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PERINATAL OUTCOME OF ALL MATERNAL DEATHS AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL FROM JANUARY 2014 TO JUNE 2019

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine.

Johannesburg 2023

Declaration

I, Dr *Nomshado Sthembile Afolayan*, student number 0503628h, declare that this research report is my own work except as indicated in the references and acknowledgements. It is submitted in partial fulfilment of the requirements for the Degree of Master of Medicine in Obstetrics and Gynaecology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in this or any other university.

Name: Nomshado Sthembile Afolayan **Signed:** 

Signed at: Alberton, Johannesburg

On the: 16 May 2023

Dedication

I dedicate this paper to my dear grandmother Roseline Nancy Nxele, who taught me that life is what you make of it and to rise with every fall. She taught me that my calling to be a doctor is not only to serve the greater population of Soweto but an act of service to God, himself. Thank you for instilling the value of healing the nation through wholistic multi-dimensional medicine and birthing the notion of healing healers as I grew and evolved in this journey through my research study.

I also dedicate this paper to my dear husband and lovely children. Thank you for reminding me of the important things in life. It was not always easy. Your smiles, hugs, words of encouragement, and love has carried me till this far and beyond.

I dedicate study to my lovely parents, my family at large and my ancestors. Thank you for the constant prayers and always believing I would finish. Thank you for instilling the importance of education and self-improvement. It all started with your hard work and always making sure I will be the best person I can be.

Lastly, I dedicate this study to God. Msibi. Nxele. Mlangeni. Ingwemabalabala.
I am my ancestors' wildest dreams activated!
By Dr Nomshado Sthembile uNokukhanya Afolayan.

Makwanade! Kukhanye!

Abstract

Background

Maternal death is a tragic event. Out of the total number of maternal deaths, 99% occur in low- and middle-income countries. Perinatal outcome is related to maternal wellbeing. Maternal death has a negative impact on the fetal and neonatal outcome in the short and long term.

Objectives

To determine the perinatal outcomes of pregnancies that end in a maternal death at CHBAH over a 5-year period, to describe the causes of maternal death and to determine the stillbirth rate and early neonatal death rate within this population.

Methods

A retrospective cross-sectional study of the maternal deaths in women with a viable pregnancy from January 2014 till June 2019 at CHBAH. All maternal deaths with gestation > 26 weeks or neonatal weight >500g were included in the study. Data was extracted from maternal and neonatal files. The following information was retrieved; demographics, booking status, antenatal care, pregnancy outcome, fetal and neonatal outcome. The data was analyzed using STATA. Approval from the University of Witwatersrand Human Research Ethics Committee *(Protocol number: M1911143)* and the CEO was obtained.

Results

There was a total of 184 maternal deaths during the study period and 147 were included in this study. The iMMR was 135 deaths per 100 000 live births. Hypertension was the highest direct cause of death at 37% (27/74) followed by pregnancy related sepsis 27.4% (20/74) and then obstetric hemorrhage 20.6% (15/74). Non-pregnancy related infections (NPRI) made up 52.1% (38/73) of indirect causes, with HIV and HIV-related complications contributing 84.2% of the NPRI causes, followed by the medical and surgical disorders respectively. One hundred and thirty-seven neonates were delivered and 14 were undelivered at the time of maternal death. There were also two set of twins and one set of triplets. Ninety-one (61.9%) were born alive and 51 (34.6%) were stillbirths. Of the 91 live births 6 (6.5%) had an early neonatal death. Of the 51 stillbirths, 14 (27.5%) were from undelivered maternal deaths and 11 (21.1%) were from perimortem caesarian sections. The SBR was 347 per 1000 total maternal deaths and an ENND rate was 66 per 1000 live births. The PNMR was high at 388 per 1000 maternal deaths which is12 times higher than the general population.

Conclusion

Maternal deaths are associated with very poor perinatal outcomes, resulting in unacceptably high stillbirth rate, early neonatal death rate and perinatal mortality rate. The health of the mother has a significant impact on the perinatal outcomes of the pregnant woman. Most of the causes of death were mostly women with comorbidities , we therefore postulate that prenatal care and stringent antenatal care may assist in optimizing women and thus reducing maternal deaths and ultimately the perinatal outcomes.

Key words: *Perinatal mortality, maternal mortality, perinatal outcomes, stillbirths, neonatal deaths*

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I, *Dr Nomshado Sthembile Afolayan,* and Prof Yasmin Adam designed the study and supervised the data extraction at the facilities. Christian Nyaundi and Siphamandla Gumede analysed the data with assistance from Yasmin Adam. Nomshado Afolayan interpreted the data and prepared the first draft of the manuscript, which was revised by Dr Mokgadi Nchinyani and Prof. Yasmin Adam and Dr Firdose Nakwa. All authors read and approved the final manuscript.

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Abbreviations

Abbreviation	*Explanation*
AIDS	Acquired Immunodeficiency Syndrome
ARVs	Antiretrovirals
CFR	Case Fatality Rate
CHBAH	Chris Hani Baragwanath Academic Hospital
CPAP	Continuous Positive Airway Pressure
ENND	Early Neonatal Death
ENNDR	Early Neonatal Death Rate
ELBW	Extreme Low Birth Weight
HDP	Hypertensive Disease in Pregnancy
HELLP	Hemolysis, Elevated Liver Enzymes, Low Platelets
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
ICD 10	International Statistical Classification of Diseases and Related Health Problems, 10^{th} edition
IQR	Interquartile range
LMIC	Low and Middle-Income Countries
MMR	Maternal Mortality Rate
NMR	Neonatal Mortality Rate
NPRI	Non-Pregnancy-Related Infection
OH	Obstetric Hemorrhage
PCP	Pneumocystis pneumonia
PNMR	Perinatal Mortality Rate
RSA/SA	Republic of South Africa
SB	Stillbirth
SBR	Stillbirth Rate
SD	Standard Deviation
STATS SA	Statistics South Africa
TB	Tuberculosis
WHO	World Health Organization

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Chapter 1: Background and Introduction

Maternal mortality is still a global challenge, with the maternal mortality ratio in developing countries at least 14 times greater than in the developed countries (1). The full impact of maternal deaths on families and communities is yet to be fully understood with minimal research in this field. (2).

The global maternal mortality ratio (MMR) decrease from 342 to 211 deaths / 100 000 live births between 2000 and 2017 (3). This represents a 38% reduction in global MMR with an estimated 2.9% annual reduction in global MMR (3). Data collected by World Health Organisation (WHO) reveal that 99% of maternal deaths occur in developing countries especially Africa (4). In the 2017-2019 Saving Mothers Report, the MMR in SA was 134/100 000 live births in 2014-2016 triennium and now 113.8/100 000 for the 2017-2019 triennium (5).

The causes of maternal mortality are grouped as direct, indirect, and incidental (6). Direct causes of maternal death occur as a consequence of the complications or management of the pregnancy and parturition: e.g., hypertension, haemorrhage and puerperal sepsis (6). Indirect causes of maternal mortality are described as a pregnancy- associated death in a woman with a pre-existing or newly developed health problem unrelated to pregnancy such as cardiac disease and non-pregnancy related infections (NPRI) such as HIV/AIDS (6,7). Incidental or non-obstetrical maternal deaths are deaths not linked to pregnancy, such as trauma and violence (6,7). Decreasing maternal death remains a global priority (6,7).

The WHO describes the perinatal mortality as the number of stillbirths (SB) and neonatal deaths in the first seven days of life per 1 000 total births (3). The definition of SB in South Africa (SA) is any fetus that has demised after 28 weeks or has a weight ≥1000g (8). Perinatal mortality is a measure of maternal healthcare, maternal well-being and nutritional status along with the fetal wellbeing; it also reveals the quality of care offered antenatally, intrapartum, postpartum and in the neonatal period (9).

