 reports were identified for possible inclusion using this strategy. Nevertheless, only for six countries multiple reports were available to assess the progress over time, for which one even used different methods for data collection. Even though Figure 2c indicates that for most of these countries, the impact of cardiac MD appears to increase over time, more data are needed to adequately assess this development.

Conclusion

To our knowledge, this is the first review assessing the frequency of maternal deaths due to cardiac disease in LMIC. Due to the limited availability of mortality reports from LMIC and the varying quality of the reports, it is hard to assess the real burden of maternal death due to cardiac disease. However, in the available reports a high incidence of cardiac-related maternal deaths was identified, which may in reality be even higher due to the likely presence of underreporting. Our findings are in line with the obstetric transition model: indirect deaths including cardiac deaths are becoming relatively more important in several countries as obstetric care improves and obstetric deaths are reduced. Since most LMIC are achieving progress in reducing maternal mortality, more attention is needed for pre-existing medical disease like cardiac disease as a cause of maternal mortality. Prospective studies on prevalence, pregnancy outcome and interventions are needed to assess the real burden or cardiac-related maternal mortality in LMIC and establish feasible and relevant guidelines.

References

1. Knight M, Nair M, Tuffnell D, Shakespeare J, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013–15. National Perinatal Epidemiology Unit, University of Oxford: Oxford, 2017.
2. Vangen S, Bodker B, Ellingsen L, Saltvedt S, Gissler M, Geirsson RT, et al. Maternal deaths in the Nordic countries. Acta Obstet Gynecol Scand 2017; 96: 1112-9.
3. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-Related Mortality in the United States, 2011–2013. Obstet Gynecol 2017; 130: 366-373.
4. Nair M, Nelson-Piercy C, Knight M. Indirect maternal deaths: UK and global perspectives. Obstet Med 2017; 10: 10-5.
5. Souza JP, Tuncalp O, Vogel JP, Bohren M, Widmer M, Oladapo OT, et al. Obstetric transition: the pathway towards ending preventable maternal deaths. BJOG 2014; 121 (Suppl 1): 1-4.
6. Bhatla N, Lal S, Behera G, Kriplani A, Mittal S, Agarwal N, et al. Cardiac disease in pregnancy. Int J Gynaecol Obstet 2003; 82: 153-9.
7. Zuhlke L, Mirabel M, Marijon E. Congenital heart disease and rheumatic heart disease in Africa: recent advances and current priorities. Heart 2013; 99: 1554-61.
8. Watkins DA, Sebitloane M, Engel ME, Mayosi BM. The burden of antenatal heart disease in South Africa: a systematic review. BMC Cardiovasc Disord 2012; 12: 23.
9. Say L, Chou D, Gemmill A, Tuncalp O, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob health 2014; 2: e323-33.
10. MDSR Action Network. Maternal Death Surveillance and Response (Available from: http://mdsr-action.net) [1-11-2017]
11. World Health Organization. Maternal mortality country profiles; 2015. (Available from: http://www.who.int/gho/maternal_health/countries/en/#E) [29-01-2018]
12. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS medicine 2009; 6: e1000097.
13. Hodorogea S. Confidential Enquiry into Maternal Deaths Moldava 2009-2013. N. Testemitanu State Medical and Pharmaceutical University, Chisinau, Republic of Moldova. Personal communication.
14. Hodorogea S, Friptu V. The Moldovan experience of maternal death reviews. BJOG 2014; 121 (Suppl 4): 81-5.
15. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2008-2010: Fifth report on the Confidential Enquiries into Maternal Deaths in South Africa, comprehensive report. Department Health: Pretoria, 2012.
16. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2011-2013: Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa, short report. Department Health: Pretoria, 2015.
17. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2014, Annual report and detailed analysis of maternal deaths due to non-pregnancy related infections. Department Health: Pretoria, 2015.
18. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2005-2007: Fourth Report on Confidential Enquiries into Maternal Deaths in South Africa. Department Health: Pretoria, 2011.
19. Paily VP, Ambujam K, Rajasekharan Nair V, Thomas B. Confidential Review of Maternal Deaths in Kerala: a country case study. BJOG 2014; 121 (Suppl 4): 61-6.
20. World Bank. Country classification by income; 2017. (Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups) [24-11-2017]
21. World Health Organization. The WHO Application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM. World Health Organization: Geneva, 2012.
22. National Committee for Confidential Enquiry into Maternal Deaths. A review of maternal deaths in South Africa during 1998. S Afr Med J 2000; 90: 367-73.
23. Abdel-Hady el S, Mashaly AM, Sherief LS, Hassan M, Al-Gohary A, Farag MK, et al. Why do mothers die in Dakahlia, Egypt? J Obstet Gynaecol Res 2007; 33: 283-7.
24. Abouchadi S, Alaoui AB, Meski FZ, Bezad R, De Brouwere V. Preventable maternal mortality in Morocco: the role of hospitals. Trop Med Int Health 2013; 18: 444-50.

25. Ahmed U, Eltigani L, Eltahir S, Mirghani S, Abd Alillah K, Abraha K. Maternal death review for maternal mortality reduction in Sudan 2010. Sudan Med J 2012; 48: 13-23.
26. Amarin Z, Khader Y, Okour A, Jaddou H, Al-Qutob R. National maternal mortality ratio for Jordan, 2007-2008. Int J Gynaecol Obstet 2010; 111: 152-6.
27. Sandoval De Baños PM. Case Study on Maternal Death Surveillance and Response, Country: El Salvador. San Salvador: Grupo de Trabajo Regional para la Reducción de la mortalidad materna, 2014.
28. Bekele A, Hassen A, Abebe S, Usmael A, Dagnew F, Hadush A, et al. Second Ethiopian national Maternal Death Surveillance and Response (MDSR) report EFY 2008. Ethiopian Public Health Institute: Addis Abeba, 2017.
29. Statistics Botswana and Ministry of Health & Wellness. Botswana - Maternal Mortality Ratio (MMR) 2011 – 2015. Statistics Botswana: Gaberone, 2017.
30. Byhell M, Nand D, Fong J, Vuadreu R. Maternal Mortality in Fiji 2008-2012. Fiji Journal of public Health 2014; 3: 32-7.
31. Campbell O, Gipson R, Issa AH, Matta N, El Deeb B, El Mohandes A, et al. National maternal mortality ratio in Egypt halved between 1992-93 and 2000. Bull World Health Organ 2005; 83: 462-71.
32. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2002-2004: Third Report on Confidential Enquiries into Maternal Deaths in South Africa. Department Health: Pretoria, 2006.
33. Du L, Qin M, Zhang L, Xu H, Zhu L. Trends in maternal mortality in resident vs. migrant women in Shanghai, China, 2000-2009: a register-based analysis. Reprod Health Matters 2012; 20: 73-80.
34. Gurina NA, Vangen S, Forsen L, Sundby J. Maternal mortality in St. Petersburg, Russian Federation. Bull World Health Organ 2006; 84: 283-9.
35. National Committee for Confidential Enquiry into Maternal Deaths. Second Interim Report on Confidential Enquiries into Maternal Deaths in South Africa, Maternal Deaths for 1999. Department Health: Pretoria, 2000.
36. Issah K, Nang-Beifubah A, Opoku CF. Maternal and neonatal survival and mortality in the Upper West Region of Ghana. Int J Gynaecol Obstet 2011; 113: 208-10.
37. Jayaratne K. Maternal Death Surveillance and Response (MDSR) – outcomes of 2014. Family Health Bureau, Ministry of Health: Colombo, 2015.
38. Maternal & Child Morbidity Surveillance Unit. Maternal Death Surveillance and Response System: Dissmenation of 2015 data. Family Health Bureau, Ministry of Health: Colombo, 2016.
39. Karimi-Zarchi M, Ghane-Ezabadi M, Vafaienasab M, Dehghan A, Ghasemi F, Zaidabadi M, et al. Maternal mortality in Yazd Province, Iran. Electron Physician 2016; 8: 1949-54.
40. Kestler E, Ramirez L. Pregnancy-related mortality in Guatemala, 1993-1996. Rev Panam Salud Publica 2000; 7: 41-6.
41. Kodan LR, Verschueren KJC, van Roosmalen J, Kanhai HHH, Bloemenkamp KWM. Maternal mortality audit in Suriname between 2010 and 2014, a reproductive age mortality survey. BMC pregnancy and childbirth 2017; 17: 275.
42. Kongnyuy EJ, Mlava G, van den Broek N. Facility-based maternal death review in three districts in the central region of Malawi: an analysis of causes and characteristics of maternal deaths. Womens Health Issues 2009; 19: 14-20.
43. Krishnan M, on behalf of National Technical Committee for the CEMD. Report on the confidential enquiries into maternal deaths in Malaysia 2006-2008. Family Health Development Division, Ministry of Health: Kuala Lumpur, 2012.
44. Madzimbamuto FD, Ray SC, Mogobe KD, Ramogola-Masire D, Phillips R, Haverkamp M, et al. A root-cause analysis of maternal deaths in Botswana: towards developing a culture of patient safety and quality improvement. BMC pregnancy childbirth 2014; 14: 231.
45. Mataya R, on behalf of Malawi National Confidential Committee on Enquiry into Maternal Death. Report on the Confidential Enquiry into Maternal Deaths in Malawi (2008-2012). Ministry of Health: Lilongwe, 2014.
46. McCaw-Binns A, Lindo JL, Lewis-Bell KN, Ashley DE. Maternal mortality surveillance in Jamaica. Int J Gynaecol Obstet 2008; 100: 31-6.
47. McCaw-Binns A, Standard-Goldson A, Ashley D, Walker G, MacGillivray I. Access to care and maternal mortality in Jamaican hospitals: 1993-1995. Int J Epidemiol 2001; 30: 796-801.
48. Munjanja SP, Nystrom L, Nyandoro M, Magwali T. Zimbabwe Maternal and Perinatal Mortality Study 2007. Ministry of Health and Child Welfare: Harare, 2009.
49. Namiq E, Jabar M, Hasson Alsenaid E, Ali Galib B. Maternal Death Surveillance and Response (MDSR) Iraq 2010-2012. Ministry of Health: Bagdad.

50. Nisar N, Sohoo NA. Maternal mortality in rural community: a challenge for achieving millennium development goal. J Pak Med Assoc 2010; 60: 20-4.
51. Olsen BE, Hinderaker SG, Bergsjo P, Lie RT, Olsen OH, Gasheka P, et al. Causes and characteristics of maternal deaths in rural northern Tanzania. Acta Obstet Gynecol Scand 2002; 81: 1101-9.
52. Qiu L, Lin J, Ma Y, Wu W, Qiu L, Zhou A, et al. Improving the maternal mortality ratio in Zhejiang Province, China, 1988-2008. Midwifery 2010; 26: 544-8.
53. Rahman MH, Akhter HH, Khan Chowdhury ME, Yusuf HR, Rochat RW. Obstetric deaths in Bangladesh, 1996-1997. Int J Gynaecol Obstet 2002; 77: 161-9.
54. National Technical Committee of The Confidential Enquiries into Maternal Deaths. Report on the confidential enquiries into maternal deaths in Malaysia 2009 – 2011. Family Health Development Division, Ministry of Health: Kuala Lumpur, 2012.
55. Sahel A, De Brouwere V, Essobli A, Elmanjra C, Zakour N. Enquête confidentielle sur les décès maternels de 2015 dans les six régions prioritaires au Maroc. Ministrère de la Santé: Marrakech, 2017.
56. Sayinzoga F, Bijlmakers L, van Dillen J, Mivumbi V, Ngabo F, van der Velden K. Maternal death audit in Rwanda 2009-2013: a nationwide facility-based retrospective cohort study. BMJ Open 2016; 6: e009734.
57. Suvedi, Krishna B, Pradhan A, Barnett S, Puri M, Rai Chitrakar S, et al. Nepal Maternal Mortality and Morbidity Study 2008/2009: Summary of Preliminary Findings. Family Health division, Department of Health Services: Kathmandu, 2009.
58. Ndavi PM, Dlamini D, Khumalo P. Report on maternal mortality review in the Kingdom of Swaziland 2001. Ministry of Health and Social Welfare: Mbabane, 2001.
59. Yang S, Zhang B, Zhao J, Wang J, Flick L, Qian Z, et al. Progress on the maternal mortality ratio reduction in Wuhan, China in 2001-2012. PloS one 2014; 9: e89510.
60. You F, Huo K, Wang R, Xu D, Deng J, Wei Y, et al. Maternal mortality in Henan Province, China: changes between 1996 and 2009. PloS one 2012; 7: e47153.
61. Zakariah AY, Alexander S, van Roosmalen J, Buekens P, Kwawukume EY, Frimpong P. Reproductive age mortality survey (RAMOS) in Accra, Ghana. Reproductive health 2009; 6: 7.
62. Otto H, Saether SG, Banteyrga L, Haugen BO, Skjaerpe T. High prevalence of subclinical rheumatic heart disease in pregnant women in a developing country: an echocardiographic study. Echocardiography 2011; 28: 1049-53.
63. ElSayed A, Elnur EE. The rebirth of cardiac surgery in Sudan. Cardiovasc Diagn Ther 2016; 6: S20-S26.
64. Zuhlke L, Engel ME, Karthikeyan G, Rangarajan S, Mackie P, Cupido B, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). Eur Heart J 2015; 36: 1115-22a.
65. Diao M, Kane A, Ndiaye MB, Mbaye A, Bodian M, Dia MM, et al. Pregnancy in women with heart disease in sub-Saharan Africa. Arch Cardiovasc Dis 2011; 104: 370-4.
66. Sliwa K, Libhaber E, Elliott C, Momberg Z, Osman A, Zuhlke L, et al. Spectrum of cardiac disease in maternity in a low-resource cohort in South Africa. Heart 2014; 100: 1967-74.
67. Rezk M, Elkilani O, Shaheen A, Gamal A, Badr H. Maternal hemodynamic changes and predictors of poor obstetric outcome in women with rheumatic heart disease: a five-year observational study. J Matern Fetal Neonatal Med 2017; 31: 1542-1547.
68. Campanharo FF, Cecatti JG, Haddad SM, Parpinelli MA, Born D, Costa ML, et al. The Impact of Cardiac Diseases during Pregnancy on Severe Maternal Morbidity and Mortality in Brazil. PloS one 2015; 10: e0144385.
69. Avila WS, Rossi EG, Ramires JA, Grinberg M, Bortolotto MR, Zugaib M, et al. Pregnancy in patients with heart disease: experience with 1,000 cases. Clin Cardiol 2003; 26: 135-42.
70. Castillo P, Hurtado JC, Martinez MJ, Jordao D, Lovane L, Ismail MR, et al. Validity of a minimally invasive autopsy for cause of death determination in maternal deaths in Mozambique: An observational study. PLoS medicine 2017; 14: e1002431.
71. Faduyile FA, Soyemi SS, Emiogun FE, Obafunwa JO. A 10 years autopsy-based study of maternal mortality in Lagos State University Teaching Hospital, Lagos, Nigeria. Niger J Clin Pract 2017; 20: 131-
72. Knight M, Nair M, Tuffnell D, Kenyon S, Shakespeare J, Brocklehorst P, et al. Saving Lives, Improving Mothers' Care Surveillance of maternal deaths in the UK 2012–14 and lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–14. National Perinatal Epidemiology Unit, University of Oxford: Oxford, 2015.
73. European Society of Gynecology, Association for European Paediatric Cardiology, German Society for Gender Medicine, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J 2011; 32: 3147-97.

74. van Hagen IM, Boersma E, Johnson MR, Thorne SA, Parsonage WA, Escribano Subias P, et al. Global cardiac risk assessment in the Registry Of Pregnancy And Cardiac disease: results of a registry from the European Society of Cardiology. Eur J Heart Fail 2016; 18: 523-33.
75. Guteta S, Yadeta D, Azazh A, Mekonnen D. Cardiac Surgery for Valvular Heart Disease at a Referral Hospital in Ethiopia: A Review of Cases Operated in the Last 30 Years. Ethiop Med J 2016; 54: 49-55
76. Barbosa PJ, Lopes AA, Feitosa GS, Almeida RV, Silva RM, Brito JC, et al. Prognostic factors of rheumatic mitral stenosis during pregnancy and puerperium. Arq Bras Cardiol 2000; 75: 215-24
77. Elkayam U, Singh H, Irani A, Akhter MW. Anticoagulation in pregnant women with prosthetic heart valves. J Cardiovasc Pharmacol Ther 2004; 9: 107-15.
78. van Hagen IM, Roos-Hesselink JW, Ruys TP, Merz WM, Goland S, Gabriel H, et al. Pregnancy in Women With a Mechanical Heart Valve: Data of the European Society of Cardiology Registry of Pregnancy and Cardiac Disease (ROPAC). Circulation 2015; 132: 132-42.
79. Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart 2006; 92: 1520-5.

Appendix 1. Search strategy

Available at https://onlinelibrary.wiley.com/doi/10.1111/tmi.13386

Appendix 2. Quality assessment for reports mentioning zero cardiac deaths and when multiple reports per country were available

Available at https://onlinelibrary.wiley.com/doi/10.1111/tmi.13386

Chapter 6.

Experiences of a dedicated Heart and Maternal Health Service providing multidisciplinary care to pregnant women with cardiac disease in a tertiary centre in Namibia

Steffie Heemelaar, Ndatiyaroo Agapitus, Thomas van den Akker, Jelle Stekelenburg, Shonag Mackenzie, Christopher Hugo-Hamman, Tangeni Auala

Trop Med Int Health. 2022 Sep;27(9):803–14

Abstract

Objective

Firstly, to describe the implementation process, benefits and challenges of a multidisciplinary service for pregnant women with cardiac disease in Namibia. Secondly, to assess pregnancy outcomes in this population.

Methods

In a tertiary hospital in Namibia, a multidisciplinary service was implemented by staff of obstetric and cardiology departments and included preconception counselling, provision of antenatal care and reliable contraception. Management guidelines developed for high-income settings were used, since no locally adapted guidelines were available. A cohort study was performed to assess cardiac, obstetric, and fetal outcomes. Included were pregnant women with cardiac disease, referred to this service between 1 August 2016 and 31 July 2018.

Results

Important benefits of this service were the integrated approach, improved access to reliable contraception and insight into drivers of poor outcome. Several challenges with use of available guidelines were encountered, as contextual factors specific to lower-income settings were not taken into consideration, such as higher rates of infection or barriers to access care. The cohort consisted of 65 women. Cardiac disease was diagnosed for the first time in sixteen (24.6%) women, of whom eleven had pre-existing cardiac disease. These women presented more often with heart failure compared to women with known heart disease (75.0% vs 6.1%, RR 12.5, 95% CI 3.9-38.0). Five women died. Cardiac events occurred in 22 women of whom eight developed thromboembolic events and two endocarditis. The majority had no indication for prophylaxis, based on available guidelines. Fetal events occurred in 36 pregnancies. After pregnancy more than half of women (35/65, 53.8%) were using long-acting reversible contraception.

Conclusion

Despite several barriers, it was possible to implement a multidisciplinary service in a high-burden setting. Cardiac and fetal event rate in this cohort were high. To improve outcomes focus should be on availability of context-specific guidelines and better detection of cardiac disease.

Introduction

Cardiac disease in pregnancy is an important contributor to maternal deaths globally. In many high-income countries cardiac disease is now the most common cause of maternal mortality, whilst in low- and middle-income countries (LMICs) its contribution to maternal mortality is increasing.[1-4]

Risk prediction tools and management guidelines have been developed for women with cardiovascular disease, who are planning pregnancy or already pregnant.[5-9] These recommendations are based mainly on findings from high-income countries, as data from LMICs are scarce.[7,8,10] Recommendations are, therefore, not easily applied to low- and middle-income settings due to the limited availability, accessibility and affordability of diagnostic and therapeutic resources, and differences in the epidemiology and severity of underlying cardiac disease.[11-14] In LMICs, there is still a high prevalence of rheumatic heart disease (RHD), whereas congenital heart disease is the most prevalent diagnosis in high-income countries.[7,8,10,11,13-15] Furthermore, more advanced disease is seen in LMICs.[12,14,16] The modified World Health Organisation (mWHO) risk classification, based on the underlying cardiac diagnosis, is considered the most accurate system for maternal cardiovascular risk assessment.[9,17-20] However, it did not perform adequately in middle-income countries, as high rates of complications were seen in pregnancies classified as low risk.[12]

In Namibia, a middle-income sub-Saharan African country, cardiac disease was one of the most common causes of maternal deaths in 2012-2015.[21] In the national referral hospital in Windhoek, the capital city, staff noted a high rate of unintended pregnancies and a high rate of complications among pregnant women with cardiac disease. However, as no data were captured, the impact of cardiac disease on maternal and fetal outcome was unclear.
To address this, a dedicated Heart and Maternal Health Service (HMH) was established by staff of the cardiology and obstetrics and gynaecology departments of Windhoek Central Hospital in 2016. The aim was to implement a multidisciplinary service for women with cardiac disease in Namibia, providing care from preconception to postpartum. A two-year prospective cohort study was performed to assess the spectrum of cardiac disease in pregnant women referred to this dedicated service and to assess cardiac, obstetric and fetal outcomes of these pregnancies. The focus of this paper is twofold: to describe the implementation process of this service, including the encountered benefits and challenges, and to present the findings of the cohort study.

Methods

Setting

This study was performed at Windhoek Central Hospital, the tertiary public hospital of Namibia, serving a population of 2.3 million.[22] This facility has approximately 12 000 births per annum.[22] During the study period the number of available obstetrician-gynaecologists ranged from three to six. This was the only public health facility in the country with availability of consultant cardiologists (2), cardiothoracic surgeons (2), and cardiac technologists (2) and where transcutaneous cardiac interventions and cardiac surgeries were performed. At one regional hospital in northern Namibia (Oshakati), about 700 kilometres from Windhoek, two cardiologists employed in the private sector provided cardiac care for patients that were referred to them.

Patients presenting to any public health facility in Namibia, pay a minimum fee (about US$ 0.65) for each healthcare visit and no additional costs are incurred for diagnostics or treatments including admissions, interventions or surgeries. Those living outside Windhoek in need of elective specialist care, such as a consultation at the cardiac outpatient department or admission for surgery, were transferred from district hospitals to Windhoek by a free bus service, once per week, provided by the Ministry of Health and Social Services.

