MATERNAL DEATHS DUE TO HYPERTENSIVE DISORDERS IN PREGNANCY: A FOUR YEAR REVIEW IN A TERTIARY HOSPITAL

MMed in Obstetrics and Gynaecology

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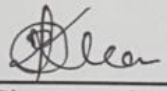
This research reported is submitted to the University of the Witwatersrand Health Sciences Faculty in partial fulfilment of the degree of Master of Medicine in Obstetrics and Gynaecology

Johannesburg, May 2023

Declaration

I, Dr Zeenat Lenina Khan, hereby declare that this research is my work and I am the main author. My supervisors Professor Hlengani Lawrence Chauke and Dr Gaynor Miranda Balie conceptualized the study. I developed the protocol and wrote the manuscript with input from my supervisors.

I am submitting this research report for the degree of Masters of Medicine in Obstetrics and Gynaecology at the University of Witwatersand, Johannesburg. This research report has not been submitted before for any degree or examination at this or any other university. This MMed research report is submitted in the format 1of a submissible research article. The article conforms to the author guidelines for the South African Journal of Obstetrics and Gynaecology.



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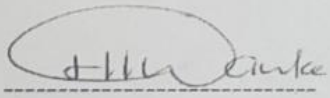

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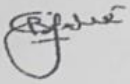

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Dedications

This MMed is dedicated to my mentor and sister Dr Rushdah Lariza Khan who was always available for advice and motivation throughout this degree.

Presentations

SASOG 2022, Cape Town- Poster presentation on 28/11/2022

Abstract

Background

Hypertensive disorders of pregnancy (HDP) are leading causes of maternal mortality worldwide. In South Africa (SA) they account for the second most important cause of maternal mortality. Despite its prevalence and devastating consequences, no progress has been made in reducing deaths due to HDP during the last decade.

Objectives

The aim of this research study is to describe maternal deaths due to complications arising from HDP, in a tertiary hospital, specifically looking at maternal characteristics, management, timing, causes and avoidable factors.

Methods

This is a retrospective cross-sectional study involving a review of patient records at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) between January 2015 and December 2018. Patient files were retrieved from records, captured onto an Excel Spreadsheet and analysed using basic statistics.

Results

Patients that died were young, booked early and attended antenatal care. Few patients had risk factors for HDP but aspirin prophylaxis was not given. Antihypertensive treatment as well as Magnesium Sulphate (MgSO4) was often not initiated appropriately. Eclampsia was the most common cause of death and 87% of patients died in the post-partum period.

Conclusions

Early, quality antenatal care, early detection of disease, referral to the appropriate level of care and adequate treatment as well as timely delivery is necessary to reduce maternal deaths due to HDP. Large scale studies are needed to identify specific quality of care issues at all levels of care in order to implement measures to improve the outcomes.

Key words

Eclampsia, Maternal Morbidity, Maternal Mortality, Pre-eclampsia

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I would like to express my sincere gratitude to my supervisors; Professor HL Chauke and Dr GM Balie for their guidance, immense motivation and support throughout this research project.