Millennium Development Goals (MDGs) four and five are aimed at improving child and maternal health and mortality respectively (10). Maternal wellbeing directly affects the fetal and neonatal outcome as the fetus is directly dependent on the mother for survival. Maternal deaths are indicative of maternal health and health care system functional adequacy. Also, fetal health is directly related to maternal health (11).

To improve on the perinatal wellbeing, it is paramount to then assess maternal health and care during antenatal and intrapartum as well postpartum to improve perinatal outcomes. Not enough work has been done to assess perinatal outcomes in relation to maternal death.

Maternal and perinatal outcomes are intrinsically related, and initiatives focused on optimizing one often has an impact on the other (9). In Sub-Saharan Africa, obstructed labour, abnormal fetal presentation, and Hypertensive diseases of Pregnancy (HDP) have been shown to increase the risk of perinatal mortality (PM) by more than 5-fold and subsequently resulting in more than a third of all perinatal deaths (8). Preterm birth, infection, hypertensive disease and intrapartum asphyxia are major contributors to perinatal deaths in Low- and middle-income countries (LMICs) (8). Data shows that an infant orphaned within 42 days of birth had a probability of surviving to one year of only 52.0% (1).

Under 5- child mortality has declined from 56 to 36 deaths /1000 live births between 2009 and 2014 and infant mortality from 39/1000 to 28/1000 during the period of 2009 to 2014 (12). However, there has been minimal change in neonatal deaths with the Neonatal mortality rate (NMR) remaining at 11-12/ 1000 live-births between 2012 and 2015 (13). The Perinatal mortality rate (PMR) was highest at 24.3 per 1000 in 2009 and lowest at 21 per 1000 in 2016 (8). According to STATS SA, the national stillbirths declined from 15.6 to 13.5 deaths per 1000 total births between 2003 and 2016 (8).

Key risk factors for death of a mother during the intrapartum period are also associated with increased neonatal mortality risk (1). Children whose mother died in the first 42 days of their birth faced 46 times greater risk of dying within one month when compared to babies whose mothers survived (1).

Chris Hani Baragwanath Academic Hospital (CHBAH) is a referral centre for seven midwifery obstetric units, a district hospital, two regional hospitals in Gauteng and two regional hospitals in the North West Province. The perinatal outcomes of pregnancies that end in a maternal death at CHBAH is unknown. This study aims to understand the perinatal outcomes of pregnancies that end in a maternal death at CHBAH to increase infant and child survival at CHBAH.

Chapter 2: Methods and materials

2.1 Setting and study design

This was a retrospective cross-sectional study conducted at CHBAH, a tertiary hospital in Soweto, Johannesburg, an area of mixed informal and urban settlements (14,15). CHBAH is an academic hospital associated with the University of the Witwatersrand that centrally provides tertiary health care services in Soweto. The Department of Obstetrics experiences high volumes of patients, with 111 551 deliveries and 108920 of those being live births between January 2014 and June 2019 (15–17).

2.2 Study Population

This study included all women with a pregnancy of at least 26 weeks or who delivered a neonate > 500g who died at CHBAH from January 2014 until June 2019. At CHBAH viability is defined as estimated gestational age of 26 weeks or birth weight of 500g or more. The population includes the neonates born to these women. All these maternal deaths were discussed at the weekly Obstetrics departmental mortality and morbidity meetings where the cause of death is evaluated and death notification filled.

2.3 Data collection

The following information was taken from the paper based maternal records; Demographic information (age, parity, employment); Pregnancy related factors (history, booking status, blood results, comorbidities, mode of delivery). The following information was extracted from the paper based neonatal files weight, sex, Apgar's scores, admission status and outcomes related to that.

2.4 Statistical analysis

Data was entered in REDCap (Research Electronic Data Capture) then exported to MS Excel (Microsoft office) for data cleaning and data quality checks. Data was transferred to STATA version 14 (Statacorp, College Station, Texas, United State of America) for statistical analysis. Categorical variables were described with frequencies and percentages, continuous variables were described with means (and SD) or medians (and IQRs). The stillbirth rate was calculated by dividing the number of stillbirths by the total number of births during the study period and expressing this per 1000. The undelivered fetuses were also documented as stillbirths for statistical purposes. The early neonatal death rate was estimated by dividing the number of deaths during the first 7 completed days of life by the total number of births during the study period and expressing this per 1000.

Means were compared with t test (if two groups) and analysis of variance [anova(if more than two groups)]. Medians were compared with rank sum test (if two groups) and Kruskal Wallis test (if more than two groups). Frequencies were compared with chi squared test and fishers exact test (if cell size was less than five). A p value of ≤ 0.05 was considered statistically significant.

2.5 Ethical Approval

Ethical approval from the University of Witwatersrand Human Research Ethics Committee was obtained (Protocol number: M1911143). Approval was also obtained from Chief Executive officers at CHBAH as well as the Obstetrics and Gynaecology department. Patient confidentiality was always ensured and anonymity was secured by use of study numbers.

2.6 Funding

The author received no financial support for the research, authorship, and/or publication of this article.

2.7 Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

2.8 Consent for publication

Not applicable.

2.9 Competing interests

The authors declare that they have no competing interests.

Chapter 3: Results

3.1 Baseline characteristics of the study population

There was a total of 183 maternal deaths at CHBAH during the study period and 147 were included in this study. Thirty-four were excluded due to gestational age being less than 26 weeks and 2 were excluded due to missing information. The iMMR was 135 deaths per 100,000 live births. Most women 85 (58.2%) were unemployed, 26 (17.8%) employed and in in 35 (24%) the employment status was unknown.

Table 1 below gives a representation of the general characteristics of the study population. The median parity was 1 (IQR: 0-2; range:0-7). The median gravidity was 3.0 (IQR: 2-4; range=1-7) pregnancies. The mean gestational age at booking was 20.2 weeks (SD± 7.7) while mean gestational age at time of death was 33.8 weeks (SD=±4,6).

Table 1: General characteristics of the study population

Characteristics	Total (N=147)
Age	
Mean (SD*)	29.2 (±6.3)
Parity	
Zero	39 (27.1%)
One	36 (25.0%)
Two	37 (25.7%)
Three or more	32 (22.2%)
Booking Status	
Unbooked	29 (19.9 %)
Booked	117 (80.1 %)
HIV	
Negative	75 (51.7 %)
Positive	68 (46.3 %)
Unknown	4 (2.7%)
CD4	
Median (IQR**)	223 (61 – 418)
HIV Treatment	
No	11 (16.1%)
Yes	53 (77.9%)
Unknown	4 (5.9%)
Gestational age at booking(weeks)	
Mean (SD*)	20.2 (7.7)

*SD=Standard déviation
** IQR=Interquartile range.

3.2 Antenatal and past obstetric history

There were 22 (15.3%) women who had a previous miscarriage, 3 (2.1%) with a previous ectopic and 1 (0.7%) who had a termination of pregnancy. The median gestational age at booking was 20 weeks (IQR=16-24; range: 3-39 weeks) and the mean Hb at booking was 11.2g/dL (SD±2.3). Two (1.4%) women were Rh negative. Most women (96.5%, n=139) had RPR test results that was negative and 5 (3.5%) had unknown RPR status. A total of 68 (46.1%) patients were HIV positive and 53 (77.9%) were on treatment. The median duration of antiretroviral treatment was 5 months (IQR: 3-12 months, range: 1-106 months). A median CD4 count was 223 cells/μL (IQR: 61-418; range: 3-2467). Of the 41 patients who had viral load results, 11 (26.8%) had lower than detectable viral load. The median viral load for those with detectable viral load was 17 583 copies/mL (IQR: 420-462000).