Reproductive health services, including contraceptive services, are free of charge. Most facilities had combined oral contraceptives and progestogen-only injectables routinely available. The United Nations Population Fund made a once off donation of hormonal implants and intra-uterine devices to the Ministry of Health and Social Services of Namibia in 2016 so these contraceptive devices were available at the study site and some other hospitals for the duration of the study.

Design and inclusion criteria of cohort study

For this two-year prospective observational cohort study all pregnant and postpartum women with cardiac disease referred to the HMH Service were included between 1st of August 2016 and 31st of July 2018. We included both women with cardiac disease diagnosed prior to conception, as well as those newly diagnosed during pregnancy or within 42 days postpartum.

Implementation of the Heart and Maternal Health Service

The HMH Service was a comprehensive service for women of reproductive age with cardiac disease. A multidisciplinary team provided antenatal, intrapartum and postpartum care for women with cardiac disease. Every two weeks this team, consisting of one or more obstetricians, cardiologist, sonographers,

echocardiographers and anaesthesiologists, was available at the antenatal clinic. Guidelines on the management of cardiovascular diseases during pregnancy of the European Society of Cardiology of 2011 were adhered to, as no local or LMICs-adapted guidelines were available at that time.[17] Based on clinical condition, severity of cardiac disease and obstetric history, each woman received an individualized management plan which outlined the frequency of follow-up visits, obstetric ultrasounds, maternal echocardiograms and birth plan. Information on postpartum contraception was provided during antenatal visits. Women who presented with newly diagnosed cardiac disease were scheduled for the earliest available clinic day if haemodynamically stable or assessed as inpatients if haemodynamically unstable. Maternal risk was assessed using the mWHO risk classification, which stratifies maternal cardiovascular risk into four classes: class I (no increased risk of maternal mortality and no/mild increase in morbidity) up to class IV (extremely high risk, pregnancy contra-indicated).[17] Risk stratification for cardiac disease not specifically mentioned in the classification, was done by a consultant cardiologist (CH) and a physician (TAu) with extensive experience in cardiology.

For women with an indication for anticoagulation, the vitamin K antagonist warfarin, unfractionated and low molecular weight heparin were available in the public health sector. If she presented early in the first trimester, a woman using warfarin was counselled about the option to change to low molecular weight heparins in the first trimester. However, dose adjustment with anti-Xa monitoring was not possible. The international normalized ratio was used to manage warfarin treatment.

In Namibia, termination of pregnancy up to 26 weeks of gestational age is legally permitted for significant maternal conditions and certain fetal conditions. Because reported cardiac event rates are 19-27% for women classified as WHO III and 40-100% for women in mWHO IV, compared to 2.5-5% for mWHO I and 5.7-10.5% for mWHO II, the option of termination of pregnancy was included in the counselling for all women classified as mWHO III and advised for women classified as mWHO IV (if they presented before 26 weeks of gestation).[6]

The HMH Service followed up all women at six weeks and at six months after the end of pregnancy. On clinical indication, the follow up period was extended up to a year. Placement of long acting reversible family planning was offered directly after birth for women who had difficulties attending follow up visits and at six weeks after birth for all other women. If a HMH visit was not feasible for the woman, the six-month follow-up was done by phone. At the last follow-up visit, all women were referred to the Cardiology service.

The HMH Service also provided preconception counselling at the cardiac outpatient department. All women of childbearing age were educated about their cardiac diagnosis, peripartum risk as determined by the mWHO risk classification and reliable contraception. A specifically designed patient information leaflet was provided to the women (Appendix 1). After counselling the woman was seen by a doctor for her cardiac follow-up and any further concerns were addressed. Women who opted for long-acting reversible contraceptives (e.g. hormonal implant or intrauterine contraceptive devices) and who had no contra-indication for these methods, could have them placed on the same day. These women were referred to the gynaecology department, as only doctors from this department had the expertise and equipment for placement of these devices. When the HMH Service was introduced, it was planned that these contraceptive devices would be placed by nursing staff of the cardiac outpatient department. This turned out to be unattainable due to an already high workload of these nurses and lack of training resources.

Due to staff shortages across all departments the integrated HMH Service ended in June 2017 and cardiac and obstetric care was continued at the respective departments. Patient assessments and management were discussed in close communication between the departments and high-risk women were discussed during multidisciplinary meetings. The provision of preconception counselling continued and long-acting reversible contraceptives could be provided on the same day at the gynaecology department.

There was no specific budget available for the HMH Service. All members of the HMH Service were employed by the Ministry of Health and Social Services and the HMH Service was part of their clinical duties. The patient information leaflet was printed by the United Nations Population Fund.

Data collection and outcome

Structured forms were developed for the HMH Service to record the women's antenatal visits and maternal and fetal outcomes. Data collected included socio-demographic characteristics, cardiac history, obstetric history, cardiac and obstetric outcome. All women were asked whether it was a planned or unplanned pregnancy and if continuation was desired.

Primary outcomes were underlying cardiac diagnoses of women referred to the HMH Service, severity of cardiac disease, risk assessment based on mWHO classification, and condition at first presentation based on the New York Heart Association (NYHA) class. Secondary outcomes were the incidences of cardiac, obstetric and fetal events. Cardiac event was defined as heart failure requiring admission or modifications

in medication, thromboembolic event, new onset or exacerbated arrhythmia, endocarditis, or a cardiac intervention during pregnancy or within 6 months after the end of pregnancy. Obstetric events that were documented included postpartum haemorrhage more than 1000 mL, pre-eclampsia or eclampsia as defined by the World Health Organisation.[23] Fetal event was defined as miscarriage or termination of pregnancy < 26 weeks of gestation, stillbirth from 26 weeks of gestation or, if the gestational age was unknown, birthweight >1000g and documented as either fresh or macerated in the medical file, premature birth <37 weeks gestation, small-for gestational age birthweight (<10th centile), born alive with congenital anomalies or neonatal death (within 28 days after birth). Maternal death was defined as death of a woman while pregnant or within 42 days of termination of pregnancy or birth, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.[24] Late maternal death was defined as the death of a woman from direct or indirect causes more than 42 days but less than one year after the end of pregnancy.[24]

The association between events and several risk factors was assessed. Risk factors were selected when listed in the guidelines of the European Society of Cardiology or identified in studies from similar settings and present in at least ten percent of our cohort.[6,16,25]

Data analysis

Data analysis consisted of frequencies of demographic and clinical variables. Data were double entered and cross checked in Epidata version 3.1 and analysed with SPSS version 26. Continuous variables are presented as means with standard deviations and differences were assessed with student t-test. Missing data regarding medical history were assumed to be 'no', whereas complete case analysis was used to handle missing data regarding outcome measures of the current pregnancy. Categorical variables are presented as percentages. Differences were assessed using chi-square test or Fisher's Exact test when indicated and risk ratio (RR) and 95% confidence interval (CI) are presented. Statistical significance was assumed at a two-sided value of $p<0.05$. All results are presented in the tables and figures and therefore not published in a separate online database. We followed the STROBE reporting guidelines.

This study was reviewed and approved by the ethics research unit of the Namibian Ministry of Health and Social Services, Reference 17/3/3 SH. Women were informed about the purpose of the cohort and verbally offered to opt out of her anonymous data being used for research purposes.

Results

Sixty-five pregnancies of women with cardiac disease were included in this cohort. Table 1 summarizes baseline characteristics according to mWHO classes of the included women. Thirty six women lived in Khomas region where the study site is located, 29 were from other regions representing nearly all 14 regions of Namibia and one woman lived in Angola. Figure 1 is a map of Namibia, indicating the study site and home regions of all women included in the cohort.

Table 1. Baseline characteristics of 65 pregnant women with cardiac disease referred to the HMH service

	Overall	mWHO I	mWHO II	mWHO III	mWHO IV	
Variables	**(N = 65)**	**(N = 6)**	**(N = 12)**	**(N = 26)**	**(N = 21)**	**P-value**
Age, years	30.0± 7.6	23.8± 6.1	30.2± 7.7	30.9± 7.3	30.5± 8.1	0.22
Nulliparous	22 (33.8)	4 (66.7)	4 (33.3)	8 (30.8)	6 (28.6)	0.4
Married/cohabiting	22 (33.8)	1 (16.7)	5 (41.7)	9 (34.6)	7 (33.3)	0.96
Attitude towards pregnancy						0.69
Desired and planned	22 (33.8)	2 (33.3)	3 (25.0)	10 (38.5)	7 (33.3)	
Desired and unplanned	20 (30.8)	3 (50.0)	6 (50.0)	6 (23.1)	5 (23.8)	
Undesired	22 (33.8)	1 (16.7)	3 (25.0)	10 (38.5)	8 (38.1)	
BMI, kg/m2	25.3± 6.9	21.1± 4.6	28.9± 8.2	24.9± 7.4	25.1± 5.3	0.15
Pre-existing hypertension	10 (15.4)	1 (16.7)	2 (16.7)	2 (7.7)	5 (23.8)	0.43
HIV	7 (10.8)	0 (0.0)	2 (16.7)	3 (11.5)	2 (9.5)	0.83
Tuberculosis	4 (6.2)	0 (0.0)	0 (0.0)	3 (11.5)	1 (4.8)	0.68
Cardiac disorder						0.02
Congenital	12 (18.5)	3 (50.0)	4 (33.3)	3 (11.5)	2 (9.5)	
RHD	31 (47.7)	2 (33.3)	7 (58.3)	15 (57.7)	7 (33.3)	
PPCM, current pregnancy	5(7.7)	0 (0.0)	0 (0.0)	2 (7.7)	3 (14.3)	
PPCM, previous pregnancy	9 (13.8)	0 (0.0)	0 (0.0)	6 (23.1)	3 (14.3)	
Cardiomyopathy other	5 7.7)	0 (0.0)	0 (0.0)	0 (0.0)	5 (23.8)	
Arrhytmia	1 (1.5)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	
Mixed	1 (1.5)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	
Pulmonary hypertension	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.8)	
Previous cardiac surgery	14 (21.5)	2 (33.3)	3 (25.0)	9 (34.6)	0 (0.0)	0.01
Previous cardiac event	27 (41.5)	0 (0.0)	5 (41.7))	16 (61.5)	6 (28.6)	0.03
NYHA III-IV at presentation	15 (23.1)	0 (0.0)	0 (0.0)	3 (11.5)	12 (57.1)	<0.001
Newly diagnosed heart condition	16 (24.6)	2 (33.3)	0 (0.0)	3 (11.5)	11 (52.4)	0.001

Values are mean ± standard deviation or n (%).
HMH, Heart and Maternal Health service; mWHO, modified World Health Organization risk classification; BMI, body mass index; HIV, human immunodeficiency virus; RHD, rheumatic heart disease; PPCM, peripartum cardiomyopathy; NYHA, New York Heart Association Functional classification

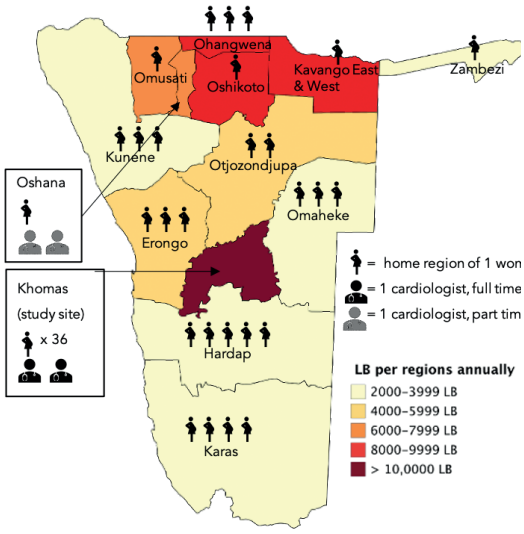


Figure 1. Map of Namibia with its 14 regions
Number of live births annually, home region of women of the cohort and distribution of cardiologists are shown. One woman lived in Angola and is not indicated on the map. Distance from the district hospital in Zambezi region to the capital, which is in Khomas region, is 1227 km.
LB, live births.

Pregnancy outcomes were available for all women. Follow-up data at 6 months was not available for six women and five babies, of whom two women already had cardiac events upon presentation to HMH Service. Incidence of cardiac events was therefore calculated based on data of 61 women. Five of the women died (5/59, 8.5%).

Cardiac history and diagnosis

Rheumatic heart disease was the most common cardiac diagnosis (31/65, 47.7%), followed by congenital heart disease (12/65,18.5%), Table 1. Nine women had previous valve replacements, four were mechanical and five bioprostheses. Appendix 2 contains baseline characteristics and outcomes of all women prosthetic valves. Eight women had an indication for anticoagulation, of whom only two presented early in the first trimester.

Sixteen (24.6%) women were diagnosed with cardiac disease for the first time during the current pregnancy, referred to as 'newly diagnosed'. Five of these women developed peripartum cardiomyopathy and the remaining women had pre-existing cardiac disease: RHD (7), congenital heart disease (2), pulmonary hypertension (1) and cardiomyopathy (1). Women with newly diagnosed cardiac disease presented in failure

with NYHA III or IV more often than women diagnosed with cardiac disease prior to pregnancy (75.0% vs 6.1%, RR 12.5, 95% CI 3.9-38.0). Women living within Khomas region were less likely to be newly diagnosed compared to women from other regions (11.1% vs 41.4%, RR 0.3, 95% CI 0.1-0.7). Over two thirds of the cohort had a high-risk cardiac condition as 47 women (72.3%) were classified as mWHO III or IV.

Cardiac events

The incidence of cardiac events was high (22/61, 36.1%), and threefold higher among women with newly diagnosed cardiac conditions compared to women with cardiac disease diagnosed before pregnancy, (13/16 vs 9/45, RR 4.1 95% CI 2.2-7.6).

The most common event was new onset heart failure (18/61, 29.5%). This occurred in two women in the second trimester, five in the third trimester and eleven postpartum. One woman with heart failure secondary to peripartum cardiomyopathy survived a cardiac arrest. Eight women had a thromboembolic event (thrombus in the left ventricle (4), stroke (2), pulmonary embolism (1) and mechanical valve thrombosis (1)). One stroke and the valve thrombosis occurred in the first trimester and the remaining six thromboembolic events occurred postpartum. Five women with a thromboembolic event had no indication for anticoagulation according to guidelines that were adhered to.[17] The remaining three women had an indication for anticoagulation, which was omitted in one case and inadequately monitored in the other two cases. Table 2 summarizes the characteristics and outcomes of women using anticoagulation during pregnancy. Three of these women developed cardiac events and there were fetal events for six of these pregnancies. Two women, who had RHD, developed infective endocarditis postpartum, both of whom died.

In this cohort five women died: two had developed peripartum cardiomyopathy and three had RHD. Three of the five deaths occurred more than 42 days after the end of pregnancy. Table 3 summarizes details of these five maternal deaths.

Table 2. Details of all women using anticoagulation during pregnancy										
Diagnosis	**mWHO**	**Age**	**Parity**	**Attitude pregnancy**	**Indication warfarin**	**GA at presentation**	**1st trimester**	**Mode of birth**	**Maternal outcome**	**Fetal outcome**
RHD, MVR	III	43	2	Desired & unplanned	AF	12 weeks	Warfarin 5 mg	Caesarean section	Death	Small-for-gestational age, alive at 6 months
RHD, MVR	III	40	4	Undesired	Mechanical valve	12 weeks	None[a]	Termination of pregnancy	Valve thrombosis	Medical abortion at 12 weeks
Cardiomyopathy	IV	28	0	Desired & planned	Previous DVT needing thrombectomy	8 weeks	None[b]	Caesarean section	CCF	Hydrocephalus, alive at 6 months
RHD, AVR	III	21	0	Unwanted	Mechanical valve	Post miscarriage	None[c]	Miscarriage	No events	Miscarriage
DCMO, EF 38%	IV	29	1	Desired & unplanned	PE prior to onset pregnancy	29 weeks	None[d]	Assisted vaginal birth	No events	Small-for-gestational age, alive at 6 months
Cardiomyopathy	IV	36	3	Undesired	Previous stroke	25 weeks	Warfarin 5 mg	Caesarean section	No events	Preterm birth at 35 weeks due to APH, alive at 6 months
RHD, AVR	III	20	0	Desired & planned	Mechanical valve	8 weeks	LMWH	Vaginal birth	No events	Alive, no complications
RHD, AVR	III	37	2	Undesired	Mechanical valve, previous stroke	23 weeks	Warfarin 7.5 mg	Vaginal birth	No events	Alive, no complications

mWHO, modified World Health Organization risk classification; GA, gestational age; RHD, rheumatic heart disease; MVR, mitral valve replacement; AF, atrial fibrillation; DCMO, dilated cardiomyopathy; DVT, deep venous thrombosis; CCF, congestive cardiac failure; AVR, aortic valve replacement; EF, ejection fraction; PE, pulmonary embolism; LMWH, low-molecular-weight heparin; MVR, mitral valve replacement.

[a] Warfarin was stopped by doctor in referral hospital when woman presented with pregnancy

[b] Woman was started at 16 weeks of gestation due to previous DVT

[c] Warfarin stopped by woman when she realized she was pregnant

[d] Woman had defaulted all medication, she was restarted at presentation to our hospital

Table 3. Details of maternal deaths									
Diagnosis	**Timing presentation**	**mWHO**	**NYHA**	**Age (yrs)**	**Parity**	**Attitude pregnancy**	**When**	**Cause of death**	**Fetal outcome**
RHD, severe MS	First trimester	IV	IV	21	1	Undesired	16 days post abortion	Stroke	Medical abortion
RHD, bioMVR & AF on warfarin	First trimester	III	I	43	2	Desired & unplanned	56 days postpartum	Infective endocarditis	Small-for-gestational age, alive at 6 months
RHD, severe MS	Postpartum	IV	IV	35	4	Unknown	16 days postpartum	Newly diagnosed RHD, CCF, infective endocarditis and septic shock	Alive at 6 months
PPCM	Postpartum	IV	IV	17	0	Undesired	3 months postpartum	Multi-organ embolism due to left ventricular thrombus	Preterm birth, alive at 6 months
PPCM	Postpartum	IV	IV	18	0	Desired & planned	8 months postpartum	CCF	Alive at 6 months

mWHO, modified World Health Organization risk classification; NYHA, New York heart association classification; RHD, rheumatic heart disease; MS, mitral valve stenosis; MVR, mitral valve replacement; AF, atrial fibrillation; PPCM, peripartum cardiomyopathy; CCF, congestive cardiac failure

Obstetric outcomes

Antenatal care commenced in the first trimester for 16 (24.6%) women, in the second trimester for 38 (58.5%), in the third trimester for five (7.7%). Three (3.1%) women did not attend antenatal care and attendance was unknown for three women.

Of the 49 women with cardiac disease diagnosed before current pregnancy, only 30 (61.2%) women had received preconception counselling and only fifteen (30.6%) had a planned pregnancy. Regarding pregnancy outcome, three women had a spontaneous miscarriage. Four women had their pregnancy terminated as they were classified as high risk: their mWHO classification was III (2) or IV (2). Of the 58 women who gave birth, 28 (43.1%) had a spontaneous vaginal birth and two (3.3%) women had an assisted vaginal birth. Twenty-eight women gave birth by caesarean section (43.1%). Two women had a cardiac indication for caesarean section as they were haemodynamically unstable, and all other women had an obstetric indication.

Obstetric events occurred among 12 women: postpartum haemorrhage (6), eclampsia (2), pre-eclampsia (5), of which one woman also had postpartum haemorrhage.

Fetal outcomes

There were 57 live births of whom two were born with congenital abnormalities (clubfoot and hydrocephalus). There were four neonatal deaths of which three were due to complications of prematurity (all born before 28 weeks of gestation) and one, born at 34 weeks of gestation, died at home due to unclear cause 15 days after birth.

There were two twin pregnancies, one resulted in two macerated stillbirths. Born prematurely were 22 babies, six were born at less than 32 weeks' gestation due to pre-eclampsia (2), spontaneous preterm birth (2), placental abruption (1) and bleeding placenta praevia (1). Seven babies had a low birthweight.

Risk factors and mWHO risk prediction

Figure 2 presents the cardiac, obstetric, and fetal events according to mWHO classes. There were cardiac events in 71.4% of women in mWHO IV, 26.9% in mWHO III and none in mWHO I and II. There was a high rate of fetal and obstetric events in all classes.

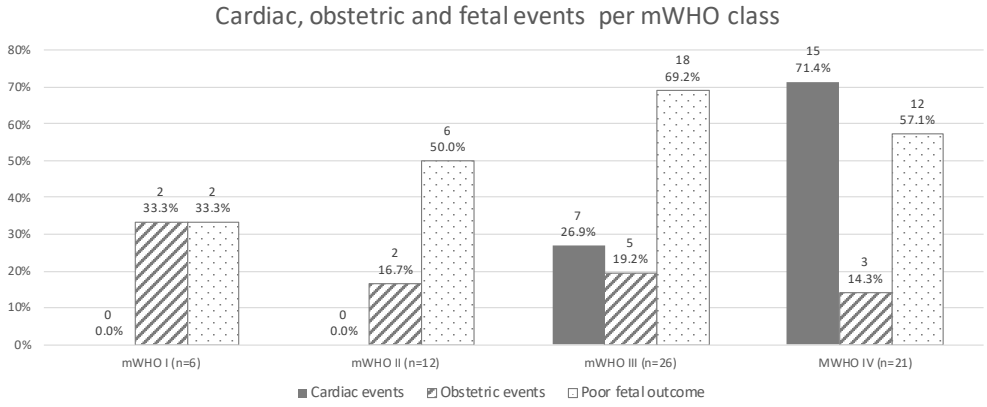


Figure 2. Events among mWHO classes.
Two women classified as mWHO III had a twin pregnancy, so for fetal outcome the denominator in mWHO III was 28.