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List of abbreviations

ANC- Antenatal care

BMI- Body Mass Index

BP- Blood pressure

CHC- Community Health Clinic

CMJAH- Charlotte Maxeke Johannesburg Academic Hospital

CPR- Cardiopulmonary resuscitation

DBP- Diastolic blood pressure

DH- District Hospitals

DM- Diabetes mellitus

DIC- Disseminated intravascular coagulopathy

EGA- Estimated Gestational age

GCS- Glasgow Coma Scale

GHPT- Gestational hypertension

HCA- High care area

HDP- Hypertensive disorders of pregnancy

HHD- Hypertensive heart disease

PCP- Pneumocystis carinni Pneumonia

ICU- Intensive Care Unit

iMMR- Maternal mortality ratio

IQR- Interquartile ratios

LDA- Low dose aspirin

LMIC- Low and Middle income countries

MgSO4- Magnesium Sulphate

MMR- maternal mortality rate

MUAC- Mid upper arm circumference

NPRI- Non-pregnancy related infections

NVD- Normal vaginal delivery

OH- Obstetric Haemorrhage

PCP- Pneumocystis Carinii~~Carinni~~ Pneumonia

PPCMO- Peri-partum cardiomyopathy

SA- South Africa

SBP- Systolic blood pressure

SSA- Sub-Saharan Africa

UPCR-Urine protein to creatinine ratio

WHO- World Health Organization

Journal article

MATERNAL DEATHS DUE TO HYPERTENSIVE DISORDERS IN PREGNANCY: A FOUR YEAR REVIEW IN A TERTIARY HOSPITAL

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Key words

Eclampsia, Maternal morbidity, Maternal mortality, Pre-eclampsia

Introduction

Maternal morbidity and mortality are global concerns and hypertensive disorders of pregnancy (HDP) are amongst the leading causes. According to the World Health Organization (WHO), 14% of maternal deaths were due to HDP worldwide [1]. The incidence of HDP ranges from 4 to 25 % and is still high in developing countries [2]. In 2015, approximately 99% of the global maternal deaths were from low and middle-income countries (LMICs), with Sub-Saharan Africa (SSA) accounting for roughly 66% [3]. Obstetric haemorrhage (OH), HDP and non-pregnancy related infections (NPRI) are the leading causes of maternal death in SSA [4]. In South Africa (SA), the maternal mortality ratio (MMR) for the 2017-2019 triennium was 113.8 per 100,000 live births [5]. HDP account for 18% of all maternal deaths [6] and were the second most common cause of maternal deaths [5]. HDP has increased in importance as a cause of potentially preventable deaths, while management of the two other major conditions has improved in the last 10 years [7].

Africa has the highest age-standardized prevalence of hypertension with 46% of adults older than 25 years being affected [8]. Preeclampsia is seen at a greater rate at the extremes of age with the highest incidences below 20 and above 35 [5]. There are greater rates of pre-eclampsia in nulliparous women, obesity, and multiple gestations [9]. Eclampsia and pre-eclampsia are the most common categories of HDP associated with maternal death [6]. Pulmonary oedema, renal failure, respiratory failure, and intra-cranial haemorrhage are the final causes of deaths in most cases [6].

In SA, 62.4% of maternal deaths and 70% of deaths related to HDP were potentially avoidable from 2016-2019 [5]. The vast majority of patients that died from HDP attended antenatal clinics, suggesting quality of care issues [5]. Major medical care problems were assessment and recognition of problems at community health clinics (CHC) and district hospitals (DH) and not following standard protocols at DH, regional hospitals, and tertiary hospitals. Inappropriate treatment of high blood pressure (BP), failure to identify patients at risk of complications, incorrect triage of patients, delays in seeking specialist advice and transport delays for referrals to a higher level of healthcare were all concerning avoidable factors [10]. Major administrative factors also contributed to maternal death in the last triennium, HDP being one of the conditions most affected by this [5].

HDP are devastating diseases and unfortunately, no progress has been made in reducing deaths during the last decade [7]. In SA, there is limited data on mortality rates from HDP and further research in this area could assist clinicians in early identification and escalation of care for such women at risk. There was previously no study that had investigated patient cases at CMJAH or within its cluster. This research study had aimed to fill this void by investigating maternal deaths arising from hypertension among pregnant women at this tertiary hospital.

Method

This is a retrospective cross-sectional study involving a review of patient records. The study site, Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), is a central hospital with 1088 beds accommodating patients from the Gauteng province as well as the neighbouring provinces. It offers level 3 and level 2 inpatient and specialist outpatient services and serves as a referral hospital to over 10 facilities. The target sample was women who died at CMJAH during pregnancy or in the puerperium due to complications of HDP which occurred in the study period.

A summary of the maternal deaths that occurred at CMJAH in patients with HDP, was compiled from patient records from the 1st of January 2015 to the 31st of December 2018, and included in the review. Maternal characteristics, causes of deaths and management of patients were collected into the data collecting sheet designed for this study. This was exported onto an excel spreadsheet and simple statistics were calculated, which included medians, interquartile ranges (IQR), ranges and percentages.

Results

There were 70 maternal deaths during the study period. HDP were identified in 23 (33%) patients. The maternal characteristics, past medical and obstetric history as well as booking information are summarised in Table 1.

Table 1: Maternal characteristics of patients with HDP

Description	n (%) or median (IQR; range)
Age in years (n=23)	27 (23-31; 18-39)
Previous Normal Vaginal Delivery (NVD)	9 (50%)