3.3 Causes of maternal death

About 80% of maternal deaths were in the postpartum period. Table 2 shows the causes of maternal death. Hypertension was the leading cause of direct maternal death, followed by pregnancy related sepsis, obstetric haemorrhage and embolism. Of the indirect causes of death due to NPRI (n=38), 32 (84.2%) were a result of HIV and related complications. For the deaths indirectly caused by medical and surgical disorders (n=35), 34.3% were due to cardiac disease and 14.8% due to respiratory diseases.

Table 2: Causes of maternal death

Characteristics	Total (N=147)
Cause of death	
Direct	74 (50.3%)
Indirect	73 (49.7%)
Direct causes	
• Hypertension related	27 (18.4%)
• Pregnancy related sepsis	20 (14.3%)
• Obstetric haemorrhage	15 (10.2 %)
• Embolism*	8 (5.4%)
• Anaesthetic related	3 (2.0%)
Indirect causes	
• Non-pregnancy related infections	38 (25.9%)
• Medical and surgical disorders	35 (23.8%)

*Embolism was based on clinical diagnosis and not radiological.

3.4 Birth outcomes

This study found that over two thirds of women (n=102, 69.4%) delivered by caesarean section, 30 (20.4%) had normal vaginal delivery (NVD), 14 (9.5%) were undelivered and 1 (0.7%) had a laparotomy for extrauterine pregnancy. Of the total caesarean section deliveries observed in this study, 79 (78.2%) were emergencies, 3 (3.0%) electives and 19 (18.8%) perimortem caesarean sections. The 30 NVDs included in this study showed that 26 (86.7%) were spontaneous whilst 4 (13.3%) were induced. There were 97 preterm deliveries observed in this study. 43.3% (n=42) of those preterm deliveries observed ended as stillbirths.

3.5 Neonatal outcomes

There was a total of 151 babies as there were two sets of twins and one set of triplets. One hundred and thirty seven babies were delivered and 14 undelivered fetuses in our study population. Of the 97 preterm births , 43.3% (n=42) ended as a stillbirth. There were 51 stillbirths with 37 (25.2%) stillbirths delivered and with 14 (9.6%) of the stillbirths were undelivered at the time of maternal death. The stillbirth rate is 347 per 1000 maternal deaths. Table 3 shows that there were 6 neonates that died with a ENND rate of 66 per 1000 maternal death live births. Eighteen (11.0%) of the neonatal data outcome was incomplete due to missing data and poor record keeping. The perinatal mortality rate was 388 per 1000 births. Out of the 38 paediatric admissions with reasons for admission, the most common reason for admission was prematurity (n=15, 39.5%), followed by respiratory distress at (n=9, 23.7%) then low Apgar's at (n=7, 15.8%).

3.6 Place of delivery

From the total 126 deliveries of the high-risk pregnant women with information on facility of delivery, 118 (93.7%) took place at CHBAH, 7 (5.6%) at other hospitals and 1 (0.8%) at a local clinic in Soweto.

Table 3 shows the comparison of perinatal outcomes in direct vs indirect causes of death. The mean GA at time of birth or death was significantly lower amongst the indirect causes of maternal deaths compared to the direct causes of maternal deaths. The direct causes of maternal deaths had significantly more live births. Indirect causes of maternal deaths showed a significantly higher rate of undelivered infants and significantly higher rates of preterm births.

Table 3: Comparison of perinatal outcomes in direct vs indirect deaths

Variables	Categories	Direct (n=74, 50.3%)	Indirect (n=73, 49.7%)	P values*
Median GA at delivery (IQR)		36.5 (32-39)	32.0 (29-36)	p<0.01
Outcome (n, %)	Alive	48 (64.9)	43 (58.9)	p<0.01
	Stillbirth	19 (25.7)	18 (24.7)	
	Undelivered	4 (5.4)	10 (13.7)	
	Unknown	3 (4.0)	2 (2.7)	
Preterm (n, %)		35 (50.0)	55 (77.5)	p<0.01
Median birthweight (IQR) (gram)		2392.5 (1885-3235)	1650 (1120-2410)	p<0.01
low birthweight (<2500g) (n, %)		36 (49.3)	46 (63.0)	p<0.010
ENND (n, %)		2 (100)	4 (80.0)	**

*p values from t-independent, Kruskal-Wallis, chi squared, fishers exact, rank-sum test.
**p value could not be calculated due to empty cells.

Table 4 compares the perinatal outcomes in different phases of pregnancy. Median GA at delivery is not significantly different in the different phase of pregnancy (p=0.21). Mothers who experienced a death at the postpartum stage had a significantly higher rate of (72.7%) of live births, with the antenatal death patients having a significantly higher rate of undelivered (72.2%) fetuses ($p < 0.001$). Birthweight at time of delivery showed no significant difference.

Table 4: Comparison of perinatal outcomes by phase of pregnancy

Variables	Categories	Antenatal (n=18, 12.2%)	Peripartum (n=12, 8.2%)	Postpartum (n=117, 79.6%)	P value
Median GA at delivery (IQR)		31 (29-33)	32 (30-38)	35 (30-39)	P=0.20
Outcome (n, %)	Alive	1 (5.5)	5 (41.7)	85 (72.7)	p<0.001
	Stillbirth	2 (11.1)	6 (50.0)	29 (24.8)	
	Undelivered	14 (77.7)	0 (0)	0 (0)	
	Unknown	1 (5.5)	1 (8.3)	3 (2.6)	
Preterm (n, %)		17 (94.4)	7 (63.6)	66 (58.4)	p=0.008
Median birthweight (IQR) (gram)		2250 (1980-2520)	2380 (1800-2880)	2075 (1375-2905)	P=0.69
Low birthweight (<2500g) (n, %)		1 (5.6)	6 (50.0)	75 (64.1)	p<0.001
ENND		0 (0)	1 (100.0)	5 (83.3)	**

*p values from t-independent, Kruskal-Wallis, chi squared, fishers exact, rank-sum test.
**p value could not be calculated due to empty cells.

Gestational age at time of delivery was higher for obstetric haemorrhage (OH) (36.3 weeks) and lowest for NPRI (30.8 weeks; [p <0.01]) as shown in table 5. There was no significant difference in the neonatal outcomes in relation to specific causes of deaths (p= 0.24). NPRI have a significantly increased rate of preterm birth compared to the other causes of maternal death (p=0.001).

Table 5: Comparison of perinatal outcomes according to the causes of maternal death

Variables	Categories	Hypertension (n=27, 23.5%)	NPRI (n=35, 30.4%)	Obstetric haemorrhage (n=15, 13.0%)	Medical and surgical disorders (n=38, 33.0%)	P value
Median GA (IQR)		34 (30-37)	30 (28.5-33.0)	38 (34-39)	32 (30-38)	p<0.01
Outcome (n, %)	Alive	17 (63.0)	21 (60.0)	8 (53.3)	22 (57.9)	p=0.243
	Stillbirth	6 (22.2)	6 (17.1)	6 (40.0)	12 (31.6)	
	Undelivered	3 (11.1)	8 (22.9)	1 (6.7)	2 (5.3)	
	Unknown	1 (3.7)	0 (0)	0 (0)	2 (5.3)	
Preterm (n, %)		18 (69.2)	29 (87.9)	5 (33.3)	26 (68.4)	p=0.002
Median birthweight (IQR) (gram)		2002.5 (1510-2405)	1275 (1020-1865)	2545 (2071-3250)	1945 (1500-2715)	p=0.01
low birthweight (n, %)		19 (70.4)	24 (68.6)	7 (46.7)	22 (57.9)	p=0.011
ENND (n, %)		2 (100.0)	3 (75.0)	0 (0)	1 (100.0)	p=1.000

*p values from t-independent, Kruskal-Wallis, chi squared, fishers exact, rank-sum test.
**p value could not be calculated due to empty cells.