Table 4. Associated factors for events					
Cardiac events					
Risk factor	**Present (%)**	**Absent (%)**	**RR**	**95% CI**	**p Value**
Prior cardiac event	6/26 (23.1)	16/35 (45.7)	0.5	0.2 - 1.1	0.07
Previous surgery	2/13 (15.4)	20/48 (41.7)	0.4	0.1 - 1.4	0.11
Pulmonary hypertension	9/11 (81.8)	13/50 (26.0)	3.1	1.8 - 5.4	0.001
Warfarin	3/8 (37.5)	19/53 (35.8)	1	0.4 - 2.7	1
NYHA III-IV at presentation	15/15 (100)	7/46 (15.2)	6.6	3.3 - 13.0	<0.001
mWHO III-IV	22/44 (50.0)	0/17 (0)			<0.001
Newly diagnosed	13/16 (81.3)	9/45 (20.0)	4.1	2.2 - 7.6	<0.001
Unplanned pregnancy	15/40 (37.5)	7/21 (33.3)	1.1	0.5 - 2.3	0.75
Fetal events					
Risk factor	**Present (%)**	**Absent (%)**	**RR**	**95% CI**	**p Value**
Prior cardiac event	18/27 (66.7)	18/38 (47.4)	1.4	0.9 - 2.2	0.12
Previous surgery	9/14 (64.3)	27/51 (52.9)	1.2	0.8 - 1.9	0.45
Pulmonary hypertension	4/11 (36.4)	32/54 (59.3)	0.6	0.3 - 1.4	0.2
Warfarin	5/8 (62.5)	31/57 (54.4)	1.1	0.6 - 2.1	0.72
NYHA III-IV at presentation	10/15 (66.7)	26/50 (52.0)	1.3	0.8 - 2.0	0.32
mWHO III-IV	28/47 (59.6)	8/18 (44.4)	1.3	0.8 - 2.4	0.27
Newly diagnosed	8/16 (50.0)	28/49 (57.1)	0.9	0.5 - 1.5	0.62
Unplanned pregnancy	24/42 (57.1)	12/23 (52.2)	1.1	0.7- 1.8	0.7
Obstetric events					
Risk factor	**Present (%)**	**Absent (%)**	**RR**	**95% CI**	**p Value**
Prior cardiac event	6/27 (22.2)	6/37 (16.2)	1.4	0.5 - 3.8	0.54
Previous surgery	3/14 (21.4)	9/50 (18.0)	1.2	0.4 - 3.8	0.72
Pulmonary hypertension	2/9 (18.2)	10/53 (18.9)	1	0.2 - 3.8	1
Warfarin	0/8 (0)	12/56 (21.4)			0.33
NYHA III-IV at presentation	5/14 (35.7)	7/50 (14.0)	2.6	1.0 - 6.8	0.12
mWHO III-IV	8/46 (17.4)	4/18 (22.2)	0.8	0.3 - 2.3	0.73
Newly diagnosed	4/15 (26.7)	8/49 (16.3)	1.6	0.6 - 4.7	0.45
Unplanned pregnancy	6/42 (14.3)	6/22 (27.3)	0.5	0.2 - 1.4	0.31

The incidence of cardiac, fetal and obstetric events presented as events/risk factor present or absent. Furthermore risk ratio and 95% confidence interval for each risk factor.
RR, risk ratio; CI, confidence interval; NYHA, New York heart association classification; mWHO, modified World Health Organization risk classification

Table 4 presents known potential risk factors for adverse events. NYHA III-IV at presentation, mWHO III-IV, pulmonary hypertension and newly diagnosed cardiac diseases were associated with cardiac events, but not with obstetric or fetal events.

Postpartum contraception

After pregnancy more than half of the women (35/65, 53.8%) were using long-acting reversible contraception, the majority were implants (26). After counselling, five women opted for sterilisation. All five had an obstetric indication for caesarean section. Eight women were not on contraceptives for the following reasons: opted for a long-acting reversible contraceptive method but did not have funds to return to the hospital (4), were not sexually active (3), or wanted another child soon (1).

Discussion

The HMH Service was introduced at Windhoek Central Hospital in Namibia to provide multidisciplinary care to women with cardiac disease referred to this tertiary centre. It was the first of its kind in the country and provided valuable insight into the spectrum and severity of cardiac disease in pregnant women in our setting, as well as the drivers of poor outcome. Several barriers to the provision of care were identified. In this section we discuss these insights and barriers.

RHD, cardiomyopathies and congenital heart disease were the most frequent cardiac diagnosis in this cohort, which is similar to findings from other LMICs.[26-29] A high proportion of women had pre-existing cardiac disease that was only diagnosed in the current pregnancy, despite these women having been symptomatic in previous pregnancies. This indicates that cardiac disease is insufficiently recognised during antenatal care. This is a missed opportunity to intervene as nearly all these women presented in poor clinical condition having already developed cardiac complications. These complications may have been prevented by initiation of treatment or cardiac intervention at an earlier stage. Late diagnosis of cardiac disease is still a common problem in LMICs.[13,14,26,30,31] Our findings suggest that women and health workers need to be made aware of symptoms and signs of cardiac disease and the importance of timeous detection and management of cardiac illness. To improve diagnosis of cardiac disease and prevent complications, targeted screening programs should be implemented at healthcare service such as antenatal care or primary healthcare clinics, as recommended by the Pan-African Society of Cardiology.[11] This requires that health workers are trained and equipped to recognize, initiate management and refer women with suspected cardiac disease accordingly. In Uganda and Eritrea, countries with a similar high RHD prevalence as Namibia, screening with an echocardiogram of asymptomatic pregnant women revealed a prevalence of subclinical cardiac disease of 1.7% and 2.3% respectively, mainly RHD.[28,29]

We identified a high mortality rate of 8.5% and over a third of the women had cardiac events. Similarly high rates were identified in other LMICs such as Kenya (9.3%) and South Africa (3.7%), and much lower mortality rates were identified in high-income settings (0.3-0.6%).[7,10,26,32] More than two thirds of the women in our cohort had high-risk conditions (mWHO III/IV), which was also the case in the Kenyan and South African cohort.[26,32] In two large cohorts, reporting on women from mainly high-income settings, only 15.0% and 17.4% of the cases were classified as high risk.[7,10] The difference in outcome between high income countries and LMICs could be due to differences in availability of resources, but another explanation could be that more advanced disease is seen in middle-income settings, as diagnosis of mild cardiac disease is often missed.

Although the definition of maternal death only includes deaths within 42 days after the end of pregnancy, many women die from medical conditions, including cardiac disease, between six weeks and one year after the end of pregnancy.[24,33] In this study three out of five maternal deaths occurred more than 42 days after birth. In a South African cohort nine of the ten maternal deaths were late maternal deaths and in a large Canadian cohort three out of six.[7,32] These findings indicate that a longer follow-up period and monitoring and registration of late maternal deaths are essential to obtain more accurate data on outcome and further improve care after the end of pregnancy.

Fetal outcome in our cohort was poor, but more data is needed to identify pregnancies at risk for poor fetal outcome in the Namibian setting. Similar rates of poor fetal outcome were found in other LMICs such as Uganda, Kenya and Egypt among women with cardiac disease.[26-28] Facilities that provided multidisciplinary care for pregnant women with cardiac disease, reported much lower rates, suggesting that joint care could improve fetal outcome.[10,16] The overall poor fetal outcome in this cohort could also be explained by the high rate of obstetric events, such as placenta praevia and pre-eclampsia, which caused premature birth for several women. The high rates of obstetric events were not reported in the other cohorts.[7,10,26,32] Considering our small cohort this finding might be due to chance.

The HMH Service quantified maternal risk using the mWHO risk classification and adopted the guidelines of the European Society of Cardiology. Several challenges with its use were encountered as neither consider barriers to the provision of care to pregnant women with cardiac disease that are specific to LMICs. For example, accurate risk classification requires access to comprehensive cardiac care and echocardiography as a bare minimum, which is not uniformly available at healthcare facilities in Namibia (Figure 1).[6] As a result, several recommendations by mWHO and guidelines of the European Society of Cardiology on the level of care or frequency of

follow up visits appeared not to be appropriate or feasible in our setting. The mWHO classification has a heavy focus on congenital cardiac diseases, the most prevalent lesion in high-income settings. However some RHD lesions are not specifically mentioned, which may make it less fit for use by doctors with limited cardiac expertise.

The guidelines of the European Society of Cardiology did not recommend routine endocarditis prophylaxis during birth and was therefore not given to our study population.[34] However, in LMICs there are considerably higher rates of maternal infections and the Pan-African Society of Cardiology recently recommended antibiotic prophylaxis during birth for all women with RHD.[11,35] We had two cases of infective endocarditis after birth in women with RHD and both women died.

Eight women had a thromboembolic event, of whom two died. Only less than half of these eight women had an indication for anticoagulation according to the adopted guidelines.[17] Among the women using anticoagulation, there was a high rate of cardiac and fetal events. These results reiterate that for all women with cardiac disease the need for anticoagulation should be assessed, taking into account both the risks and benefits of this treatment, as well as the possibilities and challenges of our setting.

Given all these considerations, context-specific guidelines, a risk stratification tool and referral algorithms are needed, based on local evidence and available expertise and resources in Namibia. An adaptation of mWHO, incorporating other recognised risk factors, such as NYHA status, cardiac history or medication use, and taking into account the aforementioned local considerations, could form the base of a Namibian referral algorithm, such as the one implemented in a South African setting.[16]

Even though almost half of the women live far from our referral centre and despite limited resources, the HMH Service was able to increase access to care for women with cardiac disease in Namibia, including improved access to long term reliable contraception. The importance of access to preconception counselling and family planning for women with cardiac disease is recognized in many reports, as it can reduce high-risk pregnancies.[6,36]. Reported barriers are lack of integrated approach and misconceptions about side effects and contra-indications for contraceptive methods among women with cardiac disease and healthcare providers.[36-39] The HMH Service sought to address some of these barriers through the integrated approach, training of health workers and counselling of women. Access to care still needs to improve as most women presented after the first trimester, two thirds of the pregnancies were unplanned and several women had to travel long distances (some greater than 700km) to receive long acting reversible contraception.

Due to staff shortages, the joint cardiac obstetric service was suspended after June 2017. Lack of staff is a common issue in LMICs and not easily solved.[40-42] Task shifting and sharing is a frequently used solution and could be considered.[43] In two studies performed in Uganda and Eritrea, echocardiograms were performed by nurses and medical students respectively and supervised by a cardiologist.[28,29]. The Namibian Ministry of Health and Social Services has an active programme of training health workers including specialists, nurses, technologists, pharmacists, and it is anticipated that the number of staff with special expertise will increase over the next few years. At last, findings of this study have been used for advocacy to ensure all stakeholders, including policy makers, prioritise cardiovascular health in women and commit to mobilise financial, technical and human resources.

Limitations

This study had several limitations. Firstly, we did not include women's perspectives in the evaluation of the HMH Service. Secondly, the severity of cardiac disease of this cohort may partially be a result of referral bias, as asymptomatic women or those with mild disease may have been undiagnosed or managed in district or regional hospitals. Thirdly, there was no Namibian data available/collected to compare the identified maternal and fetal outcomes, such as thromboembolic events or low birth weight. Considering Namibia's high maternal and neonatal mortality rates, these rates may be high in the general pregnant population as well.[44,45] Fourthly, due to the small cohort it was not possible to perform a multivariable analysis identifying risk factors for poor outcome. Lastly, no data was collected to evaluate the impact of the provision of preconception counselling for women with cardiac disease at the cardiology outpatient department.

Conclusion

A collaborative approach is essential to ensure improved care of women with cardiac disease. Despite many barriers, it was possible to implement such an approach in a high burden setting like Namibia. A high rate of maternal and fetal events was identified. Important benefit of this service was insight into spectrum and severity of cardiac disease and local drivers of these poor outcomes such as late diagnosis of pre-existing cardiac disease. To improve outcomes, studies are needed to identify effective strategies for improved diagnosis of cardiac disease, as well as for the development of context-specific guidelines for a middle-income setting like Namibia. We encourage national and regional organisations to collaborate and initiate large prospective studies to collect high quality data that will inform these interventions.

References

1. M. Knight, K. Bunch, D. Tuffnell, H. Jayakody, J. Shakespeare, R. Kotnis, et al. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Con dential Enquiries into Maternal Deaths and Morbidity 2014–16. Oxford, 2018.
2. Vangen S, Bodker B, Ellingsen L, et al. Maternal deaths in the Nordic countries. Acta Obstet Gynecol Scand. 2017;96(9):1112-1119.
3. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-Related Mortality in the United States, 2011–2013. Obstet Gynecol. 2017;130(2):366-373.
4. Heemelaar S, Petrus A, Knight M, van den Akker T. Maternal mortality due to cardiac disease in low- and middle-income countries. Trop Med Int Health. 2020 Jun;25(6):673-686.
5. Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. Eur Heart J. 2010;31(17):2124-2132.
6. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39(34):3165-3241.
7. Silversides CK, Grewal J, Mason J, et al. Pregnancy Outcomes in Women With Heart Disease: The CARPREG II Study. J Am Coll Cardiol. 2018;71(21):2419-2430.
8. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation. 2001;104(5):515-521.
9. Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart. 2006;92(10):1520-1525.
10. Roos-Hesselink J, Baris L, Johnson M, et al. Pregnancy outcomes in women with cardiovascular disease: evolving trends over 10 years in the ESC Registry Of Pregnancy And Cardiac disease (ROPAC). Eur Heart J. 2019;40(47):3848-3855.
11. Mocumbi AO, Jamal KK, Mbakwem A, Shung-King M, Sliwa K. The Pan-African Society of Cardiology position paper on reproductive healthcare for women with rheumatic heart disease. Cardiovasc J Afr. 2018;29(6):394-403.
12. van Hagen IM, Boersma E, Johnson MR, et al. Global cardiac risk assessment in the Registry Of Pregnancy And Cardiac disease: results of a registry from the European Society of Cardiology. Eur J Heart Fail. 2016;18(5):523-533.
13. Watkins DA, Sebitloane M, Engel ME, Mayosi BM. The burden of antenatal heart disease in South Africa: a systematic review. BMC Cardiovasc Disord. 2012;12):23.
14. Zuhlke L, Engel ME, Karthikeyan G, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). Eur Heart J. 2015;36(18):1115-1122a.
15. Bauersachs J, Konig T, van der Meer P, et al. Pathophysiology, diagnosis and management of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy. Eur J Heart Fail. 2019;21(7):827-843.
16. Sliwa K, Libhaber E, Elliott C, et al. Spectrum of cardiac disease in maternity in a low-resource cohort in South Africa. Heart. 2014;100(24):1967-1974.
17. European Society of G, Association for European Paediatric C, German Society for Gender M, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J. 2011;32(24):3147-3197.
18. Balci A, Sollie-Szarynska KM, van der Bijl AG, et al. Prospective validation and assessment of cardiovascular and offspring risk models for pregnant women with congenital heart disease. Heart. 2014;100(17):1373-1381.
19. Lu CW, Shih JC, Chen SY, et al. Comparison of 3 Risk Estimation Methods for Predicting Cardiac Outcomes in Pregnant Women With Congenital Heart Disease. Circ J. 2015;79(7):1609-1617.
20. Pijuan-Domenech A, Galian L, Goya M, et al. Cardiac complications during pregnancy are better predicted with the modified WHO risk score. Int J Cardiol. 2015;195):149-154.
21. Near Miss National Maternal Death, Stillbirth and Neonatal Death Review Committee. Maternal Death and Near Miss in Namibia. Report on the Confidential Enquiry into Maternal Deaths 1 April 2018 to 31 March 2019 and Near Miss 1 October 2018 to 31 March 2019. Ministry of Health and Social Services: In press.

22. Namibia Statistics Agency. Namibia Inter-censal Demographic Survey 2016. Namibia Statistics Agency: Windhoek, 2017.
23. World Health Organisation. Managing complications in pregnancy and childbirth: a guide for midwives and doctors – 2nd ed. World Health Organisation: Geneva, 2017.
24. World Health Organization. The WHO Application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM. World Health Organization: Geneva, 2012.
25. Diao M, Kane A, Ndiaye MB, et al. Pregnancy in women with heart disease in sub-Saharan Africa. Arch Cardiovasc Dis. 2011;104(6-7):370-374.
26. Lumsden R, Barasa F, Park LP, et al. High Burden of Cardiac Disease in Pregnancy at a National Referral Hospital in Western Kenya. Glob Heart. 2020;15(1):10.
27. Rezk M, Elkilani O, Shaheen A, Gamal A, Badr H. Maternal hemodynamic changes and predictors of poor obstetric outcome in women with rheumatic heart disease: a five-year observational study. J Matern Fetal Neonatal Med. 2018;31(12):1542-1547.
28. Beaton A, Okello E, Scheel A, et al. Impact of heart disease on maternal, fetal and neonatal outcomes in a low-resource setting. Heart. 2018;105(10):755-760.
29. Otto H, Saether SG, Banteyrga L, Haugen BO, Skjaerpe T. High prevalence of subclinical rheumatic heart disease in pregnant women in a developing country: an echocardiographic study. Echocardiography. 2011;28(10):1049-1053.
30. Bhatla N, Lal S, Behera G, et al. Cardiac disease in pregnancy. Int J Gynaecol Obstet. 2003;82(2):153-159.
31. Zuhlke L, Mirabel M, Marijon E. Congenital heart disease and rheumatic heart disease in Africa: recent advances and current priorities. Heart. 2013;99(21):1554-1561.
32. Sliwa K, Azibani F, Baard J, et al. Reducing late maternal death due to cardiovascular disease - A pragmatic pilot study. Int J Cardiol. 2018;272):70-76.
33. Nair M, Nelson-Piercy C, Knight M. Indirect maternal deaths: UK and global perspectives. Obstet Med. 2017;10(1):10-15.
34. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36(44):3075-3128.
35. Group WHOGMSSR. Frequency and management of maternal infection in health facilities in 52 countries (GLOSS): a 1-week inception cohort study. Lancet Glob Health. 2020;8(5):e661-e671.
36. Zuhlke L, Acquah L. Pre-conception counselling for key cardiovascular conditions in Africa: optimising pregnancy outcomes. Cardiovasc J Afr. 2016;27(2):79-83.
37. Chang AY, Nabbaale J, Nalubwama H, et al. Motivations of women in Uganda living with rheumatic heart disease: A mixed methods study of experiences in stigma, childbearing, anticoagulation, and contraception. PLoS One. 2018;13(3):e0194030.
38. Dawson AJ, Krastev Y, Parsonage WA, Peek M, Lust K, Sullivan EA. Experiences of women with cardiac disease in pregnancy: a systematic review and metasynthesis. BMJ Open. 2018;8(9):e022755.
39. Sobhani NC, Schultz H, Kheiwa A, et al. Contraceptive Choices in the Immediate Postpartum Period in Women With Cardiac Disease. Am J Cardiol. 2019;123(8):1364-1369.
40. Koblinsky M, Moyer CA, Calvert C, et al. Quality maternity care for every woman, everywhere: a call to action. Lancet. 2016;388(10057):2307-2320.
41. Miller S, Abalos E, Chamillard M, et al. Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. Lancet. 2016;388(10056):2176-2192.
42. Mahlathi P, Dlamini J. Mimimum data sets for human resources for health and the surgical workforce in South Africa's Health System. A rapid analysis of stock and migration. African Institute of Health & Leadership Development: Nairobi, 2015.
43. Joshi R, Alim M, Kengne AP, et al. Task shifting for non-communicable disease management in low and middle income countries--a systematic review. PLoS One. 2014;9(8):e103754.
44. Heemelaar S, Josef M, Diener Z, et al. Maternal near-miss surveillance, Namibia. Bull World Health Organ. 2020;98(8):548-557.
45. Ministry of Health and Social Services. Demographic and Health Survey Namibia 2013. Ministry of Health and Social Services: Windhoek, 2014.

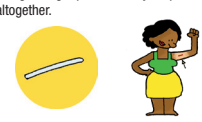
Appendix 1. Patient information leaflet

Birth control options

We strongly advise our heart patients to use birth control that works for several years. We advise the following options:

1. Hormonal loop
The loop is placed in your womb and prevents pregnancy for 5 years. Your period can become less heavy or stop altogether.

2. Implant
The implant is placed under the skin of your arm and prevents pregnancy for 3 years. The implant can cause irregular light periods and your periods may stop altogether.



Both options can be removed at any time when you want to become pregnant and there should be no delay in you getting pregnant.

*Neither the loop nor the implant protect against HIV/AIDS or other sexually transmitted diseases. Always use your birth control together with a condom.

Remember

- If you have **heart disease** pregnancy **can be dangerous** for you and your baby. Ask your doctor which risk group you are in (**green**/**orange**/**red**)
- **Plan your pregnancies with your doctor**
- If you do not want to become pregnant, we strongly recommend you use either the **hormonal loop** or the **implant**
- If you are pregnant, ask your doctor to refer you to the Heart and Maternal Health Service, in antenatal care (ANC) Windhoek Central Hospital

Heart & Maternal Health Service
Windhoek Central Hospital Maternity
Antenatal Care Clinic
Telephone: 061-203 3248

This flyer was made possible by support of:
- The Ministry of Health and Social Services (MOHSS)
- The Heart & Maternal Health (HMH) Service
- Illustrations by Margreet de Heer

Heart Disease and Womens' Health

Heart & Maternal Health Namibia

What you need to know

If you have heart disease, pregnancy can be dangerous for you and your baby as your heart has to work twice as hard.

Not all women with heart disease have the same chance of having problems during pregnancy. It depends which risk group you are in.

Ask your doctor which risk group you are in:

Green: you only have mild heart disease and there is no extra risk for you and your baby when you become pregnant (WHO I).

Orange: there is a risk of complications for you and your baby if you become pregnant (WHO II).

Red: it is very dangerous for you and your baby if you become pregnant (WHO III/IV).

We can help you

If you become pregnant go and see your doctor as soon as possible. For a healthy baby, you and your heart need to be strong and healthy. Together with you, your doctor will decide which tablets are best for you and your baby.

Get an appointment at the Heart and Maternal Health (HMH) Service so we can look after you (antenatal care), your heart and your baby all in one visit. See contact details.

Plan your pregnancy

It is important to **plan your pregnancy**. The heart doctor is there to help you plan a safe pregnancy. This will lower the chance of having problems.

If you do not want to become pregnant now, you need to use reliable **family planning**. For heart patients we advise the hormonal loop or implant. You can read more about this on the next page.

Appendix 2. Details of all women with a prosthetic valve

mWHO, modified World Health Organization risk classification; RHD, rheumatic heart disease; IUGR, intra-uterine growth restriction; TOP, termination of pregnancy; GA, gestational age.

Appendix 2. Details of all women with a prosthetic valve							
Type of valve	**Age**	**Parity**	**Diagnosis**	**mWHO**	**Details valve replacement**	**Cardiac outcome**	
Bioprothesis	43	2	RHD	III	Mitral valve replacement	Death due to infective endocarditis	
Mechanical valve	40	4	RHD	III	Mitral valve replacement	Valvethrombosis needing thrombolysis	
Bioprothesis	27	1	RHD	III	Mitral valve replacement	No events	
Mechanical valve	21	0	RHD	III	Aortic valve replacement	No events	
Bioprothesis	19	0	RHD	III	Aortic valve replacement, mitral valve replacement	No events	
Bioprothesis	20	0	RHD	II	Mitral valve replacement	No events	
Mechanical valve	20	0	RHD	III	Aortic valve replacement, mitral valve repair	No events	
Mechanical valve	37	2	RHD	III	Aortic valve replacement	No events	
Bioprothesis	33	0	RHD	III	Mitral valve replacement	Unknown	

	Obstetric complications	**Fetal outcome**
	None	Alive, IUGR
	None	TOP
	Abruptio at GA 28 weeks	Neonatal death
	None	Miscarriage
	None	IUGR
	None	Spontaneous birth at 27 weeks, alive
	None	Alive
	None	Alive
	Bleeding placenta praevia, CS done at GA 31 weeks	Unknown

Chapter 7.

Maternal and fetal outcomes of pregnancies complicated by acute hepatitis E and the impact of HIV status: A cross-sectional study in Namibia

Steffie Heemelaar, Anna Hangula, Melody Chipeio, Mirjam Josef, Jelle Stekelenburg, Thomas van den Akker, Sven Pischke, Shonag Mackenzie

Liver Int. 2022 Jan;42(1):50-58

Abstract

Objective

Namibia has been suffering from an outbreak of hepatitis E genotype 2 since 2017. As nearly half of hepatitis E-related deaths were among pregnant and postpartum women, we analysed maternal and fetal outcomes of pregnancies complicated by acute hepatitis E and assessed whether HIV-status impacted on outcome.

Methods

A retrospective cross-sectional study was performed at Windhoek Hospital Complex. Pregnant and postpartum women, admitted between 13 October 2017 and 31 May 2019 with reactive IgM for Hepatitis E, were included. Outcomes were acute liver failure (ALF), maternal death, miscarriage, intra-uterine fetal death and neonatal death. Odds ratios (OR) and 95% confidence interval (CI) were calculated.

Results

Seventy women were included. ALF occurred in 28 (40.0%) of whom 13 died amounting to a case fatality rate of 18.6%. Sixteen women (22.9%) were HIV infected, compared to 16.8% among the general pregnant population (OR 1.47, 95% CI 0.84-2.57, $P = .17$). ALF occurred in 4/5 (80%) HIV infected women not adherent to antiretroviral therapy compared to 1/8 (12.5%) women adherent to antiretroviral therapy (OR 28.0, 95% CI 1.4-580.6). There were 10 miscarriages (14.3%), five intra-uterine fetal deaths (7.1%) and four neonatal deaths (5.7%).

Conclusion

One in five pregnant women with Hepatitis E genotype 2 died, which is comparable to genotype 1 outbreaks. Despite small numbers, HIV infected women receiving antiretroviral therapy appear to be less likely to develop ALF in contrast with HIV infected women not on treatment. As there is currently no curative treatment, this phenomenon needs to be assessed in larger cohorts.

Introduction

Hepatitis E virus (HEV) is a leading cause of acute viral hepatitis in low- and middle-income countries, with an estimated 20.1 million HEV infections and 70 000 deaths annually.[1] Epidemiology and clinical presentation differ in the four main genotypes that may infect humans. Genotypes 1 and 2 are transmitted via contaminated drinking water, and outbreaks are mainly seen in Asia and Africa in regions with poor sanitation, whereas genotypes 3 and 4 are transmitted through infected swine meat and more common in high-income countries and Asia.[2-4] Usually, HEV infection is self-limiting with a low mortality rate. However, during pregnancy, a severe clinical course is frequently seen with fulminant hepatic failure, high case fatality rates and high rates of fetal complications such as miscarriage, stillbirth or premature birth. These considerable adverse outcomes are particularly described in areas where genotype 1 is endemic, and confirmed in reports from genotype 2 endemic areas, which is far less prevalent. However, it has not been identified in genotype 3 and 4 endemic areas.[5,6] The pathogenesis of the severe clinical course in pregnant women is not fully understood. It has been suggested that it may be related to the suppressed cellular immunity and immune response in general in pregnancy.[6] Currently there is no approved effective treatment available for acute HEV infections.[7,8]

Namibia has been suffering from an outbreak of HEV genotype 2 since December 2017, with more than 6000 infections reported from all 14 regions by August 2019.[9] Nearly half of the deaths because of HEV were among pregnant and postpartum women and HEV became the leading cause of maternal deaths in 2018-2019.[9,10] Namibia had a high HIV prevalence estimated at 12.6% among adults aged 15-64 years in 2017.[11] The impact of HIV/HEV co-infection on outcome is not yet clear. Some studies reported a higher seroprevalence of HEV among people with HIV in the general population, while others could not confirm this finding.[12,13] Infection with HEV genotype 3 can develop into a chronic infection among immunosuppressed patients, including HIV-infected persons with a low CD4 count, but this has not been described for the other genotypes.[4,12] Considering pregnant women there is hardly any data on HIV/HEV co-infection since most previous genotype 1 and 2 outbreaks occurred in regions with a low HIV prevalence.

As data on outcome of hepatitis E in pregnant women in the setting of an HEV genotype 2 outbreak are still scare, in particular with a focus on HIV infected women, our aim was to analyse maternal and fetal outcomes of pregnancies complicated by acute HEV in Namibia and assess whether HIV status had clinical implications in our cohort.

Methods

Study design and setting

This retrospective cross-sectional study was performed in Windhoek Hospital Complex, which has around 12 000 births annually. The first HEV case of the outbreak in Namibia was reported on 13 October 2017 in Khomas region, in which the capital Windhoek is located. The outbreak continued in the city and by August 2019, there were 6151 reported cases nationally and the outbreak had spread to 10 of the 14 regions with sporadic cases in the other regions as well.[9] The national case fatality rate (CFR) was 0.9% with 56 fatalities.[9] The majority of HEV cases were reported to be among people from informal settlements. These settlements are densely populated with limited access to sanitation, safe drinking water and hygiene. Most people live in the capital for work but travel to different parts of the country to visit family members several times a year. This continuous movement to different regions has likely facilitated the spread of HEV throughout the country. In 2018, two blood samples were tested for genotyping and showed HEV genotype 2. There are reports from two previous outbreaks in Namibia. Both were in the informal settlements of Rundu, a town in northern Namibia, of which the first outbreak was in 1983 because of HEV genotype 1 and the second outbreak in 1995 because of genotype 2.[14,15] Whereas most outbreaks last on average a year, the outbreak in Namibia which started in 2017 has been ongoing for more than 3 years.[2]

According to the national HIV guidelines, all adults with HIV are started on antiretroviral therapy (ART) in Namibia, regardless of CD4 count or clinical stage.[16] In comparison to their neighbouring countries, Namibia performs well in implementation of the ART services: in 2017, 97.1% of HIV-infected females were on ART and of these, 92.2% were virally suppressed.[11]

Study population and data collection

All pregnant women and women whose pregnancy was terminated less than 42 days earlier, who were admitted to Windhoek Hospital Complex between 13 October 2017 and 31 May 2019 with acute HEV, con- firmed by a reactive HEV immunoglobulin M (IgM), were eligible for inclusion in this study. Women were excluded if no positive IgM test result was available, the woman was not admitted to a health facility, her pregnancy or recent pregnancy could not be confirmed, or her clinical file could not be traced. The Ministry of Health and Social Services, together with the World Health Organization, developed clinical management guidelines, recommending all pregnant and postpartum women with jaundice to be admitted and tested for reactive HEV IgM, regardless if other clinical symptoms were present. Therefore, many women with mild disease were admitted and included in our cohort.

Cases were identified using a list of all suspected HEV cases in Khomas region from the Ministry of Health and Social Sciences of Namibia, which was established from the start of the outbreak, as hepatitis E is a notifiable disease. Because of budget restrictions, it was not possible to apply this list to other affected regions. Nevertheless, our cohort included the majority of pregnant women with HEV in Namibia, as the capital and it's referring regions were most severely affected by the outbreak. In the referring regions intensive care unit (ICU) facilities were not available and nearly all pregnant women with a confirmed HEV infection were therefore transferred to our study site for further monitoring and care. In the hospital complex the capital ICU facilities were available to provide supportive care for patients with ALF.

For identification of possible missed cases, data from the National Maternal Death Review Committee of the Ministry of Health and Social Services was used. This committee analysed all maternal deaths occurring in the country between 1st of April 2018 and 31st of March 2019 and all cases of severe morbidity between 1st of March 2018 and 31st of May 2018 in the capital and between 1st of October 2018 till 31st of March 2019 nationally.[10,17,18] Considering the severe clinical course among pregnant women, these cohorts contained many women with complicated pregnancies because of HEV.

For identified cases, data were collected anonymously from medical records using a structured data collection tool, including socio- demographic characteristics, maternal outcomes, fetal outcomes, obstetric complications, signs of liver failure and HIV status. This was done by AH and MC and verified by SH and MJ, both medical doctors with several years of experience providing obstetric care in Namibia.

Laboratory test results on admission and the most abnormal value during admission were collected from the database of the National Institute of Pathology, including alanine aspartate aminotransferases, alanine aminotransferases, bilirubin, haemoglobin, platelets, creatinine and international normalized ratio (INR). Serology test for hepatitis A, B and C were performed by Alinity Abbott. Hepatitis E serology was performed using Aria rapid tests. Glucose values were obtained through capillary blood tests. If the woman was HIV infected, data on ART treatment adherence, latest CD4 count and viral load value were retrieved from medical records, the database of the National Institute of Pathology and additional information was collected through the ART clinic the patient was attending. Data regarding fetal outcome was obtained from the woman's medical record. If a neonate had been admitted to neonatal ICU, survival status was obtained from neonatal ICU admission records. No neonate was tested for vertical transmission of HEV, as PCR testing was not available.

HIV prevalence among the general pregnant population was collected through the Prevention Mother to Child Transmission Program of the Ministry of Health and Social Services.

Outcomes and data analysis

Main maternal outcomes were number of women with acute liver failure (ALF) and death. ALF was defined according to the definition of European Association for the Study of the Liver; acute abnormality of liver blood tests(elevated serum transaminases) in an individual without underlying chronic liver disease followed by hepatic encephalopathy of any grade and a INR > 1.5.[19] Severity of hepatic encephalopathy was graded using the West Haven Criteria, ranging from grade 1 with mild altered mental stage up to grade 4 which is complete coma. Acute hepatitis B was identified with a reactive test for IgM anti-HBc. Chronic hepatitis B was diagnosed when a woman had a reactive test for both HBsAG and anti-HBc. Hypoglycaemia was defined as any capillary blood glucose <4.0 mmol/L. Postpartum haemorrhage was defined as >1000 mL blood loss after birth. Premature birth was defined as birth between 26 weeks and 0 days of gestation and 36 weeks and 6 days. Intra-uterine fetal death was defined as a death before birth in a fetus with a gestational age of 26 weeks and 0 days or more. For miscarriage, the threshold of less than 26 weeks and 0 days was used. Neonatal death was death during the first 28 days of life. All results were reported as numbers (n) and frequencies (%). An ART defaulter was defined as any woman who interrupted her treatment and missed at least one clinic visit.[16] Maternal case fatality rate was defined as the number of maternal deaths divided by the number of pregnancies complicated by acute hepatitis E and presented as a percentage. Fetal case fatality rate was defined as the number of intra-uterine fetal deaths and neonatal deaths, divided by the number of pregnancies complicated by acute hepatitis E and presented as a percentage.

Continuous variables are presented as means with standard deviations and differences in normally distributed variables were assessed using a student *t*-test. Missing data were assumed to be 'no' for categorical data, whereas complete case analysis was used to handle missing data for continuous variables and data regarding ART adherence. Categorical variables are presented as percentages. Differences were assessed using chi-square test or Fisher's Exact test when indicated and odds ratios (OR) with 95% confidence intervals (CI) are presented. Statistical significance was assumed at a two-sided value of $P < .05$. Data analysis was per- formed with SPSS version 26. We followed the STROBE reporting guidelines.

Table 1. Baseline characteristics	
Variables	**N = 70 (%)**
Age (years)	
< 20	3 (4.3)
20 - 34	60 (85.7)
≥ 35	7 (10.0)
Parity	
Para 0	9 (12.9)
Para 1-3	51 (72.9)
≥ 4	8 (11.4)
Unknown	2 (2.9)
Gestational age on admission (weeks + days)	
< 13 + 0	6 (8.6)
13 + 0 - 25 + 6	14 (20.0)
26 + 0 – 36 + 6	34 (48.6)
≥ 37 + 0	5 (7.1)
Unknown	11 (15.7)
HIV status	
Positive	16 (22.9)
Negative	52 (74.3)
Unknown	2 (2.9)
Hepatitis	
Hepatitis A	0 (0)
Hepatitis B, acute	0 (0)
Hepatitis B, chronic	4 (5.7)
Hepatitis C	0 (0)
Pregnancy outcome	
Vaginal birth	37 (52.9)
Caesaren section	5 (7.1)
Miscarriage	10 (14.3)
Still pregnant at discharge	18 (25.7)
Maternal outcome	
Died	13 (18.6)
Survived	53 (75.7)

Values are n (%).

Table 2. Characteristics of women with acute liver failure compared to no acute liver failure.					
	ALF	**No ALF**	**All women**		
Total	**n = 28**	**n = 42**	**n = 70**	**OR (95% CI)**	**p value**
Age	26.5 ± 4.8	28.7 ± 5.7	27.8 ± 5.4		0.11
Third trimester[a]	23 (82.1)	24 (57.1)	47 (67.1)	OR 3.45 (1.1 - 10.8)	0.04
Pregnancy outcome at discharge					
Given birth/ miscarried	25 (89.3)	27 (64.3)	52 (74.3)	OR 4.63 (1.2 - 17.9)	0.03
Still pregnant	3 (10.7)	15 (35.7)	18 (25.7)		
HIV-status	5 (17.9)	11 (26.2)	16 (22.9)	OR 0.61 (0.2 - 2.0)	0.56
On ART	1 (20.0)	7 (63.6)	8 (50.0)	OR 0.14 (0.0 - 1.8)	0.28
ART defaulted/ interrupted	4 (80.0)	1 (9.1)	5 (31.3)	OR 28.0 (1.4 - 580.6)	0.03
Unknown if on treatment	0 (0)	3 (27.3)	3 (18.8)		
Encephalopathy	28 (100)	0 (0)	28 (40.0)		
None	0 (0)	0 (0)	42 (60.0)		
Grade 1	1 (3.6)	0 (0)	1 (1.4)		
Grade 2	0 (0)	0 (0)	0 (0)		
Grade 3	6 (21.4)	0 (0)	6 (8.6)		
Grade 4	20 (71.4)	0 (0)	20 (28.6)		
Grade not specified	1 (3.6)	0 (0)	1 (1.4)		
Hypoglycemia	21 (75.0)	17 (40.5)	38 (54.3)	OR 4.41 (1.5 - 12.7)	0.01
Mechanical ventilation	24 (85.7)	0 (0)	24 (34.3)		
INR	6.2 ± 3.1	1.7 ± 0.7	3.4 ± 2.9		<0.01
AST IU/L admission	2874 ± 2232	1925 ± 1610	2302 ± 1924		0.06
AST IU/L highest	3118 ± 2579	2487 ± 1725	2734 ± 2106		0.27
ALT IU/L admission	1827 ± 847	1512 ± 1150	1634 ±1047		0.23
ALT IU/L highest	1929 ± 983	1770 ± 1111	1832 ± 1058		0.55
Total bilirubin mg/ dL admission	225 ± 95	183 ± 101	199 ± 100		0.1
Total bilirubin mg/ dL highest	278 ± 109	223 ± 132	244 ± 126		0.08

Values are mean ± standard deviation, n (%) and odds ratio (95% confidence interval).
ALF, acute liver failure; OR, odds ratio; CI, confidence interval; ARV, antiretroviral treatment ; INR, international normalized ratio; AST, alanine aspartate aminotransferases; ALT, alanine aminotransferases.
[a] ≥ 26 weeks completed weeks of gestation.

Results

Seventy women were included into this study. The Ministry data identified 196 women who had been pregnant or recently pregnant and suspected to have contracted hepatitis E. Of these, 57 women had not been admitted to a health facility or tested for HEV. Four women had a negative IgM result and for 59 women it was indicated they were tested for HEV, but no IgM result could be found on the system. We were unable to trace medical records of 20/76 women, so 56 women were included in our study from the Ministry's data. An additional 14 women were identified through the national severe morbidity and mortality registries. Table 1 shows the baseline characteristics of the 70 women in our cohort.

Maternal outcome

ALF occurred in 28/70 (40.0%) women, of whom 13 died leading to a maternal case fatality rate of 18.6%. Twelve women died because of fulminant liver failure after being in ICU for several days with hepatic encephalopathy grade 4 and one woman died because of hypovolemic shock secondary to postpartum haemorrhage and disseminated coagulopathy. Table 2 compares the characteristics of women who developed ALF and women without ALF. Women with ALF, compared to women without ALF, were more frequently in the third trimester, OR 3.45 (95% CI 1.10-10.83, *P* = .04), had one or more episodes of hypoglycaemia, OR 4.41 (95% CI 1.54-12.66, *P* = .01), and had a higher INR (6.2 ± 3.1, compared to 1.7 ± 0.7, *P* < .01). Women with ALF were more likely to give birth or lose their pregnancy because of a miscarriage compared to women without ALF during their admission for acute HEV, OR 4.63 (95% CI 1.20-17.93, *P* = .03). Of the women with ALF, 20/28 (71.4%) developed hepatic encephalopathy grade 4 and 24/28 (85.7%) needed mechanical ventilation. An INR >1.5 was found in 42/70 (60.0%) of our study population. We identified a trend of higher elevated serum transaminases for women with ALF. For six patients with ALF birth was complicated by postpartum haemorrhage. Two women developed pregnancy-induced hypertension and four had pre-existent hypertension. There were no other hypertension-related complications such as pre-eclampsia/eclampsia.

HIV

In our study population 16/70 (22.9%) women were HIV infected, compared to a prevalence of 16.8% among the general pregnant population in Namibia in 2018, which was not significantly higher OR 1.47, 95% CI 0.84-2.57, P = .17).[10] Among the women with ALF, HIV prevalence was lower compared to women without ALF (17.9% vs 26.2%), but there was no statistical significance (OR 0.61, CI 0.19- 2.01, P = .56). Notably 4/5 HIV infected women who interrupted their ART (80%) developed ALF compared to

Table 3. Details of HIV positive women with acute hepatitis E during pregnancy							
	Outcome	**Gestational age**	**ARV adherence**	**ARV regimen**	**CD4 cells/mm3**	**Viral load (copies/mL)**	**Comments**
1	ALF - died	3rd trimester	On treatment	TDF/3TC/ AZT/ ATVr		< 20 copies	2nd line regimen[a]
2	ALF - died	3rd trimester	Defaulted	N/A	279		
3	ALF - survived	3rd trimester	Defaulted		739		
4	ALF - survived	3rd trimester	Defaulted	TDF/3TC/EFV	560		Restarted in ICU 2 weeks after onset ALF
5	ALF - survived	2nd trimester	See comments	TDF/FTC/EFV	639		No ARVs from day 1 admission, ALF on day 5, restarted ARVs in ICU on day 7
6	No ALF	3rd trimester	On treatment	TDF/FTC/EFV		< 20 copies	
7	No ALF	3rd trimester	On treatment	Unknown		< 20 copies	
8	No ALF	3rd trimester	On treatment	TDF/AZT/3TC/ LPV-r		< 20 copies	2nd line regimen[a]
9	No ALF	3rd trimester	Defaulted	TDF/FTC/EFV	329		Restarted on admission before signs ALF
10	No ALF	2nd trimester	Unknown				
11	No ALF	2nd trimester	On treatment	TDF/3TC/EFV			
12	No ALF	1st trimester	Unknown				Started in 2016, lost to follow up
13	No ALF	3rd trimester	On treatment	TDF/FTC/EFV	559	< 20 copies	
14	No ALF	3rd trimester	On treatment	TDF/3TC/AZT/ ATVr		< 20 copies	
15	No ALF	3rd trimester	Unknown			< 20 copies	
16	No ALF	3rd trimester	On treatment	TDF/FTC/EFV	600	< 20 copies	

All available data is presented.
ARV, antiretroviral; ALF, acute liver failure; TDF, tenofovir; 3TC, lamivudine; AZT, zidovudine; ATVr, atazanavir/ritonavir; N/A not applicable, EFV, efavirenz; ICU, intensive care unit; LPV-r, lopinavir/ritonavir.
[a]no recent amendments in drug regimen.

1/8 (12.5%) HIV infected women adherent to their ART (OR 28.0, 95% CI 1.4-580.6, P = .03). Table 3 presents the ART regimen, adherence, most recent available CD4 count and viral load of all HIV-infected women in our study. One woman with ALF forgot her ART when she was admitted for observation with HEV infection during pregnancy in a stable condition. She developed encephalopathy 5 days after admission and was transferred to ICU where she developed hepatic encephalopathy grade 3. Her ART was restarted 7 days after admission and she fully recovered. For three women we were unable to trace information regarding their ART regimen or adherence, of whom one woman had a recent viral load blood test indicating she was virally suppressed and therefore on treatment.