3.7 Perimortem caesarean section

Table 6 is a description of the perimortem caesarean sections. Two of the fetuses born at perimortem caesarean section had missing documents and thus outcome is unknown. The causes of deaths in women who had a Perimortem caesarean section were mostly from of NPRI (n=7,36.8%) with TB and PCP as the cause followed by thromboembolic disease (n=4;21%) with pulmonary embolus and amniotic fluid embolus as the cause, then HT (n=3,15.7%), DKA (N=2, 10.5%) then abruptio and asthma and peripartum cardiomyopathy at 5.3% each.

Table 6: Perimortem caesarean section outcomes

Variable	Categories	C/S-perimortem (n=19)
Median GA (IQR)		32 (30-37)
Median birthweight (IQR) (gram)		2380 (1510-2855)
Outcome (n, %)	Alive	6 (31.6)
	Stillbirth	11 (57.9)
	Unknown	2 (10.5)
Low birthweight (<2500g) (n, %)		10 (52.6)
ENND (n, %)		1 (5.3)

Chapter 4: Discussion

This study determined the causes of maternal deaths and their perinatal outcomes over a 5-year period. This is the first study to use routinely collected data to report the perinatal outcomes in association with maternal deaths in South Africa.

The iMMR was 135 per 100 000 live births. This MMR is higher than the national MMR of 113.8 per 100 000 live births in the last 2017-2019 triennium (5). This is probably because CHBAH receives more critical and high-risk patients. The perinatal mortality rate (PNMR) in CHBAH during the study period specific to women who had a maternal death was higher than the rate in South Africa (388 per 1000 births versus 30.9 per 1000 births) (5). The PNMR for CHBAH for this time period was 36 per 1000 births. Our study then highlights that the perinatal outcomes are dire in a maternal death population as the PNMR is 12 times higher in than that in the general population. The perinatal mortality is a comprehensive indicator for estimating the true level of mortality around time of delivery as it analyses both live births and the stillbirths of a target population studied (18).

A study conducted in SA posited that pregnancy accelerates HIV disease progression due to the immunosuppression associated with pregnancy (19). The authors of that study further posited that NPRI and HIV related conditions such as pulmonary TB, pneumonia heighten the mortality in pregnant and postpartum women (19). The findings of this study are similar to the causes of maternal deaths in SA, more specifically caused by NPRI, hypertension, obstetric haemorrhage, as well as medical and surgical diseases (5). However, this is different from developed countries, for example the UK, where the leading causes of direct and indirect maternal deaths are thromboembolic and cardiac diseases respectively (20). The plausible reason for this high rate of NPRI in SA is due to the HIV prevalence in the country as well as its associated co infections such as pulmonary TB.

The neonates/fetuses of most patients who had maternal death were delivered via caesarean section and almost four fifths of these were emergency caesarean sections with 19% being peri-mortem caesarean sections. Almost three quarters of the deliveries were preterm, which is associated with increased risk of neonatal death in CHBAH (21). This study shows that indirect deaths were significantly associated with lower gestation at birth and as well as low birth weight when compared to direct causes of death. Indirect causes of maternal death are co-morbid conditions which are prone to earlier complications during the course of the pregnancy.

Furthermore, antenatal maternal deaths were associated with a higher rate of stillbirths compared to intrapartum or postnatal deaths. The reason for this observation is not clear but it could also be related to the fact that intrapartum and postpartum causes of maternal deaths are acute and therefore unlikely to affect the fetus as compared to co-morbid conditions which may have a higher rate of placental insufficiency and poor fetal growth and survival (22). Obstetric haemorrhage was associated with significantly better neonatal outcomes (estimated GA at birth, live births and birth weights) whilst NPRI had the worst outcomes. This can be explained by the fact that NPRI are chronic diseases thus associated with earlier insults on the developing fetus.

About one fifth of the caesarean sections were perimortem caesarean sections. More than half of these resulted in neonates who were low birth weight and almost two thirds who were stillbirths. A perimortem caesarean section is performed in a mother who is being resuscitated. These cases have a high maternal and perinatal mortality rate (23).

4.1 Limitations of the study

This study was based on routine clinical data which has missing information. The maternal data is routinely collected which is not routinely linked to the perinatal outcomes data. The study also focused on early neonatal outcome and not at late neonatal (>7 days to 30 days of life) outcomes. A strength of the study is that the cause of death is determined by a multidisciplinary team

Chapter 5: Conclusion

Maternal deaths are associated with poor perinatal outcomes. The causes of deaths were similar to maternal deaths in Saving Mothers report. The worst perinatal outcomes were in women who died in the antenatal period and these were deaths mainly due to Indirect causes. NPRI infections were associated with the worst perinatal outcomes. Of the poor fetal and neonatal outcomes stillbirth was the most common. Maternal deaths are associated with very high stillbirth and early neonatal death rates. Whilst we have made strides in antiretroviral treatment initiation, we need to focus on opportunistic infections and adherence. We suggest that routinely collected data on maternal deaths include Perinatal outcomes as a standard. Prenatal care may assist in optimising the health of women with co-morbidities, therefore future research needs to be done to evaluate whether Pre-natal care and its effects on improving and averting maternal deaths and subsequently improving perinatal outcomes. More work also needs to be

done to improve HIV programmes and prevention of HIV related opportunistic infections as these still are a leading cause of maternal death and thus poor perinatal outcomes.

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APPENDIX A: Approved protocol

PERINATAL OUTCOME OF ALL MATERNAL DEATHS AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL FROM JANUARY 2014 TO JUNE 2019

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1. Introduction

1.1.Background

Maternal death is defined as the demise of a female while pregnant or within 42 days of termination of pregnancy, regardless of the gestation and location of the pregnancy, from any cause related to or potentiated by the pregnancy or its management, but not from accidental or incidental causes (ICD-10). Maternal mortality is assessed using the maternal mortality rate, which is the number of deaths per 100 000 live births (1). Deaths of women during pregnancy, childbirth, and puerperium remain a serious public health issue, particularly in low- and middle-income countries, such as SA (2).

The global maternal mortality ratio came down from 342 to 211 deaths / 100 000 live births between 2000 and 2017 (3). This represents a 38% drop in global MMR with an estimated 2.9% annual drop in global MMR (3). There were 35% fewer maternal deaths in 2017 compared to 2000; 255 000 vs 451 000 deaths (3). Data collected by WHO reveals that more than 500 000 maternal mortalities take place worldwide every year with developing countries yielding 99%, mostly in Africa, and developed countries yielding only 1% (4). In the 2014-2016 Saving Mothers Report the MMR in SA was 154/100 000 live births in (2011-2013 tri-annum) and now 134/100 000(2014-2016 triennium (5).

The WHO describes the perinatal mortality as the number of stillbirths and neonatal deaths in the initial seven days of life per 1000 total births (6). The definition of SB in SA is any fetus that has demised after 28 weeks or 500g (6). Perinatal mortality is a measure of maternal healthcare, maternal well-being and nutritional status along with the fetal wellbeing; it also reveals the quality care offered antenatally, intrapartum, postpartum and in the neonatal period (7). Maternal and perinatal outcomes are intrinsically related, and initiatives focused on optimizing one often has an impact on the other (7).

Under 5- child mortality has declined from 56 to 36 deaths /1000 live births between 2009 and 2014 and infant mortality from 39/1000 to 28/1000 from 2009 to 2014(8). However, there has been minimal change in neonatal deaths with the NMR remaining at 11-12/ 1000 live-births between 2012 and 2015(9). The PMR was highest at 24.3 per 1000 in 2009 and lowest at 21 per 1000 in 2016 according to Statistics SA (6). The global SBR is roughly calculated at 18 deaths /1000 births or 2.6 million stillbirths in a year (10). According to STATS SA stillbirths declined nationally from 16 to 13 deaths per 1000 total births respectively between 2003 and 2005 which turned out to be the lowest recorded rate. In 2016 the SBR was 13.5 per 1000 live births (6).

Millennium Development Goals four and five are aimed at improving child and maternal health and mortality respectively (11). Maternal wellbeing directly impacts the fetal and neonatal outcomes as the fetus is directly dependent on the mother for survival. Chris Hani Baragwanath Academic Hospital (CHBAH) is a secondary/tertiary that surrounding clinics and hospitals refer to around Soweto, surrounding towns and provinces such as North West. It receives patients that are at high risk. The perinatal mortality amongst women who have a maternal death at CHBAH is unknown.

2. Literature review

Deaths of women during pregnancy, childbearing and after delivery remains a crucial public health issue, especially in LMICs (2). MDG 4 and MDG 5 are inextricably linked, as maternal health is rudimentary to the health of the newborn infant (11). A continuance of care approach that focuses on prenatal and intrapartum care and solidifies immediate newborn and postpartum care for mother and newborn is therefore considered essential in improving the health of mother and infant (11).

2.1.Causes of maternal deaths

The causes of maternal mortality are grouped as direct, indirect, and incidental (12). Direct causes of maternal demise occur as a consequence of the complications or management of the pregnancy and parturition: e.g. pre-eclampsia/eclampsia, hemorrhage and puerperal sepsis (12). Indirect causes of maternal mortality are described as a pregnancy-associated death in a woman with a pre-existing or newly developed health problem unrelated to pregnancy, such as cardiac disease, HIV/AIDS, or chronic hypertension (12). Incidental or non-obstetrical maternal deaths are deaths

not linked to pregnancy, such as trauma and violence (12). Decreasing maternal death remains a global priority (13).

According to the WHO systematic analysis, hemorrhage and indirect causes are the greatest causes of mortality worldwide (14). Hemorrhage was documented as a dominating cause of indirect mortality followed by HDP and sepsis (14). In a low- and middle-income country review, it was noted that hemorrhage and hypertensive diseases came close to or went above 40% of maternal mortalities (15). In Sub-Saharan Africa 61% of maternal mortalities were due to direct causes, 35% were due to indirect causes and 4% were not known (15). Indirect complications and causes in sub-Saharan Africa were reported as malaria contracted in pregnancy, HIV/AIDS and severe anemia in pregnancy (15). NPRIs remain the most common cause of maternal mortality in SA and all provinces (5). The leading cause of maternal mortality is still respiratory infections with TB, PCP pneumonia and other types of pneumonia attributes for 69% of deaths as per Saving Mothers Report 2014-2016. Altogether 68% of maternal mortalities were as a result of respiratory failure followed by immunosuppression at 63% and septic shock at about 15% (5). According to Moodley et al, there has been a major reduction in death owing to NPRI in SA (2). It is also noted that 95% of these women were HIV positive and the reduction indicates the major success of PMTCT and ARV roll-out programs in the country (2,13).

Currently, HDP is the most frequent direct cause of maternal death with Gauteng, Kwazulu-Natal, and Limpopo having the highest number of mortalities (5). The main problems during the pregnancy period were eclampsia, severe hypertension, HELLP and liver rupture with eclampsia being the most popular subcategory of HDP to cause mortality (5).

OH is the third commonest cause of maternal death in SA with the MMR of almost 23deaths/100 000 live births (5). As per a study done on improvements in maternal mortality in SA, OH had a small decrease in the number of deaths (2). There has also been an alarming rise in the number of case fatality rates (CFR) for excessive bleeding associated with cesarean delivery (BLDACD) which rose from 78 to 221 cases during the tri-annum of 2002-2004 and 2011-2013 tri-annum with a slight reduction to 217 during 2014-2016(2). Most maternal deaths are considered preventable and avoidable (5). Lack of appropriately trained medical personnel was the avoidable factor recorded in 39% and 23% of maternal deaths respectively where an avoidable factor was recorded

(16). The three conditions contributing most to the potentially preventable deaths were OH (24,4%), HDP (19,5%) and non-pregnancy related infections (NPRI)(18%)(16).

2.2.Perinatal mortality causes

Perinatal outcomes include the stillbirths and early neonatal period (birth to day7 of life) (6). Perinatal deaths remain globally inappropriately high with up to 3 000,000 stillbirths (SBs) and 3 000,000 neonatal deaths every year (7). Out of about 6 million perinatal mortalities estimated across the world, about 3.3 million are SBs with LMICs accounting for more than 97% (17). In Africa, the perinatal mortality rate (PMR) is recorded to be as high as 75 per 1000 with the lowest PMRs recorded to be from rural SA at 31/1000 total births (17). Tanzania showed a PMR OF 92 per 1000, Ethiopia had a PMR OF 57/1000 (17). The PMR in SA was highest at 24.3 per 1000 in 2009 and lowest at 21 per 1000 in 2016(6).

Causes of death are classified using ICD-10 and STATS SA used an analysis that focused mainly on the underlying cause of death, which is described as the disease or insult that began the sequence of events leading directly to death, or the consequences of the accident or violence which led to the fatal injury (WHO, 1992) (6). In developing countries, obstructed labor, abnormal fetal presentation, and HDP are well known for increasing the risk of PM by more than 5-fold and subsequently resulting in more than a third of all perinatal deaths (17). Another study states that preterm birth, infection, hypertensive disease, and intrapartum asphyxia are recurrently presented as the major regular contributors to perinatal deaths in LMICs (7). The top five causes of stillbirth in SA were (6):

i. The fetus and newborn affected by maternal factors and by complications of pregnancy, labor, and delivery
ii. Respiratory and cardiovascular disorders specific to the perinatal period
iii. Disorders related to the length of gestation and fetal growth
iv. Other congenital malformations
v. Congenital malformations of the nervous system**.**

2.3.Maternal and perinatal outcomes

Maternal mortalities are relatively sparse even in areas with high MMRs resulting in few studies able to investigate maternal deaths and their relationship and correlation to neonatal outcomes (7).

Those studies that have been carried out have been generally restricted to hospital births and have included a small number of deaths in comparison to the general population (7). Thus, making it difficult to extrapolate from these studies.

The mortality of a mother is particularly disturbing, more so when death occurs during the childbearing or puerperal period (8). A randomized controlled trial of vitamin A, beta carotene and placebo supplement in Nepal found that maternal mortality showed a statistically compelling association with early infant mortality, even after controlling for other applicable predictors (8). Although the timing of mothers' death and the underlying condition ending in the mother's demise does also have a substantial influence on the risk of fetal or neonatal death, the conditions that cause maternal mortality contributes to the risk (7).

In Tanzania, a qualitative study was done which illustrated the effect of maternal mortality on the survival life span, nutritional, health and other intergenerational outcomes for children, while Research in Haiti found that a household with maternal mortality had a 55% higher chance of suffering a death of a child under age 12 years, but that there were no elevated chances of child mortality in the case of other adult deaths not being the mother (8). It is clear that the demise of a mother is not only a calamitous single event to the household but has formidable adverse effects on the surviving offspring, the male partner and society (18).

A study in Tanzania revealed how a maternal death compromised a household in numerous ways as fathers were not well equipped for childcare thus siblings were often disunited and sent to different relatives and the household crumbled (8). Mothers were more involved in nurturing and feeding children and caring for them so if a mother is lost these duties are left to older surviving siblings or elderly and this compromised the quality of care and challenged the life expectancy of the surviving neonate even if born well and healthy (18). As per a prospective study in rural China, it was found that 14/120 index children (11.6%) demised in the maternal death group and noted to be within 15 months of maternal death as compared to no death of comparison group without maternal death (18). The index child death rate in rural Tanzania was 48% which is significantly higher than 11.6% in rural China which is most likely due to worse socioeconomic status in Africa. Unfortunately, also 14 0f 120 index children (11.6%) were deserted in the maternal death group whilst only 1 was abandoned in the control group (18). There is a significantly increased pervasiveness of malnutrition in the index group than control (18). There is also an unfortunate

higher probability of not going to school on time and quitting school for the older pre-existing siblings of maternal death patients (18).