Twelve (75.0%) HIV positive women were in the third trimester, compared to 35/54 (64.8%) HIV negative women, which was not a significant difference (P = .45). For women in the third trimester, there was a trend of a lower HIV prevalence in women with ALF compared to women without ALF (17.4% vs 33.3%, OR 0.42, 95% CI 0.11-1.66, P = .21).

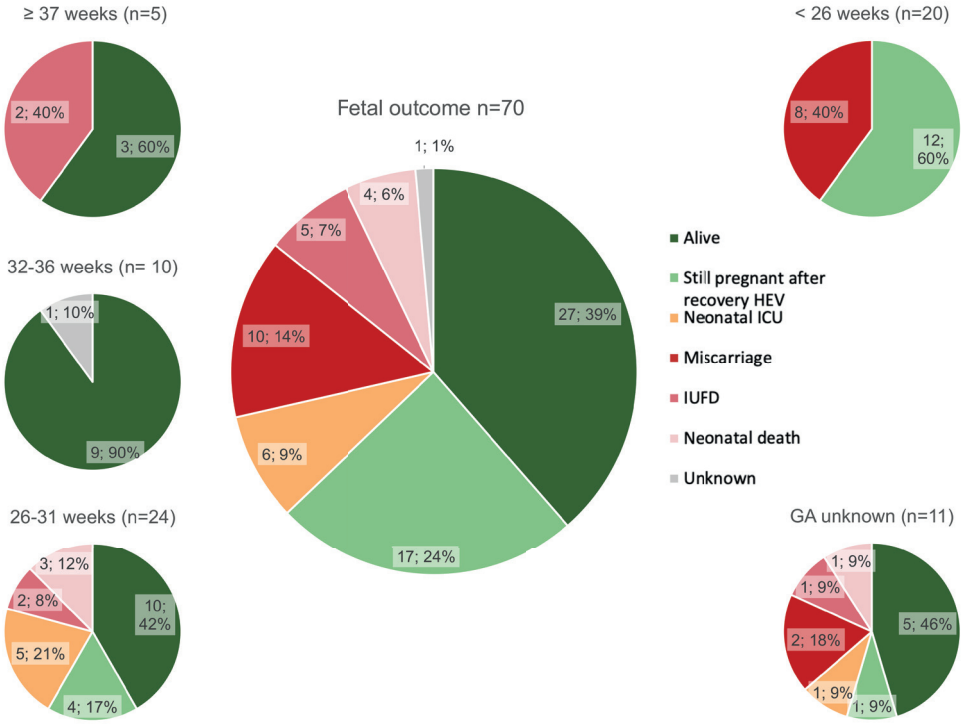


Figure 1. Fetal outcome according to gestational age
Largest pie chart presents fetal outcome of the complete cohort. Smaller pie charts present fetal outcome based on gestational age at end of pregnancy. One woman died while still pregnant, fetal outcome in this woman was counted as intra-uterine fetal death.
NICU, neonatal intensive care unit; IUFD, intra-uterine fetal death; GA, gestational age.

Fetal outcome

Even though only 5/70 (7.1%) of the women had a term pregnancy at the time they were admitted with acute HEV, 42/70 (60.0%) gave birth during admission for HEV and 10/70 (14.3%) had a miscarriage. One woman died while still pregnant and only 17/70 (24.3%) were discharged still pregnant after they had recovered from their HEV infection. There were five intra-uterine fetal deaths and four neonatal deaths leading to a fetal-neonatal case fatality rate of 12.9%. Six neonates were admitted to neonatal ICU and we were unable to verify whether they were discharged alive. One woman gave birth at 35 weeks of gestation but was admitted postpartum with signs of ALF and no information regarding fetal outcome was available. Figure 1 presents the fetal outcome of our cohort, according to gestational age at the time of HEV infection. Preterm birth took place among 30/70 (42.9%) women and 20 neonates needed admission to neonatal ICU for this reason.

Discussion

In our cohort of pregnant women with acute hepatitis E in the setting of an HEV genotype 2 outbreak we identified a high maternal case fatality rate, as well as a high fetal case fatality rate. Women who were HIV positive seemed to be more frequently infected with HEV, although not statistically significant. Also HIV infected women appeared to have a better outcome, especially when on ART.

To our knowledge, this is the first cohort reporting acute HEV in pregnancy caused by genotype 2. Our high maternal case fatality rate corresponds with the available literature for genotype 1, as well as the more severe outcome among women in the third trimester and a high mortality rate among women who develop ALF.[5,20] A systematic review and meta-analysis performed by Jin et al, identified a CFR of 21%, reporting on 3968 pregnancies from both community-based and facility-based studies, whereas Berglov et al, identified a CFR of 26%, reporting on 1338 pregnancies from facility-based studies only.[5,20] It's important to realize, even though most review articles present CFR for genotype 1 and 2 combined, data regarding pregnancy outcomes of genotype 2 are actually scarce as genotype 1 is far more prevalent, especially in Asia.[2,5,6,20-22] Besides Namibia, genotype 2 has only been identified in Mexico, Chad, Nigeria, Burkina Faso and Central African Republic.[22-24] Berglov et al[20] solely included studies from areas with genotype 1. Jin et al included only one report from an African country where genotype 2 was prevalent, namely Central African Republic, reporting on seven pregnant women with acute HEV, of which one died.[25] We were able to identity one additional study from Chad, reporting on four pregnant women with acute HEV, of whom two died.[26]

Our fetal outcome also corresponds with the fetal outcome identified in cohorts reporting on genotype 1. The review of Berglov included miscarriage in the intra-uterine stillbirth rate and identified a stillbirth rate of 33% and a neonatal CFR of 8%.[20] Jin et al[5] identified a fetal case fatality rate of 34%, but it is unclear whether miscarriages were included in their definition. Berglov et al[20] reported a similar high premature birth rate to ours of 52%. There was no premature birth rate available in the report of Jin et al[5] We did not test for vertical transmission in our cohort. Berglov et al reported a vertical transmission rate ranging from 28% to 79%, based on the findings of five studies.[20]

This is one of the first cohorts reporting on the outcome of pregnant women with HIV and acute HEV. The literature is scarce regarding the clinical impact of HIV/HEV co-infection in pregnant women, as in most of the areas with outbreaks of genotype 1 and 2 there was a low HIV prevalence. Firstly, we identified a slightly higher HIV prevalence in our cohort, compared to the general pregnant population, although not statistically significant. This finding may suggest that HIV positive women are more easily infected by HEV. For all genotypes, the literature is conflicting on whether or not there is a higher seroprevalence of HEV among people with HIV.[12,13] We found three reports from other African countries. Only in the report from Gabon, a slightly higher sero-prevalence was reported among 183 asymptomatic HIV positive pregnant women, as 7% were IgG positive for HEV, compared with 5% of their control group.[27] In a Ethiopian cohort with 386 asymptomatic pregnant women, 31.6% were IgG positive and two women were IgM positive. Only 18 women were HIV positive and HEV prevalence did not differ between both groups.[28] In the Central African Republic, they found a seroprevalence of 68% among 200 HIV positive adults, which was comparable to the general population.[28] Secondly, in our cohort of HIV infected women, in particular those receiving ART, appeared to be at lower risk of a severe clinical course including developing ALF. Although this finding needs to be interpretated with caution because of the small numbers, it is an interesting observation as, with most infections among HIV infected individuals, a more severe outcome could be anticipated. Possible mechanisms contributing to our observations are a reduced immune response, resulting in a mitigated level of hepatitis or a direct effect of the antiretroviral therapy against HEV. Among the eight women on ART there were four different drug regimens and therefore we could not further assess the potential protective role of individual ART drugs. Also the duration of pregnancy could not explain this finding as the number of women in the third trimester appeared to be similar for both HIV positive and negative women. Furthermore, a similar trend of a lower HIV prevalence among women with ALF compared to no ALF was identified,

when analysing data of women in the third trimester only. To our knowledge, there are no studies available reporting the outcome of pregnant women with acute HEV comparing HIV infected and non-infected women. However, a recent large meta-analysis revealed that ongoing chronic HEV was seen significantly less frequently among HIV infected adults in comparison to transplant recipients, which also suggests that HIV infected adults tend to clear the HEV virus more easily com- pared to those who are not infected.[29]

We identified a trend of higher elevated serum transaminases for women with ALF compared to women without ALF, which was not significant and there was a very wide range for these parameters. This is most likely explained by a large variation in condition on admission of the women. While some women presented asymptomatic, others presented after the onset of signs of acute liver failure and a few women only presented in the terminal phase when serum transaminases are decreasing again.

The hepatitis E outbreak had a significant impact on the limited resources of the public healthcare system of Namibia. There were only 14 ICU beds available in the hospital complex in the capital, serving the entire population. A woman with hepatic encephalopathy because of HEV often needed ventilatory support for two to three weeks. Since the start of the outbreak on average one to two ICU beds have been occupied by a young woman with HEV. This increased demand on an already overburdened ICU resulted in more referrals to ICUs of private institutions, resulting in high costs for the Ministry of Health. Similar problems were seen at the neonatal ICU, because of the high frequency of extreme premature birth of HEV infected women. Lastly, the frequent loss of a young woman and unavailability of an effective treatment had an enormous impact on the mental well-being of our staff. The number of maternal deaths has nearly doubled since the start of the outbreak. One of the consultants stated: ‘it feels like the HIV era, when we could only hope for the best’.

In our facility we experienced challenges with providing good care to the HEV patients, because of unfamiliarity with the disease, fear of transmission and lack of resources. Especially at the start of the epidemic, several women were misdiagnosed with alcohol intoxication when they presented with hepatic encephalopathy. Others were brought in by the police, accused of performing an illegal abortion when they had a spontaneous premature birth at home. Furthermore, out of fear for transmission, observations were not always done as requested and subsequently deterioration was noted at a late stage. As a result of limited availability of glucose strips, diagnosis of hypoglycaemia was in some cases delayed until clinical symptoms were present. We feel glucose monitoring is essential for all pregnant women with acute HEV, as hypoglycaemia was often the first sign of the progression towards

acute liver failure. To improve care, healthcare workers working in regions affected by the HEV outbreak, were trained in the management of pregnant women with jaundice. This was through video conferencing and sharing management guidelines, which resulted in the provision of better care.

Our study has several limitations. Firstly, there might have been selection bias as hospitalized women were included only. We identified additional patients through our severe morbidity and mortality registry and it is highly likely that the true case fatality rate might be lower. Secondly, our cohort was small and because of the retrospective design some important data, such as HIV status of two women or ART regimen of four women, were missing. Thirdly, we did not determine the HEV genotype or subtype in our cohort, while genotype 2 has been proven to be the causative agent of the outbreak. Lastly, we did not test for vertical transmission from mother to baby, which may have assisted with the interpretation of our poor fetal outcome. A prospective cohort with larger numbers may have resulted in more answers but was not feasible because of limited resources and the sudden onset of the outbreak.

Conclusion

Hepatitis E is a disease with many faces: while sporadic chronic HEV infections in immunosuppressed individuals and extrahepatic manifestations are of main interest in high-income countries, low- and middle-income countries suffer from endemic outbreaks involving large populations causing a high mortality in pregnant women. HEV genotype 2 infections and outcome of pregnancy have not been studied in detail previously. This retrospective study shows a mortality rate of almost 20% caused by an ongoing HEV genotype 2 outbreak in Namibia, which is similar to outbreaks with genotype 1. For the first time it was possible to study a potential role of underlying HIV infection and ART in pregnant women threatened by HEV infection. Despite the total numbers being low, it is surprising that HIV infected women in particular those on ART, seem to be less likely to developed acute liver failure in contrast with non-HIV infected pregnant women. These data for the first time indicate that underlying HIV infection or the ART itself might attenuate the severity of HEV genotype 2 infections in pregnant women. More research is urgently needed to confirm or refute this phenomenon in larger cohorts. Understanding the underlying mechanism may potentially lead to treatment options to alter the often fatal outcome of this disease among pregnant women.

References

1. Rein DB, Stevens GA, Theaker J, Wittenborn JS, Wiersma ST. The global burden of hepatitis E virus genotypes 1 and 2 in 2005. Hepatology. 2012;55(4):988-997.
2. Hakim MS, Wang W, Bramer WM, et al. The global burden of hepatitis E outbreaks: a systematic review. Liver Int. 2017;37(1):19-31.
3. Aggarwal A. The Global Prevalence of Hepatitis E Virus Infection and Susceptibility: A Systematic Review. World Health Organization: Geneva, 2010.
4. Kamar N, Bendall R, Legrand-Abravanel F, et al. Hepatitis E. Lancet. 2012;379(9835):2477-2488.
5. Jin H, Zhao Y, Zhang X, Wang B, Liu P. Case-fatality risk of pregnant women with acute viral hepatitis type E: a systematic review and meta-analysis. Epidemiol Infect. 2016;144(10):2098-2106.
6. Perez-Gracia MT, Suay-Garcia B, Mateos-Lindemann ML. Hepatitis E and pregnancy: current state. Rev Med Virol. 2017;27(3):e1929.
7. Organization WH. Hepatitis E vaccine: WHO position paper, May 2015. Wkly Epidemiol Rec. 2015;90(18):185-200.
8. Nishiyama T, Kobayashi T, Jirintai S, et al. Screening of novel drugs for inhibiting hepatitis E virus replication. J Virol Methods. 2019;270):1-11.
9. Ministry of Health and Social Services. Outbreak of Hepatitis E Virus (HEV) in Namibia, Situation Report (SITREP No. 64). Ministry of Health and Social Services: Windhoek, 2019.
10. Near Miss National Maternal Death, Stillbirth and Neonatal Death Review Committee. Maternal Death and Near Miss in Namibia. Report on the Confidential Enquiry into Maternal Deaths 1 April 2018 to 31 March 2019 and Near Miss 1 October 2018 to 31 March 2019. Ministry of Health and Social Services: In press.
11. Ministry of Health and Social Services. Namibia Population-Based HIV impact assessment NAMPHIA 2017. Ministry of Health and Social Services: WIndhoek, 2019.
12. Debes JD, Pisano MB, Lotto M, Re V. Hepatitis E virus infection in the HIV-positive patient. J Clin Virol. 2016;80):102-106.
13. Krain LJ, Nelson KE, Labrique AB. Host immune status and response to hepatitis E virus infection. Clin Microbiol Rev. 2014;27(1):139-165.
14. Isaacson M, Frean J, He J, Seriwatana J, Innis BL. An outbreak of hepatitis E in Northern Namibia, 1983. Am J Trop Med Hyg. 2000;62(5):619-625.
15. Maila HT, Bowyer SM, Swanepoel R. Identification of a new strain of hepatitis E virus from an outbreak in Namibia in 1995. J Gen Virol. 2004;85(Pt 1):89-95.
16. Ministry of Health and Social Services Directorate of Special Programmes. National Guidelines for Antiretroviral Therapy, Fifth Edition. Ministry of Health and Social Services: Windhoek, 2016.
17. Heemelaar S, Josef M, Diener Z, et al. Maternal near-miss surveillance, Namibia. Bull World Health Organ. 2020;98(8):548-557.
18. Heemelaar S, Kabongo L, Ithindi T, et al. Measuring maternal near-miss in a middle-income country: assessing the use of WHO and sub-Saharan Africa maternal near-miss criteria in Namibia. Glob Health Action. 2019;12(1):1646036.
19. European Association for the Study of the Liver. Electronic address eee, Clinical practice guidelines p, Wendon J, et al. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. J Hepatol. 2017;66(5):1047-1081.
20. Berglov A, Hallager S, Weis N. Hepatitis E during pregnancy: Maternal and foetal case-fatality rates and adverse outcomes-A systematic review. J Viral Hepat. 2019.
21. Hartl J, Wehmeyer MH, Pischke S. Acute Hepatitis E: Two Sides of the Same Coin. Viruses. 2016;8(11.
22. Aggarwal R, Goel A. Natural History, Clinical Manifestations, and Pathogenesis of Hepatitis E Virus Genotype 1 and 2 Infections. Cold Spring Harb Perspect Med. 2019;9(7.
23. Dimeglio C, Kania D, Mantono JM, et al. Hepatitis E Virus Infections among Patients with Acute Febrile Jaundice in Burkina Faso. Viruses. 2019;11(6.
24. Kim JH, Nelson KE, Panzner U, Kasture Y, Labrique AB, Wierzba TF. A systematic review of the epidemiology of hepatitis E virus in Africa. BMC Infect Dis. 2014;14):308.
25. Goumba CM, Yandoko-Nakoune ER, Komas NP. A fatal case of acute hepatitis E among pregnant women, Central African Republic. BMC Res Notes. 2010;3):103.

26. Coursaget P, Buisson Y, N'Gawara MN, Van Cuyck-Gandre H, Roue R. Role of hepatitis E virus in sporadic cases of acute and fulminant hepatitis in an endemic area (Chad). Am J Trop Med Hyg. 1998;58(3):330-334.
27. Caron M, Bouscaillou J, Kazanji M. Acute risk for hepatitis E virus infection among HIV-1-positive pregnant women in central Africa. Virol J. 2012;9):254.
28. Demi Sibiro OA, Manirakiza A, Komas NP. Seroprevalence of Hepatitis E Virus Infection Among People Living With HIV in the Central African Republic. Open Forum Infect Dis. 2018;5(12):ofy307.
29. Buescher G, Ozga AK, Lorenz E, et al. Hepatitis E seroprevalence and viremia rate in immunocompromised patients: a systematic review and meta-analysis. Liver Int. 2021;41(3):449-455.

Part III.

Discussion and summary

Chapter 8.

General discussion

Aims of this thesis were to enhance implementation of a national obstetric surveillance system and assess requirements to improve maternal health in Namibia. The findings of chapters 2-7 provided insight into several important drivers of severe maternal outcome. Obstetric surveillance played a crucial role in obtaining these insights. Based on these, targeted recommendations could be formulated.

Understanding the poor maternal outcome in Namibia

In Namibia, the incidence of severe maternal outcome was much higher than expected for an upper middle-income country.[1] For example, in 2017 the reported maternal mortality ratio (MMR) was three times higher than the average reported MMR for upper middle-income countries.[2,3] This thesis showed that the two most important contributors to severe maternal outcome were challenges in timely access to care for some women, and poor quality of facility-based care. Access was hampered particularly among vulnerable women. This disparity results from gross inequities present in Namibia, impacting all three elements of the system supposed to support women in terms of their reproductive health needs, Figure 1. The poor-quality care provided within facilities can be summarized as 'too little, too late' and was the result of the combination of health workers having insufficient knowledge and skills to timely diagnose and manage complications, an inconsistent supply of basic and essential resources, and high levels of understaffing.

The structure of this general discussion is based on the conceptual framework (Figure 1), with the identified challenges impacting the support structure for the woman discussed first, followed by that for the health worker.

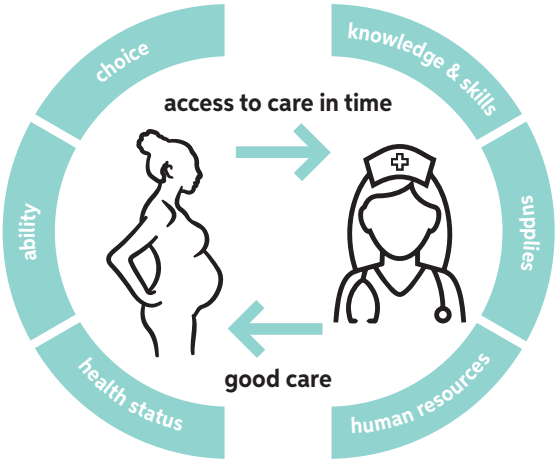


Figure 1. Framework mapping the requirements for functioning support systems for women to ensure they can access care in time and the requirements for health workers to ensure they can provide high-quality care.

Inadequate support for (some) women

Namibia has one of the largest socioeconomic inequalities in the world.[4] Unsurprisingly, there are large differences in access to reproductive health services and outcomes. For example, while contraceptives are supposed to be freely available, the alarmingly high teenage pregnancy rate of 18% and the high rate of unintended pregnancies among women with cardiac disease identified in this thesis clearly indicate that there is a large unmet need of family planning (choice, chapter 2, 6). A school-based sexual and reproductive health educational approach or a focus on increased use of long-acting reversible contraception, interventions proven to be effective elsewhere, could assist in the reduction of unintended pregnancies among teenagers in Namibia.[5,6] Several modern long-acting contraceptive methods, such as hormonal implants, recently became available in public health facilities through donations by the United Nations Population Fund to the Ministry of Health.[7] As described in chapter 6, an integrated approach with the provision of reliable contraception at the cardiology department increased access to contraception for women with cardiac disease. This approach should be implemented across other departments to reach all women with high-risk pre-existing medical conditions such as HIV or tuberculosis.[8]

The socioeconomic inequalities also affect the ability of girls and women to access care. For example, the caesarean section rate was only 6% among the poorest quintile of the population compared to 35% among the richest, one of the widest disparities in sub-Saharan Africa.[9] As identified in chapter 4, several rural district hospitals were unable to provide access to basic surgery, such as caesarean section or laparotomy for ectopic pregnancy, due to a lack of resources. For several women, especially those living in rural areas, lack of access to basic surgery was the main underlying cause of maternal near-misses, particularly when uterine rupture or shock requiring prompt surgery occurred during transport to a referral hospital. Findings of chapters 2 and 4 were shared with decision makers at the Ministry of Health and Social Services and immediate steps were taken to improve availability of basic surgery in all district hospitals. At last, also among women with cardiac disease more complications were seen in those with delayed access to care (chapter 6). The ability of these women to access care in time could be improved through enhanced implementation of high-quality counselling, ideally starting prior to conception, to increase knowledge on danger signs (chapter 5, 6).[10]

Communicable diseases were mainly found among women of lower socioeconomic status, and these conditions had considerable impact on women's health status and, thereby, pregnancy outcome. Hepatitis E was the leading cause of maternal deaths, mainly seen among the poorest women living in the least serviced informal

settlements without access to sanitation or safe drinking water (chapter 7). Other examples are tuberculosis, HIV and rheumatic heart disease, which are all more prevalent among women of lower socioeconomic status and as well associated with severe maternal outcome in Namibia (chapters 2, 5, 6).[11,12] To improve the health status, ideally these diseases are prevented through primary prevention. However, this is not easy to attain given the fact that complex interventions, such as better housing conditions or universal test and treat strategies, are needed.[13,14] Several effective interventions are available for secondary prevention, such as the provision of isoniazid preventive therapy to prevent tuberculosis co-infection among HIV-positive women, improved detection of mild cardiac disease among women of reproductive age or secondary antibiotic prophylaxis for women with mild rheumatic heart disease (chapter 5,6).[11,15]

The unequal outcomes that we identified are not unique to Namibia. Even though around the globe an overall reduction in maternal mortality has been observed over the past decades, health disparities between the (moderately) rich and the poor only seem to have increased, both between and within countries.[16] Although access to care improved for some, vulnerable populations are lagging behind.[16] Of women accessing health facilities, the poor and disadvantaged are the ones most likely to reach precisely those grossly overburdened and severely understaffed facilities that provide low-quality care.[17]

Addressing maternal health inequities is a complex undertaking and a multisectoral approach is needed. Most of the origins of inequity lie outside the health sector and the differences in health outcome are just another symptom of such inequity.[16] The importance of reducing health disparities has been recognized by authors of many authoritative papers and is a key item of the 2030 Agenda of Sustainable Development.[18,19] Also from within the health sector significant progress is required. Health systems will need to be strengthened, to enable health workers to provide universal coverage of good health care to all women.[17] The specific requirements to strengthen the Namibian maternity care system will be discussed in the following section.

Inadequate support for health workers

The combination of insufficient **knowledge and skills** of attending health workers, inconsistent **supplies** of essential medication and medical equipment, and understaffing (**human resources**) had considerable impact on maternal outcome in Namibia. As a result, conditions such as septic shock or cardiac disease were diagnosed or managed with substantial delay (chapter 2, 6). These delays contributed considerably to maternal deaths and near-misses (chapter 2-4).

Insufficient knowledge and skills of the attending health workers is likely to be predominantly the result of lack of availability of continuous postgraduate training as well as lack of senior staff.[20,21] In high-income countries lifelong learning is ensured through mandatory and optional courses. Furthermore, freshly graduated doctors and nurses receive extensive on-the-job guidance from senior colleagues before they get the ultimate responsibility for the care of individual patients.

Personal example: during my specialty training as a medical doctor in Global Health and Tropical Medicine I performed 60 caesarean sections under close supervision of a consultant obstetrician-gynaecologist and completed a compulsory basic surgical skills course before I was allowed to do this procedure independently, which I could do only when it was anticipated to be an uncomplicated one. My Namibian colleague medical officers would do about fifteen caesarean sections under supervision of a more senior medical officer. Subsequently, they had to do most procedures independently, regardless of the anticipated difficulty of the surgery.

In Namibia, it is common that a newly graduated doctor or nurse works independently, with very limited postgraduate training or supervision by more senior peers. Also, locally adapted guidelines that could support them in providing clinical care were hardly present. Not seldom, junior staff had to take decisions or perform procedures beyond their competency level (chapter 2). In such situations, the occurrence of 'too little, too late' was a logical consequence.

To increase the knowledge and skills of health workers in Namibia, a continuous training program needs to become available. It is essential that such efforts would take the form of a 'low-dose high frequency' program: low-dose to ensure it can be combined with clinical duties without causing staff shortages for the duration of the training, and high-frequency to ensure lifelong learning, training of future staff and that it is incorporated into the clinical routine. In Ghana and Uganda it was feasible to implement such programs in busy facilities, contributing to improved maternal and perinatal outcomes.[22-24] Importantly, participating health workers appeared to prefer this training method over traditional once-off trainings. In Tanzania, the development of context-specific guidelines was combined with ongoing low-dose high-frequency training, which was associated with marked improvements in quality of care and perinatal outcome.[25,26] In Namibia, all hospitals have well-functioning equipment in place to facilitate video conferencing, which was used successfully to feedback findings of maternal death surveillance to health workers throughout the country (chapter 2). Considering the long distances between Namibian facilities, this is an

ideal set-up for a monthly or weekly national clinical meeting, which could be part of a routine continuous training program, as health workers can remain in their facility. These meetings could be used to implement new guidelines, or discuss feedback of obstetric surveillance. Through case discussion, medical officers from district hospitals can receive guidance from consultant obstetrician-gynaecologists in referral hospitals.

To further achieve better on-the-job guidance, a balanced mixed of skills needs to be present among available staff, and policy makers should focus on retaining more experienced personnel (chapter 2).[17] A system of career progression could stimulate staff retainment.[27] A mentorship program could help to facilitate coaching of junior peers by senior staff.[28,29] Such a program was implemented successfully in the obstetric department of the national referral hospital and the Ministry of Health should ensure that similar efforts are undertaken around the country.[29] Last, national guidelines based on the Namibian setting need to become available.

There was inconsistent **supply** of essential medical resources (chapter 2, 4). While magnesium sulphate should be routinely available, delays in the supply chain resulted in temporary unavailability in some facilities. A critically ill woman had to be transferred more than 100 kilometres to the nearest hospital to access treatment. Another example, in several district hospitals there was a lack of sufficient equipment to monitor vital signs, which resulted in delayed monitoring. Subsequently, for several women a severe complication, such as shock or raised blood pressure, was only noticed at a late stage. These and other findings of obstetric surveillance were used for advocacy and several steps were taken by the Ministry of Health and Social Services to resolve these issues.

In addition to the need for training and context-specific guidance, the need for higher numbers of staff (**human resources**) also remains unquestionable, as illustrated by the following story.

Story of a woman who died

A 38-year old G3P2, with two previous vaginal births, was admitted in active labour. There were signs of fetal distress when her cervix was fully dilated. She was prepared for emergency caesarean section but in theatre the head was crowning and doctor John, a medical officer, assisted vaginal birth with a vacuum pump. Directly after birth the woman lost a lot of blood and it was noted she looked very pale. Oxytocin was given to make the uterus contract. She received one unit of blood and the bleeding stopped. After a few hours she was doing better, and was breastfeeding her baby. There was no record of ongoing vaginal bleeding, and she was moved to the postnatal ward at 18:30 hours. Her vital parameters were obtained and her blood pressure was 60/43 mmHg. The blood pressure was repeated with another machine since the machine was thought to be malfunctioning. The second recording was documented as 118/63 mmHg. Both the labour ward and postnatal ward were busy that afternoon. Nurse-midwife Mary, recently graduated, was the only member of staff on duty in the high-risk postnatal ward caring for up to 24 postpartum women. During her 12-hour shift Mary had to provide medication and intravenous fluids to all women at least twice. Moreover, she was supposed to check their general condition at least three times during her shift, assess whether or not they were bleeding, and obtain their parameters. Doctor John, who had started as a medical officer four months earlier, was busy in theatre. Due to the staff shortage, the woman was monitored infrequently on the high-risk postnatal ward. She suddenly died at 20:30. Autopsy revealed a ruptured uterus with retroperitoneal bleeding, as well as signs of severe hypovolaemic shock.

As this story shows, it is unrealistic to expect good care being consistently provided by health workers working in severely understaffed and overburdened facilities. Currently, most Namibian health workers encounter one or more similar situations in the beginning of their careers. Not surprisingly, the consequences of understaffing may negatively impact their mental wellbeing and contribute to the high turnover of staff. Many health workers opt for other settings with better working conditions, such as private health facilities or other departments with fewer emergencies and the devastations pertaining to young patients in critical conditions.[30] The consequences of pregnancy-related calamities on staff wellbeing were seen in two recent studies among doctors and nurses working in the obstetric department in Windhoek, which showed that more than half of participating doctors frequently experienced physical and mental exhaustion and among nurse-midwives high levels of stress and anxiety were seen.[29,31] Both studies developed support structures to improve the mental

wellbeing of health workers, which should be implemented nationally to benefit all health workers involved in maternity care.

While health workers in low- and middle-income countries are used to working in a situation of critical staff shortages, many health workers in high-income settings had their first experience with working in an overburdened facility during the COVID-pandemic. Some hospitals were extremely overwhelmed, whereby elective care had to be postponed and the availability of ventilatory support could not be guaranteed.[32] Worldwide, there were several initiatives to thank and support health workers. Youtube exploded with movies of people clapping their hands for health workers.[33] Banners with supportive notes were placed on hospital walls and free food and gifts were handed out.[34,35]

Personal reflection: I found myself wondering: where was the global applause for health workers before, particularly for those working in facilities in low- and middle income countries who are permanently overburdened, day in day out, without any prospect of improvement within the near future? As described in chapter 2, even the opposite was happening in Namibia: individual health workers sometimes received the blame when a woman died, rather than the failing health system.

Also in Namibia health workers, involved in care of COVID-patients, were overwhelmed with thank-you notes from patients, hospital management and policy makers.[36,37] Although a positive development, it should be ensured that not only during a disease outbreak, but routinely, health workers receive such recognition. A culture change is needed in the maternity care system, exchanging blame culture for continuous support and recognition (chapter 2).[29,31,38] Such recognition and support may not change the day-to-day working conditions, but will have a positive impact on the work experience, as described in chapter 4. Both recognition and support for mental wellbeing can have a positive effect on staff shortages by preventing burn-out and reducing high turnover rates.[29,30] Moreover, health workers who received recognition from their seniors are more likely to deliver respectful maternity care.[38]

Needs for Namibia to improve maternal health

Improving maternal health in Namibia is not an easy task, given the complexity and diversity of the underlying problems. To achieve significant impact and reduce adverse health outcomes, all elements of both support systems need to function. For example, a well-trained health worker will still not be able to provide good care when

she does not have the appropriate resources or when she works in an understaffed facility. Proposed interventions to improve the maternity care system, based on findings of this thesis, are summarized in Figure 2.

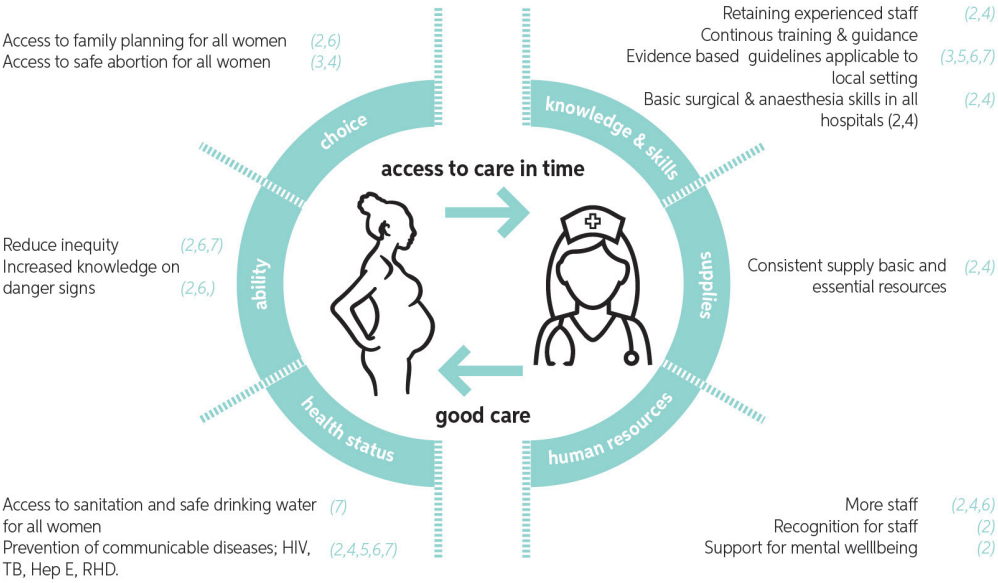


Figure 2. Framework mapping the requirements to improve maternal health in Namibia
Numbers in brackets refer to the chapters of this thesis.
HIV, human immunodeficiency virus; TB, tuberculosis; Hep E, hepatitis E; RHD, rheumatic heart disease.

The added value of obstetric surveillance

In this thesis obstetric surveillance including maternal near-miss was used to assess the maternity care system, instead of maternal death surveillance only. This approach had several advantages. For example, through collection of morbidity data, staff could take more pride in their jobs by acknowledging the number of women they had saved, rather than only reporting numbers of those lost (chapter 3, 4). Furthermore, obstetric surveillance provided insight into local drivers of severe maternal outcome, making it possible to propose context-specific interventions as presented in Figure 2. These insights will contribute to successful implementation, as for any intervention, it is key it addresses a local need in a context-specific manner.[27]

Local needs

In addition to national surveillance of maternal death and near-miss, obstetric surveillance included two facility-based studies into specific potentially life threatening conditions. These two studies provided insight into the outcomes of pregnant women with cardiac disease and those with acute hepatitis E. Women with a delayed diagnosis of cardiac disease appeared to be at higher risk of cardiac complications, while HIV-infected women receiving antiretroviral therapy appeared to be less likely to develop acute liver failure due to hepatitis E (chapter 6,7). National maternal near-miss surveillance provided better insight into the challenges of smaller health facilities, such as lack of access to surgery and essential resources (chapter 3,4).

With near-miss surveillance it was possible to better map the burden of severe maternal complications in Namibia. Maternal deaths are only the tip of the iceberg, while underneath there is a much larger burden of maternal morbidity.[16] When the near-miss approach was introduced by the World Health Organization, it was stated that maternal near-misses and deaths have similar underlying causes and characteristics.[39] However, we remarkably identified in the Namibian setting that the underlying causes differed between maternal deaths and near-misses. Near-misses were mainly caused by direct obstetric complications, while this was the case in only half of the maternal deaths, the other half of which were caused by medical conditions (chapter 2,4).

A similar pattern was seen in high-income countries, such as Scotland and the Nordic countries, and middle-income countries such as Brazil, South Africa, China and Suriname.[40-46] In Ethiopia and Nigeria, countries with high MMRs estimated at 401 and 917 per 100 000 live births respectively, obstetric complications were the main underlying cause of both maternal near-misses and deaths.[47,48] This is in line with the obstetric transition: as obstetric care improves, deaths from obstetric complications are increasingly avoided. As a result, the proportion of maternal deaths caused by medical conditions increases. Even though deaths due to obstetric complications are avoided, these are still the most common causes of maternal near-miss, even in high-income settings. This is important, as maternal near-miss occur far more frequently than maternal deaths. Therefore, the largest burden of severe maternal outcome will still be caused by obstetric complications. As most low- and middle-income countries only have some sort of maternal death review system in place, maternal near-miss goes unreported. When progress is achieved and maternal deaths due to obstetric complications are reduced, focus may incorrectly shift towards non-obstetric causes.

Context-specific

An intervention shown to be effective in a given setting to improve maternal outcome may not work elsewhere. Three examples are found in this thesis. First, rather than simply implementing a national confidential enquiry into maternal deaths in Namibia, for it to be successful, fear of being blamed among health workers had to be addressed first (chapter 2). Second, for maternal near-miss surveillance, the World Health Organization recommends a set identification criteria, that were postulated to be implementable across all settings, but chapter 3 showed that adaptations of these criteria to the local context were essential to avoid underreporting. Lastly, guidelines for the management of pregnancies of women with cardiac disease were only available from high-income settings (chapter 5).[10] Implementation of these guidelines were a challenge in the Namibian setting due to differences in (severity of) the underlying cardiac disease and in availability of resources and staff (chapter 6).

Globally, the adaptation of interventions to the local context is hampered by limited availability of data from lower-income settings and vulnerable populations such as poor and/or pregnant women. There are many examples of interventions that appeared less effective in these understudied populations. For example, in the past two decades it became clear that outcome of hypertension-related complications was worse among African Americans when applying standard management guidelines.[49] These guidelines, based on studies performed primarily in white men, were only assessed in this part of the population after being implemented in routine practice. Even today, the effectiveness of many interventions remains unclear for pregnant women, as they are commonly excluded from clinical trials out of fear of potential side effects on the fetus.[50] For instance, pregnant women were excluded from most COVID-19, Ebola and hepatitis E vaccine trials, despite being at higher risk of complications.[51-53] Fear of side effects on the fetus was one of the major reasons a hepatitis E vaccine trial was not initiated in Namibia, which could have resulted in a decline in maternal and perinatal mortality (chapter 7).[54] The exclusion of pregnant women from most COVID-19 vaccine trials resulted in low vaccination uptake as, unsurprisingly, pregnant women tended to perceive the vaccine as being unsafe.[55,56] The low vaccination rate impacted negatively on maternal outcome.[57]

The implementation of interventions in low- and middle-income countries, whereby only efficacy data from high-income settings is available, may have negative consequences for health outcomes in these lower income settings. An illustrative example is the provision of corticosteroids to pregnant women at risk of premature birth to reduce neonatal mortality. Only recently its effectiveness was assessed in two large randomized trials performed in several low- and middle-income countries.[58,59] The effects on neonatal outcome were inconsistent in these settings, but especially in

rural settings corticosteroids seemed to be associated with worse outcomes among women and babies, due to the increased risks of infection.[60] Another example is the available guidance for routine intrapartum monitoring.[61] Although recommended to be implemented globally, intensive monitoring appeared to be unrealistic when assessed within the day-to-day reality of an understaffed referral hospital in Tanzania.[62] Worrisome is the impact of the Term Breech Trial, published in 2000, which resulted in increased rates of caesarean section for women presenting with a baby in breech presentation around the world.[63] In the trial, birth by caesarean section was associated with a reduction in perinatal mortality. Even though the study population included women from several middle-income countries and one low-income country, this finding may not be applicable to such settings in general, since participating facilities were generally the more advanced within these countries. Of concern are the high maternal and perinatal complication rates of caesarean sections in low- and middle-income countries.[64] Moreover, the Term Breech Trial did not assess the increased risks of mortality for woman and baby in subsequent pregnancies in presence of a scarred uterus. This is especially important for countries like Namibia, where timely access to caesarean section is not guaranteed for all women (chapter 4).

It is clear that locally performed research is urgently needed, representing both the local setting and local populations in settings like Namibia. Only then it will be possible to establish evidence-based guidance, applicable to the local context, which may lead to improved maternity care.

Conclusion

This thesis showed a high incidence of maternal mortality and morbidity in Namibia. A large contributor was poor quality of facility-based care and particularly vulnerable women appeared to be at higher risk of severe maternal outcome. Or, as phrased in a Dutch proverb, the risk of poor maternal outcome mostly depended on 'the location of the crib of the woman herself' at the time she was born. Equal and better maternal health outcomes for all Namibian women can be achieved by focusing on more support for these vulnerable women. Access to family planning needs to be improved, to ensure that women get pregnant when they choose to be **(choice)**. Their **ability** to access care in time must be improved. Thirdly, to reduce the risks of complications, women's general **health status** needs to improve, for example, through better prevention and management of HIV, tuberculosis, RHD and hepatitis E. Besides more support for women, to achieve a significant positive impact on maternal outcome, it is crucial to simultaneously address the poor quality of facility-based care. Health workers will be able to improve the quality of the care they provide, when they

are adequately supported themselves. Therefore, guidance and continuous post-graduate training programs are needed, to increase their knowledge and skills. Also, there is a need of a consistent supply of essential resources (supplies). At last, more staff is needed and experienced staff needs to be retained (human resources), by improved recognition of staff and support for their mental wellbeing.

To improve maternal health, obstetric surveillance holds promise as a useful tool for a country like Namibia, by enabling identification of key drivers of severe maternal outcome as well as local opportunities to address these. Nevertheless, obstetric surveillance is not the silver bullet to improve maternal health. It all depends on that crucial next step, namely acting on recommendations coming out of surveillance. With the insights obtained, targeted, context-specific interventions can be implemented. If we follow track, it will be possible for Namibia to progress towards maternal health for all.

Future perspectives

Although it should be the next step, acting on the recommendations from surveillance, often referred to as 'the response', was difficult to achieve in many countries.[65,66] The failure to respond, commonly referred to as the 'knowledge-act' gap, can be addressed by strong leadership and supportive systems.[27,65,66]

For Namibia, to overcome the 'knowledge-act' gap, first and foremost strong leadership is needed to ensure all relevant stakeholders collaborate and recommended interventions are implemented. Unfortunately, there is currently no national association uniting obstetricians, which could contribute to such leadership. There is a small Independent Midwife Association of Namibia, uniting the midwives, who are trained abroad. The obstetric surveillance system was implemented by a national committee, appointed by the Ministry of Health and Social Services. Either the midwifery association or the national committee should take leadership and set up a team tasked with the response. All stakeholders should be represented within this team. Inclusion of women representatives will be crucial for successful implementation of recommendations related to choice, ability and women's health status, as depicted in the framework. This team should work in close collaboration with the Ministry of Health and Social Services of Namibia, ensuring integration of interventions into routine services. To ensure the executing team can implement an effective response, members must be made available fulltime or parttime and receive an appropriate salary.