Neonatal and infant survival fluctuated quite significantly between the maternal death group and control groups of women; with just above a 1/4 of live births (27%) to women who died of maternal causes dying before becoming a month of age (between 0-28 days), as compared to zero deaths in women who demised of non-maternal causes, and one death among live births to similar mothers who survived (8). See the chart in Appendix 1. Antepartum hemorrhage, HDP, uterine rupture, obstructed labor, and malpresentation were the prevalent obstetric complications in a case-control study of perinatal mortality and associated risk factors (17). Preeclampsia and eclampsia are critical causes of maternal death and considerable contributors to fetal and neonatal deaths due to their affiliation with asphyxia and preterm birth (19). Hemorrhage and obstructed labor both escalate the risk of stillbirths and early neonatal deaths attributed to birth asphyxia (19).

Maternal, fetal, and neonatal deaths in LMICs were reviewed in a prospective study, which found that 2/3 of SBs were considered as developing around the delivery time since the fetuses were fresh stillborn (19). This is a sign of the poor quality of care and the detection of most endangered fetuses. Furthermore, approximately 1/3 of neonatal deaths happened on day one of life and another 25% took place in two days following delivery (19). There is a great concern that babies born healthy and documented as alive are then discharged and die at home within the neonatal period and more so in the early neonatal period (17).

Prematurity is at the forefront of neonatal mortalities in SA, with those born weighing <1000g(ELBW) adding significantly to mortality figures (9) Reduction of ELBW death lies primarily in the beneficial factors associated with the administration of antenatal steroids and frequent antenatal visits but not necessarily building more specialized neonatal care units (9). This further proves that we need healthier mothers in the antenatal phase to secure healthier babies at birth. Studies in LMICs show that ensuring that these surviving infants are breastfed, receive kangaroo mother care and continuous positive airway pressure (CPAP) are simple cost-effective ways of reducing neonatal mortality (9). This means more emphasis must be made to keep mothers alive postpartum to care for these vulnerable infants.

Between September 2011 and March 2012, Pande et al evaluated the outcome of maternal death in rural Kenya and found that above ¾ of the women who died had more chores within the family when they were healthy such as agricultural duties, cooking, childminding, laundry, dishwashing, and shopping at the market (8). After their death, these duties were taken over primarily by the immediate and extended family (8).

Maternal and child mortality is still an essential gauge of the capacity of the healthcare system to provide preventive, promotive and curative health services in SA (4). The relationship between maternal and child morbidity and mortality and the fragility of women is often not adequately problematized and managed by policymakers, culminating in inefficient action plans (4). This then creates an ongoing problem in the healthcare system that is already under immense pressure.

3. Problem statement

The perinatal mortality rate in SA for infants of 500g or more is approximately 36/1000 (16). This fluctuates widely among different institutions from 35 per 1000 in metropolitan areas, such as Cape Town to more than 50 per 1000 in some underprivileged, rural areas (6).

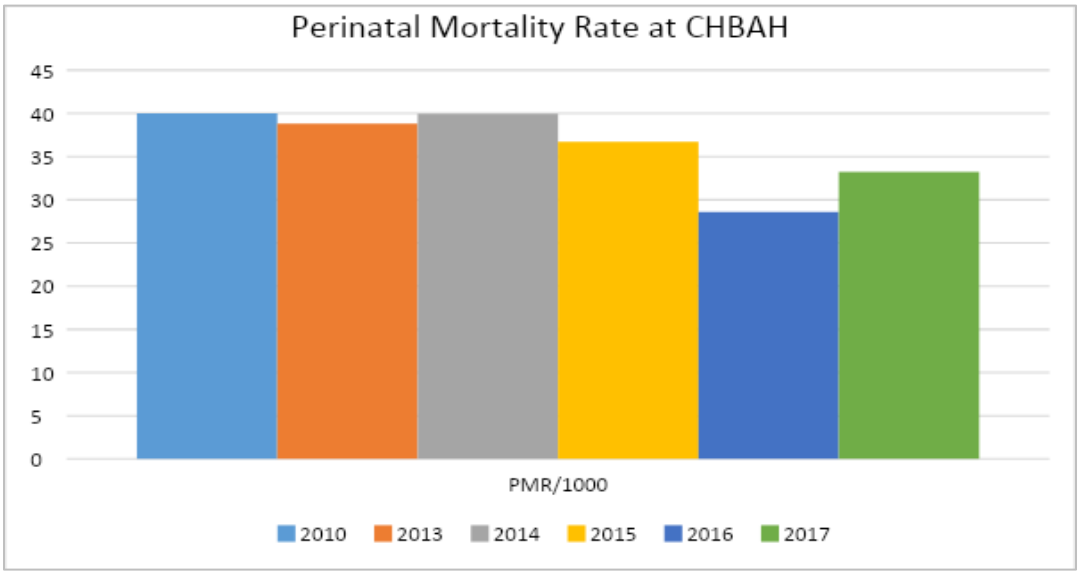


Figure 1: Perinatal mortality rate at CHBAH

From departmental data at CHBAH, the perinatal mortality amongst women who died at CHBAH is unknown. Maternal deaths are indicative of maternal health and health care system functional adequacy. Also, fetal health is directly related to maternal health. To improve on the perinatal wellbeing, it is paramount to then assess maternal health and care during antenatal and intrapartum as well as postpartum to improve perinatal outcomes. Not enough work has been done to assess perinatal outcomes in relation to maternal death. Approximating these outcomes in developing countries is challenging due to the poor availability of accurate, valid and reliable data.

This study intends to evaluate perinatal outcomes in women who have died during pregnancy, labor, or the postpartum period. Understanding the maternal and newborn outcomes captured at health care centers presents an opportunity for health care professionals and decision-makers to analyze and strategize on what can be improved (15).

4. Justification of study

Maternal and child mortality remain a foremost concern to health systems worldwide (4). The global MMR came down from 380/100 000 live births in 1999 to 210/100 00 live births in 1990(WHO, UNICEF, UNFPA, World Bank and the United Nations population divisions 2014) (4). The MMR at CHBAH was 171(1997-2003), 209(2004-2009), 170(2010-2012) and 162 during 2013-2015 according to Mnyani et al. If perinatal outcomes are related to maternal outcomes, then it is important to review the outcome if the mother demises. If we look into offspring of maternal death, we can be more readily prepared to optimize and prevent bad outcomes in the presence of a high-risk pregnancy threatened by maternal mortality.

5. Main aim

This study aims to determine the perinatal outcomes of the offspring of women whose deaths were classified as a maternal death at CHBAH between January 2014 and June 2019.

5.1.Key objectives

i. To describe the causes of maternal death
ii. To describe the perinatal outcomes of women who have died
iii. To determine the stillbirth rate of the women who have died
iv. To determine the early neonatal death rate of the women who have died.

6. Methods

6.1.Study Setting

This study will be conducted at CHBAH, a referral hospital in Soweto, Johannesburg, an area of mixed informal and urban settlements (13). CHBAH is the third-largest hospital in the world with an estimated 3200 beds and 6760 staff members. The maternity unit has 222 beds. It is a tertiary institution that is a referral center for seven midwifery obstetric units, a district hospital, two regional hospitals and two regional hospitals in the North West. The obstetric department at the CHBAH obstetrics department experiences high volumes, documented 19,804 live births recorded for 2015(13) and approximately 22000 deliveries in 2018.

6.2.Study Design

This will be a retrospective cross-sectional study.

6.3.Study Population

The population comprises all women with fetuses >26 weeks or who have delivered a 500g fetus who died at CHBAH during the antenatal period, in labor or postpartum between January 2014-June 2019. The population will also include the neonates born to these women.