As previously described, to achieve significant impact several interventions will need to be implemented simultaneously. Therefore, adequate human resources, both in numbers and skills, are needed to create local capacity for a sustainable response. In the past two decades, the Namibian government successfully managed to increase the number of locally trained doctors and nurses.[67,68] This motivated young generation of health workers will need to be guided and trained by local experts. If local expertise is not available, assistance of international experts, who implemented similar interventions elsewhere, could be invited to fulfil this task. Guided by the executing team, the following interventions should be implemented:

- Improved access for teenagers to reliable contraception, including long-acting reversible contraceptives, through a school-based approach.
- The provision of reliable contraception to women with high-risk pre-existing medical conditions such as tuberculosis or HIV, through an integrated approach.
- Implementation of (preconception) counselling, to increase knowledge on danger signs, especially for high-risk women.
- Enhanced provision of isoniazid preventive therapy to prevent tuberculosis co-infection among HIV-positive women.
- Improved detection of mild cardiac disease among women of reproductive age by increasing knowledge and skills of health workers to pick up cardiac symptoms.
- Development of a continuous postgraduate training program for all health workers working in the maternity care system. This should be developed in close collaboration with the Health Professions Councils of Namibia, the institute responsible for the registration of health workers as well as the monitoring of their development and education.
- Nationwide implementation of a mentorship program, to ensure senior colleagues provide guidance to junior staff.[36]
- Development of context-specific guidelines, implemented through a 'low-dose high-frequency' program including regular meetings through video conferencing.
- Availability of basic surgery in all hospitals, through increased training of medical officers in basic surgical and anaesthesia skills, as well as the provision of all the required equipment and medication for functioning operating theatres in all hospitals.
- Employment of more staff, to ensure all facilities have a more appropriate number of doctors and nurse-midwives, based on the current workload.[69]
- More recognition of health workers by hospital management and policy makers.
- Support for mental wellbeing of health workers through the nationwide implementation of two available Namibian programs.[29,31]

References

1. Bishai DM, Cohen R, Alfonso YN, Adam T, Kuruvilla S, Schweitzer J. Factors Contributing to Maternal and Child Mortality Reductions in 146 Low- and Middle-Income Countries between 1990 and 2010. PLoS One. 2016;11(1):e0144908.
2. USAID. International Data & Economic Analysis (IDEA) Country Dashboard Namibia. (Available from: https://idea.usaid.gov/cd/namibia/health) [30-08-2021]
3. Maternal Mortality Estimation Inter-Agency Group. Maternal mortality in 2000-2017. Internationally comparable MMR estimates by the Maternal Mortality Estimation Inter-Agency Group (MMEIG), Namibia. World Health Organisation: Geneva, 2017.
4. World Bank. GINI index. (Available from: https://data.worldbank.org/indicator/SI.POV.GINI) [25-10-2021]
5. Diedrich JT, Klein DA, Peipert JF. Long-acting reversible contraception in adolescents: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017;216(4):364 e361-364 e312.
6. Lopez LM, Bernholc A, Chen M, Tolley EE. School-based interventions for improving contraceptive use in adolescents. Cochrane Database Syst Rev. 2016(6):CD012249.
7. United Nations Population Fund. UNFPA hands over N$ 7.4m contraceptives to Health Ministry; 2018. (Available from: https://namibia.unfpa.org/en/news/unfpa-hands-over-n-74m-contraceptives-health-ministry) [26-06-2022]
8. Ford N, Newman M, Malumo S, Chitembo L, Gaffield ME. Integrating Sexual and Reproductive Health Services Within HIV Services: WHO Guidance. Front Glob Womens Health. 2021;2):735281.
9. Boatin AA, Schlotheuber A, Betran AP, et al. Within country inequalities in caesarean section rates: observational study of 72 low and middle income countries. BMJ. 2018;360):k55.
10. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39(34):3165-3241.
11. Zuhlke L, Engel ME, Karthikeyan G, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). Eur Heart J. 2015;36(18):1115-1122a.
12. Ministry of Health and Social Services. Demographic and Health Survey Namibia 2013. Ministry of Health and Social Services: Windhoek, 2014.
13. Kielmann K, Karat AS, Zwama G, et al. Tuberculosis infection prevention and control: why we need a whole systems approach. Infect Dis Poverty. 2020;9(1):56.
14. Brault MA, Spiegelman D, Hargreaves J, Nash D, Vermund SH. Treatment as Prevention: Concepts and Challenges for Reducing HIV Incidence. J Acquir Immune Defic Syndr. 2019;82 Suppl 2):S104-S112.
15. Directorate of Special Programmes Ministry of Health and Social Services. Namibian HIV Guidelines Fifth Edition. Ministry of Health and Social Services: Windhoek, 2016.
16. Graham W, Woodd S, Byass P, et al. Diversity and divergence: the dynamic burden of poor maternal health. Lancet. 2016;388(10056):2164-2175.
17. Koblinsky M, Moyer CA, Calvert C, et al. Quality maternity care for every woman, everywhere: a call to action. Lancet. 2016;388(10057):2307-2320.
18. Morton S, Pencheon D, Squires N. Sustainable Development Goals (SDGs), and their implementation: A national global framework for health, development and equity needs a systems approach at every level. Br Med Bull. 2017;124(1):81-90.
19. The Regional Office for Europe of the World Health Organization. Health and reduced inequalities, policy brief. World Health Organization: Copenhagen, 2019.
20. Miller S, Abalos E, Chamillard M, et al. Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. Lancet. 2016;388(10056):2176-2192.
21. Christians F. Country profile - Primary healthcare and family medicine in Namibia. Afr J Prim Health Care Fam Med. 2020;12(1):e1-e3.
22. Evans CL, Bazant E, Atukunda I, et al. Peer-assisted learning after onsite, low-dose, high-frequency training and practice on simulators to prevent and treat postpartum hemorrhage and neonatal asphyxia: A pragmatic trial in 12 districts in Uganda. PLoS One. 2018;13(12):e0207909.
23. Gomez PP, Nelson AR, Asiedu A, et al. Accelerating newborn survival in Ghana through a low-dose, high-frequency health worker training approach: a cluster randomized trial. BMC Pregnancy Childbirth. 2018;18(1):72.

24. Asiedu A, Nelson AR, Gomez PP, Tappis H, Effah F, Allen C. “It builds your confidence… you’ve done well”: Healthcare workers’ experiences of participating in a low-dose, high-frequency training to improve newborn survival on the day of birth in Ghana. Gates Open Res. 2019;3):1470.
25. Maaloe N, Housseine N, Meguid T, et al. Effect of locally tailored labour management guidelines on intrahospital stillbirths and birth asphyxia at the referral hospital of Zanzibar: a quasi-experimental pre-post study (The PartoMa study). BJOG. 2018;125(2):235-245.
26. Maaloe N, Andersen CB, Housseine N, Meguid T, Bygbjerg IC, van Roosmalen J. Effect of locally tailored clinical guidelines on intrapartum management of severe hypertensive disorders at Zanzibar’s tertiary hospital (the PartoMa study). Int J Gynaecol Obstet. 2019;144(1):27-36.
27. Balabanova D, Mills A, Conteh L, et al. Good Health at Low Cost 25 years on: lessons for the future of health systems strengthening. Lancet. 2013;381(9883):2118-2133.
28. Morof D, Serbanescu F, Goodwin MM, et al. Addressing the Third Delay in Saving Mothers, Giving Life Districts in Uganda and Zambia: Ensuring Adequate and Appropriate Facility-Based Maternal and Perinatal Health Care. Glob Health Sci Pract. 2019;7(Suppl 1):S85-S103.
29. Bruckner T. Healthcare Worker Burnout in Namibia. Developing a staff support structure in the obstetric department of Namibia’s national referral hospital. Amsterdam: Vrije Universiteit Amsterdam (Master thesis); 2021.
30. Dubale BW, Friedman LE, Chemali Z, et al. Systematic review of burnout among healthcare providers in sub-Saharan Africa. BMC Public Health. 2019;19(1):1247.
31. Endjala T. An employee assistance programme (EAP) to support midwives affected by maternal deaths and stillbirths in Khomas region, Namibia. Windhoek: University of Namibia (PhD thesis); 2022.
32. Horowitz J. Italy’s Health Care System Groans Under Coronavirus – a Warning to the World. New York Times, 12-03-2020.
33. Hess A. In Praise of Quarantine Clapping. The New York Times, 09-04-2020.
34. Medical University of South Carolina. Messages to Our Health Care Heroes. (Available from: https://muschealth.org/heroes) [03-07-2022]
35. Western Sussex Hospitals. Thank you to all our wonderful staff who’ve been working in new ways and in new areas; 2021. (Available from: https://www.westernsussexhospitals.nhs.uk/news/thank-you-to-all-our-wonderful-staff-whove-been-working-in-new-ways-and-in-new-areas-to-support-each-other-during-the-pandemic/) [03-07-2022]
36. Namene J. ‘Thank you for saving my life’. the Namibian, 10-08-2021.
37. Xinhuanet Africa. Young frontline workers in Namibia showing resilience in fight against COVID-19; 2021. (Available from: http://www.xinhuanet.com/english/africa/2021-07/25/c_1310084659.htm) [03-07-2022]
38. Wesson J, Hamunime N, Viadro C, et al. Provider and client perspectives on maternity care in Namibia: results from two cross-sectional studies. BMC Pregnancy Childbirth. 2018;18(1):363.
39. World Health Organization. Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. World Health Organization: Geneva, 2011.
40. Cecatti JG, Costa ML, Haddad SM, et al. Network for Surveillance of Severe Maternal Morbidity: a powerful national collaboration generating data on maternal health outcomes and care. BJOG. 2016;123(6):946-953.
41. Heitkamp A, Vollmer Murray L, van den Akker T, et al. Great saves or near misses? Severe maternal outcome in Metro East, South Africa: A region-wide population-based case-control study. Int J Gynaecol Obstet. 2022;157(1):173-180.
42. Soma-Pillay P, Pattinson RC, Langa-Mlambo L, Nkosi BS, Macdonald AP. Maternal near miss and maternal death in the Pretoria Academic Complex, South Africa: A population-based study. S Afr Med J. 2015;105(7):578-563.
43. Verschueren KJ, Kodan LR, Paidin RR, et al. Applicability of the WHO maternal near-miss tool: A nationwide surveillance study in Suriname. J Glob Health. 2020;10(2):020429.
44. Mu Y, Wang X, Li X, et al. The national maternal near miss surveillance in China: A facility-based surveillance system covered 30 provinces. Medicine (Baltimore). 2019;98(44):e17679.
45. Marr L, Lennox C, McFadyen AK. Quantifying severe maternal morbidity in Scotland: a continuous audit since 2003. Curr Opin Anaesthesiol. 2014;27(3):275-281.
46. Vangen S, Bodker B, Ellingsen L, et al. Maternal deaths in the Nordic countries. Acta Obstet Gynecol Scand. 2017;96(9):1112-1119.
47. Adeniran AS, Ocheke AN, Nwachukwu D, et al. Non-obstetric causes of severe maternal complications: a

secondary analysis of the Nigeria Near-miss and Maternal Death Survey. BJOG. 2019;126(3):41-48.
48. Tura AK, Zwart J, van Roosmalen J, Stekelenburg J, van den Akker T, Scherjon S. Severe maternal outcomes in eastern Ethiopia: Application of the adapted maternal near miss tool. PLoS One. 2018;13(11):e0207350.
49. Williams SK, Ravenell J, Seyedali S, Nayef S, Ogedegbe G. Hypertension Treatment in Blacks: Discussion of the U.S. Clinical Practice Guidelines. Prog Cardiovasc Dis. 2016;59(3):282-288.
50. Shields KE, Lyerly AD. Exclusion of pregnant women from industry-sponsored clinical trials. Obstet Gynecol. 2013;122(5):1077-1081.
51. Rubin R. Pregnant People's Paradox-Excluded From Vaccine Trials Despite Having a Higher Risk of COVID-19 Complications. JAMA. 2021;325(11):1027-1028.
52. Gomes MF, de la Fuente-Nunez V, Saxena A, Kuesel AC. Protected to death: systematic exclusion of pregnant women from Ebola virus disease trials. Reprod Health. 2017;14(Suppl 3):172.
53. Dashraath P, Nielsen-Saines K, Madhi SA, Baud D. COVID-19 vaccines and neglected pregnancy. Lancet. 2020;396(10252):e22.
54. Zhu F-C, Zhang J, Zhang X-F, et al. Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: a large-scale, randomised, double-blind placebo-controlled, phase 3 trial. The Lancet. 2010;376(9744):895-902.
55. Egloff C, Couffignal C, Cordier AG, et al. Pregnant women's perceptions of the COVID-19 vaccine: A French survey. PLoS One. 2022;17(2):e0263512.
56. Shamshirsaz AA, Hessami K, Morain S, et al. Intention to Receive COVID-19 Vaccine during Pregnancy: A Systematic Review and Meta-analysis. Am J Perinatol. 2022;39(5):492-500.
57. Engjom H, van den Akker T, Aabakke A, et al. Severe COVID-19 in pregnancy is almost exclusively limited to unvaccinated women - time for policies to change. Lancet Reg Health Eur. 2022;13):100313.
58. Althabe F, Belizan JM, McClure EM, et al. A population-based, multifaceted strategy to implement antenatal corticosteroid treatment versus standard care for the reduction of neonatal mortality due to preterm birth in low-income and middle-income countries: the ACT cluster-randomised trial. Lancet. 2015;385(9968):629-639.
59. Collaborators WAT, Oladapo OT, Vogel JP, et al. Antenatal Dexamethasone for Early Preterm Birth in Low-Resource Countries. N Engl J Med. 2020;383(26):2514-2525.
60. Mooij R, Mwampagatwa IH, van Dillen J, Stekelenburg J. Antenatal corticosteroid therapy for foetal maturation in women with eclampsia and severe pre-eclampsia in a rural hospital in Western Tanzania. BMC Pregnancy Childbirth. 2016;16):235.
61. World Health Organization. Managing complications in pregnancy and childbirth: a guide for midwives and doctors. World Health Organization: Geneva, 2007.
62. Housseine N, Punt MC, Mohamed AG, et al. Quality of intrapartum care: direct observations in a low-resource tertiary hospital. Reprod Health. 2020;17(1):36.
63. Hannah ME, Hannah WJ, Hewson SA, Hodnett ED, Saigal S, Willan AR. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. Term Breech Trial Collaborative Group. Lancet. 2000;356(9239):1375-1383.
64. Sobhy S, Arroyo-Manzano D, Murugesu N, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. Lancet. 2019;393(10184):1973-1982.
65. Jayakody H, Knight M. Implementation assessment in confidential enquiry programmes: A scoping review. Paediatr Perinat Epidemiol. 2020;34(4):399-407.
66. Moodley J, Pattinson RC, Fawcus S, et al. The Confidential Enquiry into Maternal Deaths in South Africa: a case study. BJOG. 2014;121(Suppl 4):53-60.
67. BBC news. Namibia's 'home-grown doctors' start to make a difference; 2016. (Available from: https://www.bbc.com/news/world-africa-37780777) [03-07-2022]
68. Sibeene P. More Nurses Graduate. New Era, 28-04-2008.
69. Ministry of Health and Social Services. Namibia National WISN Report 2015: A Study of Workforce Estimates for Public Health Facilities in Nambia. Ministry of Health and Social Services: Windhoek, 2016.

Chapter 9.

Summary / samenvatting

Summary

Over the past decades increasing efforts have aimed to improve the health of pregnant women around the world. Despite the overall reduction of maternal deaths globally, health disparities between the rich and the poor only seem to have increased, both between and within countries. Namibia has made limited progress in reducing severe maternal outcomes (i.e maternal deaths and maternal near-misses), with a higher incidence than expected for an upper middle-income country (chapter 1).

It has been obvious for a considerable time that Namibia's high burden of severe maternal outcome must be addressed. However, it was unclear how a reduction could be achieved. For the development of applicable and effective interventions, we first needed to gain more insight into the drivers of severe maternal outcomes, as well as the challenges and opportunities within the Namibian maternity care system. In this thesis, enhanced implementation of national obstetric surveillance system was used to obtain these insights. Based on these, targeted recommendations could be formulated.

The obstetric surveillance system consisted of three components. The first was a confidential enquiry into maternal deaths, the second a maternal near-miss surveillance system, and the third were facility-based cohort studies to assess the outcomes of pregnancies complicated by cardiac disease and hepatitis E.

The confidential enquiry into maternal deaths assesses why women in Namibia die during pregnancy, childbirth or the postpartum period. Since 2010 this methodology has been used to assess the Namibian maternity care system. However, successful implementation was hampered by a blame culture that allegedly made clinicians refrain from reporting cases to the enquiry committee. For review period 2018-2019 its implementation was enhanced by focussing on obtaining trust among health workers (chapter 2). To achieve this, a "no name, no blame" policy, aiming to identify health system failures, rather than mistakes of individuals, was implemented. Furthermore, the enquiry committee ensured dissemination of findings to staff at all levels and focussed on acting on the recommendations forthcoming from the enquiry. The leading causes of maternal deaths in 2018-2019 were obstetric haemorrhage and hepatitis E (both 11/70, 15.7%) (chapter 2). Majority of women who died received poor quality care within the health facilities, and most deaths (40/70, 57.1%) could have been prevented with improved quality of care. Recommendations to address poor quality of provided care include the need for continuous training and guidance of health workers, the consistent supply of basic and essential resources, more staff and retaining experienced staff.

The national maternal near-miss surveillance system studied women who nearly died but survived a severe complication of pregnancy (chapter 3,4). In a sparsely populated country such as Namibia (2.5 million inhabitants and 70 000 births per annum), the absolute number of maternal deaths is low, especially in district hospitals. As maternal near-misses occur in larger numbers, the maternal near-miss approach provides better insight into the functioning of all Namibian health facilities.

To avoid underreporting we adapted the near-miss identification criteria as proposed by the World Health Organization to the Namibian context (chapter 3). In 2018-2019, obstetric haemorrhage and hypertensive disorders were the commonest causes of maternal near-miss (each 92/298, 30.9%) (chapter 4). Several challenges were identified, such as the structural lack of access to basic surgery in several rural district hospitals. These findings were shared with policy-makers at national and regional levels and several steps were taken to ensure access to basic surgery in all hospitals.

The facility-based studies assessed the outcomes of pregnant women with cardiac disease and hepatitis E, both common causes of maternal deaths in Namibia, in greater detail. While cardiac disease is the most common cause of maternal deaths in high-income countries, it is rarely discussed in reports on maternal health in low- and middle-income countries. Yet, we found a high incidence of cardiac-related maternal deaths in these countries (chapter 5).

A multidisciplinary approach was developed and implemented for women with cardiac disease, from the preconception up to postpartum period, in the national referral hospital of Namibia (chapter 6). Important benefits of this service were the integrated approach and improved access to care including reliable contraception. With no existing locally adapted guidelines, we applied management guidelines developed for high-income settings. Several challenges were encountered, as contextual factors specific to lower-income settings were not taken into consideration, such as higher rates of infection, or barriers to access of care. A high rate of maternal and fetal events was identified in a two-year cohort study, especially among women with newly diagnosed cardiac disease (chapter 6). While many of these women presented to a health care facility with cardiac related symptoms in their previous pregnancy, diagnosis was often missed. Rheumatic heart disease was the most common cardiac diagnosis (31/65, 47.7%), mainly seen among women of lower socio-economic classes. Outcomes of women with cardiac disease can be improved in Namibia with improved detection of pre-existing cardiac disease and development of context-specific guidelines.

Hepatitis E emerged relatively recently in Namibia. A nationwide outbreak of hepatitis E, with its first case reported in 2017, had a devastating impact on maternal and fetal health (chapter 7). As hepatitis E is transmitted through contaminated drinking water, infections were mainly seen among poor women living in the informal settlements with no access to safe sanitation. Both maternal and fetal outcomes were extremely poor. Nearly half of the pregnant women admitted to the national referral hospital with hepatitis E developed acute liver failure needing intensive care unit admission (28/70, 40.0%) and nearly one in five women died. Surprisingly, we found that HIV infected women, in particular those on antiretroviral treatment, seem to be less likely to develop acute liver failure in contrast with non-HIV infected pregnant women. As there is no known treatment capable of altering the course of acute hepatitis E, more research is urgently needed to confirm or refute the phenomenon we found in larger cohorts.

The most important contributor of the high-incidence of severe maternal outcome in Namibia was poor quality of facility-based care and particularly vulnerable women appeared to be at higher risk of severe maternal outcome (chapter 8). The maternity care system needs to be strengthened, to enable health workers to provide universal coverage of good health care to all women in Namibia. It is therefore crucial the next step will follow, which is to act on the proposed recommendations. The insights obtained through obstetric surveillance will contribute to such action, as for any intervention, it is key it addresses a local need in a context-specific manner.

Samenvatting

Wereldwijd zijn er dagelijks ongeveer 5000 vrouwen die ernstig ziek worden of zelfs overlijden als gevolg van complicaties tijdens zwangerschap, bevalling of kraambed. Het merendeel vindt plaats in lage- en midden-inkomenslanden en kan voorkomen worden met betere zorg (hoofdstuk 1). In de afgelopen decennia is er wereldwijd veel aandacht geweest voor het verbeteren van de zorg voor zwangere vrouwen. Ondanks dat er een afname lijkt te zijn in het aantal vrouwen dat overlijdt rondom de zwangerschap, lijken de verschillen tussen arm en rijk alleen maar toe te nemen. Arme zwangere vrouwen blijven een veel hoger risico houden op moedersterfte. Deze toenemende ongelijkheid wordt zowel tussen landen gezien, als tussen verschillende inkomensgroepen binnen een land. Ook in Namibië is slechts beperkte vooruitgang geboekt en blijft de moedersterfte veel te hoog voor wat je mag verwachten van een middeninkomensland (hoofdstuk 1).

De auteur werkte vier jaar als arts op de verloskamers van het nationale verwijsziekenhuis van Namibië, genaamd Windhoek Hospital Complex. Hier werkte ze samen met diverse collega's die, net als zij, gemotiveerd waren om iets te doen aan de hoge moedersterfte. Dit proefschrift beschrijft het resultaat van hun gezamenlijke inspanningen. De auteur en haar collega's realiseerden zich dat er gerichte interventies nodig waren om de zorg voor zwangeren te verbeteren. Echter, voor het ontwikkelen van lokaal relevante en effectieve interventies was allereerst meer inzicht nodig: ten eerste in de onderliggende oorzaken van de slechte uitkomsten; en ten tweede in de huidige problemen en mogelijkheden van het Namibische zorgsysteem.

Om dergelijke inzichten te verkrijgen, werd een nationaal obstetrisch registratiesysteem ontwikkeld, bestaande uit drie onderdelen:

- Nationale audit van maternale sterfte
- Nationale maternale near-miss registratie
- Cohortstudies voor analyse van specifieke zwangerschappen, zoals vrouwen met een hartaandoening of hepatitis E.

Dit proefschrift beschrijft de uitkomsten van deze drie methodes.

Analyse van moedersterfte

Middels een nationale audit van maternale sterfte wordt geanalyseerd waarom vrouwen in Namibië sterven tijdens de zwangerschap, bevalling of in het kraambed. Deze audit wordt al verricht sinds 2010, maar functioneerde aanvankelijk niet goed omdat moedersterfte vaak niet werd gerapporteerd door de betrokken hulpverleners (hoofdstuk 2). Door de onderrapportage, voortkomend uit angst voor verwijten van nalatigheid of schuld, kon een groot deel van de moedersterfte niet worden meegenomen in de analyse.