6.4.Data management

Files will be accessed from the department and each file will be given a number and data collected on each sheet using numbers and not GT/GP numbers**.**

6.5.Data Acquisition

The data will be acquired in the following manner:

i. Evaluation of maternal death files from January 2104 to December 2018 and the following variables will be extracted:
    a. Demographic information
    b. Booking status
    c. Comorbidities
    d. Antenatal, perinatal, and postpartum information
    e. Cause of death as decided by the M&M meeting
    f. Timing of death (antenatal, intrapartum, or postpartum).

ii. The following neonatal information will be retrieved from the maternal records and pediatric file if there is one:
    a. Gestational age at delivery
    b. Weight, height
    c. Mode of delivery
    d. APGAR scores
    e. Presence of fetal distress defined by attending doctors
    f. Neonatal resuscitation
    g. Admission to neonatal care units
    h. Cause of stillbirth if known
    i. Cause of neonatal death if known.

6.6.Sample size

The sample size is subject to the number of maternal deaths from January 2014 to June 2019 that fit the below criteria.

6.7.Inclusion Criteria

i. All maternal deaths with a fetus above 26 weeks and or weight greater than 500g.
ii. Maternal deaths that occurred at CHBAH.

6.8.Exclusion Criteria

i. Any maternal death before arrival to CHBAH.

7. Ethics application

Permission to perform the study will be requested from the University of Witwatersrand Human research ethics committee (HREC).

8. National health research database

Register with the NHRD.

9. Limitations

This is a retrospective study, incomplete records or missing data can be a limitation. Any baby discharged before seven days but demises at home.

10. Funding

No funding is needed to conduct this study.

11. Timeline

The timelines of the research project are as follows:

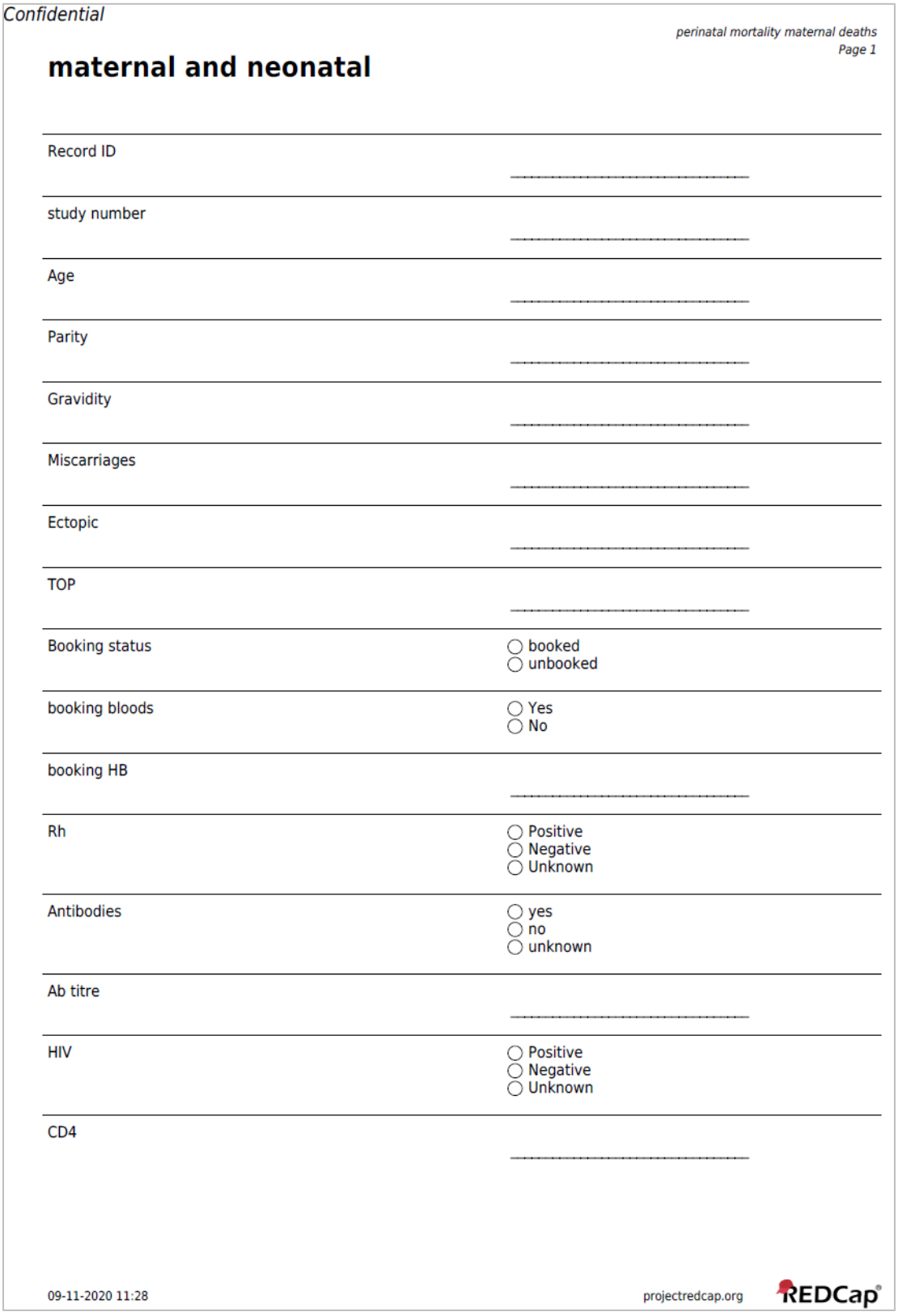
Stage 1	November 2019	Protocol
Stage 2	November 2019	Handing to ethic
Stage 3	November 2019	Handing to postgraduate
Stage 4	March 2019	Data collection
Stage 5	April 2020	Write up start
Stage 6	April – June 2020	Handing MME

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APPENDIX B: Data collection sheet



Confidential

perinatal mortality maternal deaths
Page 1

maternal and neonatal

Record ID	_____
study number	_____
Age	_____
Parity	_____
Gravidity	_____
Miscarriages	_____
Ectopic	_____
TOP	_____
Booking status	◯ booked ◯ unbooked
booking bloods	◯ Yes ◯ No
booking HB	_____
Rh	◯ Positive ◯ Negative ◯ Unknown
Antibodies	◯ yes ◯ no ◯ unknown
Ab titre	_____
HIV	◯ Positive ◯ Negative ◯ Unknown
CD4	_____

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Viral load	_____ (if LDL put in 19)
hepatitis B	◯ Positive ◯ Negative ◯ Unknown
Treatment	◯ Yes ◯ No ◯ Unknown
Duration Tx in months	_____
Tx Specify	_____ (if less than 1 month)
RPR	◯ Positive ◯ Negative ◯ Unknown
RPR_specify	_____
HB value	◯ < 10 ◯ >10
Gestation at booking	_____
Comorbidities	◯ Hypertension ◯ Diabetes ◯ Anemia ◯ Thyroid disease ◯ cardiac disease ◯ Other ◯ Epilepsy ◯ Asthma ◯ None
Other specify	_____
HPT type	◯ Chronic ◯ Gest ◯ PET ◯ Imminent Eclamp ◯ HELLP ◯ Eclampsia
DM type	◯ Pregestational ◯ Gestational ◯ DKA
Thyroid disorder type	◯ Hyperthyroidism ◯ Hypothyroidism