Tijdens het 'Vertrouwelijke Onderzoek' (Confidential Enquiry) naar moedersterfte in 2018-2019, werd daarom veel aandacht geschonken aan het verhogen van het vertrouwen van hulpverleners in deze methode. Hen werd duidelijk gemaakt dat de analyse geheel anoniem verloopt en dat het doel is hen te ondersteunen bij het leveren van goede zorg. Het gaat erom problemen in het zorgsysteem op te sporen, niet fouten van individuen. Deze aanpak droeg waarschijnlijk bij aan het feit dat meer moedersterftes werden gerapporteerd, zodat betere analyses konden worden gedaan.

Zo werd vastgesteld dat in de periode 2018-2019 postpartum bloedverlies en hepatitis E de meest voorkomende oorzaken van moedersterfte in Namibië waren (hoofdstuk 2). De meerderheid van de vrouwen die overleden, hadden in Namibische gezondheidsinstellingen zorg van lage kwaliteit ontvangen. Bij 40 van de 70 vrouwen (57.1%) had het overlijden mogelijk voorkomen kunnen worden als betere zorg was geleverd. Aan de hand van de geanalyseerde casus werden diverse aanbevelingen opgesteld, zoals het verbeteren van onderwijs en begeleiding van hulpverleners, permanente beschikbaarheid van essentiële middelen, en het aantrekken en behouden van ervaren personeel.

Analyse van maternale near-miss

Via een nationale registratie van zogenaamde 'maternale near-misses' worden casus geanalyseerd van vrouwen die ernstig ziek worden door zwangerschapscomplicaties en deze ternauwernood overleven ('Maternal Near-Miss', hoofdstukken 3 en 4). Namibië is heel dun bevolkt. Er wonen slechts 2,5 miljoen mensen en er zijn gemiddeld 70 000 bevallingen per jaar. Het absolute aantal maternale sterftes is daarom relatief laag en sterfte vindt slechts zelden plaats in een klein district ziekenhuis. Echter, tegenover iedere vrouw die overlijdt staan gemiddeld vijf 'near-misses'. Omdat een maternale near-miss dus veel vaker voorkomt, kunnen middels een maternale near-miss registratie sneller meer data verkregen worden over het functioneren van het zorgsysteem, inclusief op lokaal niveau in de kleinere districtsziekenhuizen.

Deze maternale near-miss registratie is ontwikkeld door de Wereldgezondheidsorganisatie in 2004, waarbij internationale criteria zijn opgesteld om te classificeren welke casus geregistreerd dienen te worden. Deze criteria zouden wereldwijd gebruikt moeten kunnen worden, zodat bevindingen internationaal vergeleken kunnen worden. Toch bleken deze internationale criteria niet goed toepasbaar in de Namibische ziekenhuizen (hoofdstuk 3). Door onder andere een gebrek aan diagnostische en therapeutische mogelijkheden in Namibië, vielen meerdere ernstige zieke vrouwen niet binnen de criteria. Aanpassingen aan de lokale situatie in Namibië waren nodig om onderrapportage van maternale near-miss te

voorkomen. Pas hierna kon een goed functionerend registratiesysteem landelijk worden ingevoerd.

Hoofdstuk 4 presenteert de uitkomsten van de nationale maternale near-miss registratie, uitgevoerd tussen 1 oktober 2018 en 31 maart 2019. Postpartum bloedverlies en complicaties gerelateerd aan een te hoge bloeddruk tijdens de zwangerschap waren de meest voorkomende oorzaken van maternale near-miss. Beide complicaties kwamen even vaak voor, namelijk bij 92 van de 298 vrouwen (30.9%). Bijdragende factoren waren het feit dat er in enkele afgelegen districtsziekenhuizen niet altijd toegang was tot basale chirurgische zorg, bijvoorbeeld een keizersnede, onder andere omdat operatiekamers gesloten moesten blijven door gebrek aan personeel, personeel met voldoende chirurgische vaardigheden en/of benodigd materiaal. De bevindingen werden gedeeld met beleidsmakers op nationaal en regionaal niveau. Zo konden diverse stappen worden genomen om het zorgsysteem te verbeteren, inclusief betere beschikbaarheid van basale chirurgische zorg in alle ziekenhuizen.

Analyse van zwangerschappen van vrouwen met een hartaandoening of hepatitis E

Hartaandoeningen en acute hepatitis E waren beide een veel voorkomende oorzaak van moedersterfte in Namibië. Derhalve werden twee cohort studies uitgevoerd in het nationale verwijsziekenhuis 'Windhoek Hospital Complex', om meer in detail te kijken naar de uitkomsten van zwangere vrouwen met een hartaandoening of acute hepatitis E infectie. Terwijl hartaandoeningen één van de meest frequente oorzaken vormen van moedersterfte in hoge inkomenslanden, wordt deze oorzaak zelden uitgebreid beschreven in rapporten over moedersterfte in lage- of middeninkomenslanden. Hoofdstuk 5 laat echter zien dat er wel degelijk ook in lagere inkomenslanden een hoge incidentie is van moedersterfte gerelateerd aan hartaandoeningen.

In 2016 werd multidisciplinaire zorg geïntroduceerd in Windhoek Hospital Complex voor vrouwen met een hartaandoening (hoofdstuk 6). Een multidisciplinair team, bestaande uit één of meerdere gynaecologen, cardiologen, anesthesiologen, echoscopisten en echocardiografisten, was iedere twee weken beschikbaar voor het leveren van zorg aan zowel zwangere als niet zwangere vrouwen met een hartaandoening. Een belangrijk voordeel van deze opzet is de verbeterde toegang tot zorg, inclusief de bereikbaarheid van betrouwbare anticonceptie. De richtlijnen die beschrijven hoe deze zorg goed kan worden opgezet, waren alleen beschikbaar vanuit hoge inkomenslanden. Invoering van deze richtlijnen in Namibië leverde diverse problemen op, omdat contextuele factoren specifiek voor lage- en middeninkomenslanden, zoals een hogere incidentie van infecties en verminderde

toegang tot zorg, hierin niet waren meegenomen. In een tweejarige cohortstudie werd een hoge incidentie waargenomen van complicaties bij een groep van 65 zwangere vrouwen en hun (ongeboren) baby's (hoofdstuk 6). Bij vrouwen waarbij in de huidige zwangerschap hun hartaandoening pas voor het eerst gediagnosticeerd was, werden relatief vaker complicaties gezien. Veel van deze vrouwen hadden tijdens hun vorige zwangerschap een ziekenhuis bezocht met symptomen passend bij een hartaandoening, maar de diagnose was toen gemist door gebrek aan kennis of materiaal van de betreffende hulpverlener. Reumatische hartziekte was de meest voorkomende aandoening in het cohort (31/65, 47.7%). Deze aandoening wordt vooral gezien onder vrouwen van een lagere sociaaleconomische klasse. Om de zwangerschapsuitkomsten van vrouwen met een hartaandoeningen in Namibië te verbeteren, moet er meer aandacht komen voor het diagnosticeren van een hartaandoening in een vroeger stadium. Tevens moeten er richtlijnen beschikbaar komen voor het verlenen van zorg aan vrouwen met een hartaandoening die toepasbaar zijn op de lokale situatie van Namibië.

In Namibië begon hepatitis E pas in 2017 een impact te hebben op de gezondheid van zwangere vrouwen en hun baby's, toen er sprake was van een nationale uitbraak (hoofdstuk 7). Omdat hepatitis E verspreid wordt via besmet drinkwater, worden infecties eigenlijk alleen gezien onder arme vrouwen die in de sloppenwijken wonen en geen toegang hebben tot schoon drinkwater. Zwangerschappen die gecompliceerd worden door een acute hepatitis E infectie, laten zeer slechte uitkomsten zien, zowel voor de moeder als haar (ongeboren) baby. Bijna de helft van de zwangere vrouwen die tussen 2017 en 2019 opgenomen waren in het Windhoek Hospital Complex met hepatitis E ontwikkelde acuut leverfalen. Deze vrouwen moesten dan worden opgenomen op de intensive care. Bijna een op de vijf overleed. Opvallend genoeg zagen we dat vrouwen die ook geïnfecteerd waren met HIV, en dan met name vrouwen die HIV medicatie gebruikten, minder ernstig ziek leken te worden en minder vaak leverfalen ontwikkelden. Omdat er nu geen genezende behandeling beschikbaar is voor hepatitis E, is het belangrijk dat deze observatie in een groter cohort wordt onderzocht.

De belangrijkste factor die bijdraagt aan de hoge incidentie van ernstige maternale uitkomsten in Namibië was een lage kwaliteit van zorg in de zorginstellingen en met name kwetsbare vrouwen hadden een hoger risico op ernstige maternale uitkomsten. Het Namibische zorgsysteem moet verbeterd worden, zodat het voor hulpverleners mogelijk is om goede kwaliteit zorg aan alle vrouwen in Namibië te leveren. Het is daarom cruciaal dat de voorgestelde aanbevelingen nu ook omgezet worden in acties. De inzichten die zijn verkregen door dit nationaal obstetrisch registratiesysteem zullen bijdragen aan een succesvolle invoering. Het is immers

essentieel, zoals bij elke interventie, dat een lokaal probleem wordt aangepakt op een manier die aansluit bij de lokale context.

Publications

Brückner TY, **Heemelaar S**, Endjala T, van den Akker T. Healthcare Worker Burnout: Exploring the experiences of maternity unit healthcare workers in Namibia. Submitted

Heemelaar JC, **Heemelaar S**, Hertel SN, Jukema JW, Sueters M, Louwerens M, Antoni ML. Cardiac and obstetric outcomes of pregnancies for women after cardiotoxic therapy in childhood: a single center observational study. BMC Cancer. 2023 Feb 2;23(1):115.

Mackenzie S, **Heemelaar S**, Callard B, (Eds.) on behalf of National Maternal Death, Near-miss, Stillbirth And Neonatal Death Review Committee. Maternal death, stillbirths and neonatal Deaths in Namibia: Report on the confidential enquiry into maternal deaths, stillbirths and neonatal deaths (1 April 2018 to 31 March 2021). Ministry of Health and Social Services: Windhoek, 2022.

Heemelaar S, Callard B, Shikwambi H, Ellmies J, Kafitha W, Stekelenburg J, van den Akker T, Mackenzie S. Confidential enquiry into maternal deaths in Namibia, 2018-2019: findings and lessons learned from implementation. Submitted

Heemelaar S, Agapitus N, van den Akker T, Stekelenburg J, Mackenzie S, Hugo-Hamman C, et al. Experiences of a dedicated Heart and Maternal Health Service providing multidisciplinary care to pregnant women with cardiac disease in a tertiary centre in Namibia. Trop Med Int Health. 2022 Sep;27(9):803–14.

Heemelaar S, Hangula AL, Chipeio ML, Josef M, Stekelenburg J, van den Akker T, Pischke S, Mackenzie SBP. Maternal and fetal outcomes of pregnancies complicated by acute hepatitis E and the impact of HIV status: A cross-sectional study in Namibia. Liver Int. 2022 Jan;42(1):50-58.

Heemelaar S, Josef M, Diener Z, Chipeio M, Stekelenburg J, van den Akker T, Mackenzie S. Maternal near-miss surveillance, Namibia. Bull World Health Organ. 2020 Aug 1;98(8):548-557.

Heemelaar S, Petrus A, Knight M, van den Akker T. Maternal mortality due to cardiac disease in low- and middle-income countries. Trop Med Int Health. 2020 Jun;25(6):673-686.

Heemelaar S, Kabongo L, Ithindi T, Luboya C, Munetsi F, Bauer AK, Dammann A, Drewes A, Stekelenburg J, van den Akker T, Mackenzie S. Measuring maternal near-miss in a middle-income country: assessing the use of WHO and sub-Saharan Africa maternal near-miss criteria in Namibia. Glob Health Action. 2019;12(1):1646036.

Heemelaar S, Nelissen E, Mdoe P, Kidanto H, van Roosmalen J, Stekelenburg J. Accuracy of indication for caesarean sections in maternal death and "near-miss" cases in a rural hospital in Tanzania. Trop Med Int Health. 2016 Apr;21(4):525-34.

Heemelaar S, Habets N, Makukula Z, van Roosmalen J, van den Akker T. Three monthly HIV re-testing: missed opportunities peripartum in a rural district hospital in Zambia. Trop Med Int Health. 2015 Mar;20(3):277-83.

van de Mheen L, Everwijn SM, Knapen MF, Oepkes D, Engels M, Manten GT, Zondervan H, Wirjosoekarto SA, van Vugt JM, Erwich JJ, Nij Bijvank SW, Ravelli A, **Heemelaar S**, van Pampus MG, de Groot CJ, Mol BW, Pajkrt E. The effectiveness of fetal reduction in trichorionic triplet pregnancy. Am J Obstet Gynecol. 2014 Nov;211(5):536.e1-6.

Surendran RP, Visser ME, **Heemelaar S**, Wang J, Peter J, Defesche JC, Kuivenhoven JA, Hosseini M, Péterfy M, Kastelein JJ, Johansen CT, Hegele RA, Stroes ES, Dallinga-Thie GM. Mutations in LPL, APOC2, APOA5, GPIHBP1 and LMF1 in patients with severe hypertriglyceridaemia. J Intern Med. 2012 Aug;272(2):185-96

Heemelaar S, Hooker AB, Bakkum E. Een incomplete curettage: re-curettage of hysteroscopie resectie? Nederlands Tijdschrift Obstetrie en Gynaecologie. Vol 129, jun 2012; 246-250.

The Safe Motherhood Series

The Dutch Working Party 'International Safe Motherhood and Reproductive Health' aims to contribute to improvement of the reproductive health status of women around the globe, in particular by collaborating with local health workers (http://www.safemotherhood.nl). The Working Party is part of both the Dutch Society of Obstetrics and Gynaecology (NVOG) and the Dutch Society for International Health and Tropical Medicine (NVTG). The activities that are undertaken under the umbrella of the Working Party can be grouped into four pillars: education, patient care, research and advocacy.
Research activities are undertaken by (medical) students, Medical Doctors International Health and Tropical Medicine and many others. Some research activities develop into PhD-trajectories. PhD- candidates all over the world, Dutch and non-Dutch, work on finding locally acceptable and achievable ways to improve the quality of maternal health services, supervised by different members of the Working Party. Professor Jos van Roosmalen initiated the Safe Motherhood Series, which started in 1995.

- The role of oral (methyl)ergometrin in the prevention of postpartum haemorrhage. (**Akosua de Groot**), Radboud UMC, Nijmegen, the Netherlands, 1995
- Perinatal assessment in rural Tanzania. (**Gijs Walraven**), Radboud UMC, Nijmegen, the Netherlands, 1995
- Confidential enquiries into Maternal Deaths in the Netherlands, 1983- 1992. (**Nico Schuitemaker**), Leiden UMC, the Netherlands, 1998
- Confidential enquiries into Maternal Deaths in Surinam. (**Ashok Mungra**), Leiden UMC, the Netherlands, 1999
- Reproductive health matters in rural Ghana. (**Diederike Geelhoed**), Leiden UMC, the Netherlands, 2003
- Vaginal birth after caesarean section in Zimbabwe and The Netherlands (**Wilbert Spaans**), AMC Amsterdam, the Netherlands, 2004
- Safe Motherhood and Health systems research: Health care seeking behaviour and utilization of health services in Kalabo District (**Jelle Stekelenburg**), VU Amsterdam, the Netherlands, 2004
- Enhancing survival of mothers and their newborns in Tanzania (**Godfrey Mbaruku**), Karolinska Institute, Stockholm, Sweden, 2005
- Beyond the numbers: confidential enquiries into maternal deaths in Accra- Ghana (**Afisah Yakubu Zakariah, Accra, Ghana**), Vrije Universiteit Brussel, Belgium, 2008
- Severe maternal morbidity in the Netherlands: the LEMMoN study (**Joost Zwart**), UMC Leiden, the Netherlands, 2009
- Obstetric audit in Namibia and the Netherlands (**Jeroen van Dillen**), VU Amsterdam, the Netherlands, 2009

- Confidential enquiries into maternal deaths in the Netherlands 1993- 2005 (**Joke Schutte**), VU Amsterdam, the Netherlands, 2010
- Delay in Safe Motherhood (**Luc van Lonkhuijzen**), UMC Groningen, the Netherlands, 2011
- Medical Mirrors: Maternal care in a Malawian district (**Thomas van den Akker**), VU University Medical Centre, Amsterdam, the Netherlands, 2012
- Leading change in the maternal health care system in Tanzania: application of operations research (**Angelo Nyamtema**, Ifakara, Tanzania), VU Amsterdam, the Netherlands, 2012
- Health professionals and maternal health in Malawi: mortality and morbidity at district level (**Jogchum Beltman**), VU Amsterdam, the Netherlands, 2013
- Obstetric emergencies in primary midwifery care in the Netherlands (**Marrit Smit**), Leiden UMC, the Netherlands, 2014
- Improving maternal outcome in rural Tanzania using obstetric simulation-based training (**Ellen Nelissen**), VU Amsterdam, the Netherlands, 2014
- The aberrant third stage of labour (**Giel van Stralen**), UMC Leiden, the Netherlands, 2015
- Terugvinden van waardigheid, community-based sociotherapie in Rwanda, Oost-Congo en Liberia (**Cora Bakker**), VU Amsterdam, the Netherlands, 2016
- Severe acute maternal morbidity, risk factors in the Netherlands and validation of the WHO Maternal Near-Miss Tool (**Tom Witteveen**), Leiden UMC, the Netherlands, 2016
- Getting the job done, providing lifelong HIV-treatment in settings with limited human resources for health: innovative approaches (**Marielle Bemelmans**), VU Amsterdam, the Netherlands, 2016
- Identifying needs for optimizing the health work force in Ethiopia (**Tegbar Yigzaw Sindekie**), VU Amsterdam, the Netherlands, 2017
- Improving frontline health workers' performance in low resource settings; the case of Ethiopia (**Firew Ayalew Desta**), VU Amsterdam, the Netherlands, 2017
- Increasing access to anesthesia in Ethiopia: task shifting (**Sharon J.N. Kibwana**), VU Amsterdam, the Netherlands, 2017
- Diagnostic and clinical decision support systems for antenatal care: is mHealth the future in low-resource settings? (**Ibukun-Oluwa O. Abejirinde**), VU Amsterdam, the Netherlands, 2018
- Assisting birth attendants in providing acceptable care under unacceptable clinical realities: The Partoma Intervention Study at Zanzibar's Tertiary Hospital (**Nanna Maaløe**), University of Kopenhagen, Denmark, 2019
- Severe Maternal Morbidity and Mortality in Eastern Ethiopia (**Abera Kenay Tura**), UMC Groningen, the Netherlands, 2019
- Maternity Waiting Homes in Ethiopia to improve women's access to maternity care (**Tienke Vermeiden**), UMC Groningen, the Netherlands, 2019

- Improving access to quality maternal and newborn care in lowresource settings: the case of Tanzania (**Dunstan Raphael Bishanga**), UMC Groningen, the Netherlands, 2019
- Towards better prognostic and diagnostic strategies for major obstetric haemorrhage (**Ada Gillissen**), Leiden UMC, the Netherlands, 2019
- Hospital based audit of obstetric care and birth preparedness in rural Rwanda (**Richard Kalisa**), VU University Amsterdam, the Netherlands, 2019
- Re-introduction of vacuum extraction in a tertiary referral hospital in Uganda (**Barbara Nolens**), VU University Amsterdam, the Netherlands, 2019
- Health system determinants of maternal and neonatal health in Rwanda (**Felix Sayinzoga**), Radboud UMC, Nijmegen, the Netherlands, 2019
- Context-appropriate innovative solutions for improving the access to quality intra- and immediate postpartum care in India (**Somesh Kumar**), UMC Groningen, the Netherlands, 2019
- Quality of maternal and newborn health care in health facilities in Afghanistan (**Nasratullah Ansari**), VU Amsterdam, the Netherlands, 2019
- Safe Motherhood: Improving the quality of maternal and perinatal health care in a rural hospital in Tanzania (**Rob Mooij**), UMC Groningen, the Netherlands, 2020
- Strategies to improve intrapartum care: foetal monitoring in low resource settings (**Natasha Housseine**), UMC Utrecht, the Netherlands, 2020
- Maternal mortality in Suriname: Implementation of Maternal Death Surveillance and Response to reduce preventable maternal deaths (**Lachmi Kodan**), UMC Utrecht, the Netherlands, 2020
- Maternal mortality, near-miss and stillbirths in Suriname: time to respond (**Kim Verschueren**), UMC Utrecht, the Netherlands, 2020
- Key factors to improve maternal and child health in Sindh province, Pakistan (**Jin Won Noh**), UMC Groningen, the Netherlands, 2021
- Innovative partnerships for Safe Motherhood: participation and transdisciplinary collaboration as tools towards increasing skilled birth attendants (**Yadira Roggeveen**), VU University Amsterdam, the Netherlands, 2021
- Improving respectful maternity care provision in Ethiopia (**Ephrem Daniel Sheferaw**), UMC Groningen, the Netherlands, 2021
- Improving access to quality Family Planning Services in Kenya by Addressing Contraceptive Discontinuation (**Susan Ontiri**), UMC Groningen, the Netherlands, 2021
- Postpartum Hemorrhage: From Insight to Action (**Paul Ramler**), Leiden UMC, the Netherlands, 2022
- Optimizing care and patient experience of preeclampsia in low- and and middle-income countries – the case of Ghana (**Titus Kofi Beyuo**), UMC Utrecht, the Netherlands, 2022

- Epidemiology and etiology of genital fistulas in East Africa (**Carrie J.Ngongo**), Ghent University, Belgium, 2023
- Maternal morbidity and mortality in the Netherlands and their association with obstetric interventions (**Athanasios Kallianidis**), Leiden UMC, the Netherlands, 2023
- Maternal health in Namibia: Lessons learned from obstetric surveillance (**Steffie Heemelaar**), Leiden UMC, the Netherlands, 2023
- Maternal deaths, near misses and great saves: severe maternal outcomes in Metro East, the Western Cape Province, South Africa (**Anke Heitkamp**), Stellenbosch University, Cape Town, South Africa/VU University Amsterdam, the Netherlands, 2023