Cardiac disorder type	◯ pregestatioal cardiac disorder ◯ peripartum cardiac disorder
social History	◯ Smoking ◯ Alcohol ◯ None ◯ unknown
Employment status	◯ unemployed ◯ employed ◯ unknown
Mode of delivery	◯ NVD ◯ Caesarean section ◯ Undelivered ◯ Laparotomy
Caesarean section	◯ Emergency ◯ Elective ◯ Perimortaum ◯ Laparotomy for rupture
NVD	◯ assisted ◯ spontaneous
Date of death	_____
Gestation at death	_____
Period of death	◯ antenatal ◯ peripartum ◯ postpartum
cause of death	_____
Cause of death classified	◯ Direct ◯ Indirect ◯ Unanticipated complcations of management ◯ Coincidental
Direct cause	◯ Hypertension related ◯ Obstetric hemorrhage ◯ Pregnancy related sepsis ◯ Anaesthetic complication ◯ Acute collapse cause unknown ◯ Embolism ◯ Adverse drug reaction ◯ Miscellaneous
Indirect causes	◯ Non pregnancy -related infections ◯ Medical and surgical disorders ◯ Unknown

Coincidental cause	◯ Accidental ◯ Suicide
NPRI cause	◯ HIV and HIV related infections ◯ HPV ◯ Other
Med and Surg causes	◯ Thyroid disease ◯ Cardiac ◯ Diabetic complication ◯ Visceral surgical injury ◯ Neurological disease ◯ Renal ◯ Haematological ◯ Malaria ◯ Respiratory
Gestational age at birth	_____
Birthweight	_____
Gender	◯ Male ◯ Female ◯ Uknown
Place of Delivery	◯ CHBAH ◯ Clinic ◯ BBA: Home ◯ BBA: Ambulance ◯ Other hospital
Apgars at Birth	_____
Admission to Paeds	◯ Yes ◯ No
Paeds admission	◯ NICU ◯ TICU ◯ Ward 66 ◯ Other ◯ Nursery
Reason for admission	◯ Prematurity ◯ Respiratory Distress Syndrome ◯ Hypoglycemia ◯ Apnea ◯ Encaphalopathy ◯ Low agars ◯ Meconium Aspiration ◯ Maternal choriamnionitis ◯ Neonatal Jaundice ◯ Congenital Abnormalities ◯ observations ◯ Other

Length of admission	◯ < 7Days ◯ >7Days
specific days	◯ 1 ◯ 2 ◯ 3 ◯ 4 ◯ 5 ◯ 6 ◯ 7 ◯ < 1
Management	◯ Stimulated and warmed ◯ Suction ◯ IV Fluids ◯ Meconium aspiration ◯ CPR ◯ CPAP ◯ Ventilated ◯ Cooled ◯ Antibiotics ◯ Blood transfusion ◯ Surfactant ◯ Exchange transfusion ◯ Phototherapy ◯ Growth monitoring ◯ Observations
Complications	◯ Sepsis ◯ AKI ◯ NEC ◯ Poor growth ◯ Other ◯ None
Other complication	_____
Date of discharge	_____
Discharge status	◯ < 7 days ◯ 7 days ◯ < 30 days ◯ >30 days
Date of death	◯ Stillbirth ◯ < 7days ◯ 7-30days ◯ >30days
Cause of death	◯ Sepsis ◯ NEC ◯ RDS ◯ HIE ◯ Seizures ◯ Other

Other death cause _____

APPENDIX C : Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr NS Afolayan

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M1911143

NAME: (Principal Investigator)	Dr NS Afolayan
DEPARTMENT:	School of Clinical Medicine Department of Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Perinatal outcomes of all women with a maternal death at Chris Hani Baragwanath Academic Hospital from January 2014 to June 2019
DATE CONSIDERED:	2019/11/29
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor Y Adam
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/03/25

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore reports and re-certification will be due early in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

APPENDIX D: Author Guideline from the South African Medical Journal

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.
Do not replicate data in tables and in text .

Structured abstract

This should be 250-400 words, with the following recommended headings:

- Background: why the study is being done and how it relates to other published work.
- Objectives: what the study intends to find out
- Methods: must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.

- Results: first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
- Conclusion: must be supported by the data, include recommendations for further study/actions.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomization, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:

- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

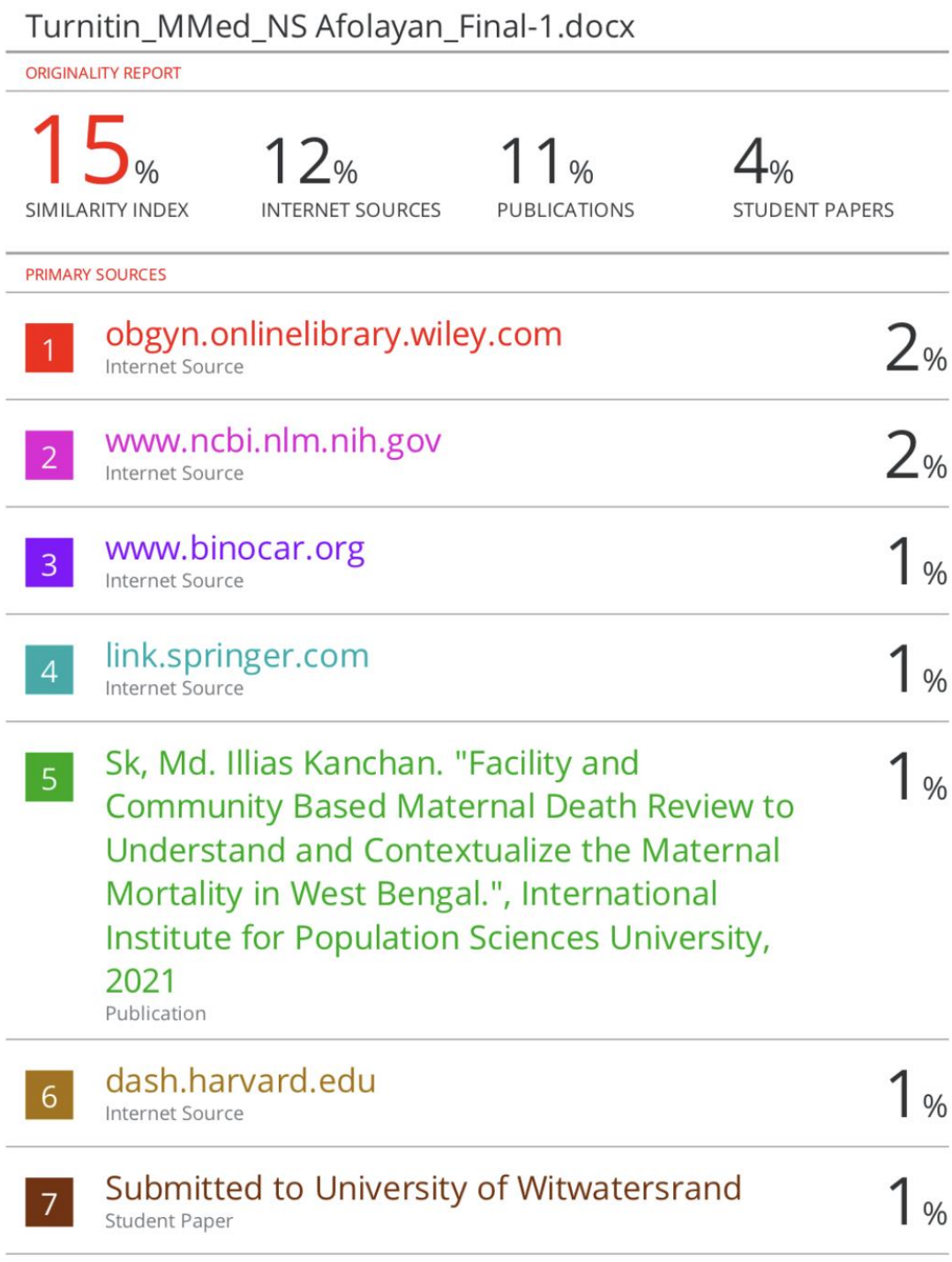
This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state ‘none’.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).

- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

APPENDIX E: Turnitin plagiarism report



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