(n=18)	
Previous Caesarean (n=18)	3 (16.7%)
Median parity (n=23)	1(0-2; 0-2)
Booking status (n=21)**	
Booked	16 (76.2%)
Unbooked	5 (23.8%)
Estimated Gestational Age (EGA) in completed weeks at booking (n=14)	15 (11.75-22.25; 6.0-30)
EGA in completed weeks at first presentation to health care facility (n=23) (booked and unbooked patients)	21(14-30; 6-36)
Booking variables	
HIV positive (n=22)	6 (27.3%)
CD4+ cell count (cell/uL) n=5*	157 (77.5-296.5, 66-362)
Systolic Blood Pressure (SBP) (at first presentation to health care facility (mmHg) (n=13)	135 (114-178; 104-238)
Diastolic Blood Pressure (DBP) at first presentation to health care facility (mmHg)	79 (69-94; 60-139)
Body Mass Index (BMI) (kg/m^2) (n=8)	33.5 (26.5-36.5; 19.5-49.9)
Co-morbidities	
Chronic Hypertension (CHPT) (n=22)	3(13.6%)
Diabetes Mellitus (DM) (n=21)	1 (4.8%)
Previous Gestational Hypertension (GHPT) (n=18)	4 (22.2)
Time interval between referral and arrival at CMJAH (minutes) (n=14)	117.5 (102.3-312.3; 27-672)
Anti-hypertensive initiated at booking	1 (6.3%)
Low Dose Aspirin (LDA) initiated at booking	1 (6.3%)
Number of Antenatal Care (ANC) visits (n=20)	3 (0.3-5; 0-6)

EGA at diagnosis of HDP (n=23)	30 (25-35; 19-39)
SBP at diagnosis (n=21)	177 (143.5-208; 134-241)
DBP at diagnosis (n=21)	103 (91.5-118.5; 74-165)

*Only one patient had a viral load documented which was 165 750 copies/ml

** The N value is 21 and not 23 because two patients arrived to CMJAH without any history or antenatal card and their booking status could not be determined with the available records.

The median age of death was 27. There were 10 (43.5%) patients with at least one risk factor for HDP. Information to calculate BMI was available for 8 patients and 7 were classified as overweight to obese. The median BMI was 33.5kg/$m^{2.}$ Only 3 (13.6%) patients had CHPT and 1 (4.8%) had type 1 DM. Previous GHPT with proteinuria was identified in 3 (13%) patients. The median parity was 1 with 6 (26.1%) patients being nulliparous.

There were 16 (76.2%) booked and 5 (23.8%) unbooked patients. The median number of ANC visits was 3 and 9 (56.3%) patients attended 4 or more visits. The median EGA at booking was 15 weeks. The median SBP and DBP at presentation to a health care facility were 135mmHg and 79mmHg respectively. The medical and obstetric management at the referral hospitals and CMJAH is summarised in Table 2.

Table 2: Medical and obstetric management at referring centre and CMJAH

	Referring centre	**CMJAH**
Description	**n (%) or median (IQR; range)**	**n (%) or median (IQR; range)**
SBP (mmHg)	(n=15) 170 (151-196; 130-241)	(n=22) 149.5 (136.8-183; 101-238)
DBP (mmHg)	(n=15) 110 (96-122; 80-163)	(n=22) 103.5 (89-124; 65-165)
Proteinuria on urine dipstick	(n=17) 17 (100%)	(n=21) 19 (90.5%)
Spot Urine protein to creatinine Ratio (UPCR) (mg/mmol)		(n=5) 0.52 (0.21-0.65; 0.20-0.72)
Signs and Symptoms of	(n=17)	(n=23)

Severity	15 (88.2%)	16 (69.6%)
Seizures	3 (20%)	6 (37.5%)
Frontal headache	5 (33.3%)	4 (25%)
Epigastric pain	3 (20%)	4 (25%)
Visual disturbance	1 (6.7%)	3 (18.8%)
BP > (160/110)	10 (66.7%)	10 (62.5%)
Glasgow Coma Scale (GCS) less than 15	3 (20%)	7 (43.8%)
Urgent Antihypertensive Treatment †	(n=18)	(n=23)
Nifedipine	6 (33.3%)	6 (26.1%)
Labetalol		(n=23) 7 (30.4%)
Prevention of Eclampsia	(n=15)	(n=23)
MgSO4 given	10 (66.7%)	13 (56.5%)
Loaded	10 (66.7%)	9 (39.1%)
Maintenance	7 (46.7%)	11 (47.8%)
Anti-hypertensive initiated	(n=18)	(n=23) 15 (65.2%)
First line	9 (50%)	15 (100%)
Amlodipine	1 (11.1%)	5 (33.3%)
Methyldopa	8 (88.9%)	4 (26.7%)
Labetalol		5 (33.3%)
Adalat XL		1 (6.7%)
Second line		4 (26.7%)
Third line		2 (13.3%)
Maternity High Care Area (HCA)		(n=23) 18 (78.3%)
Duration (min)		(n=13) 870 (569.5-1440; 35-4320)
Intensive Care Unit (ICU)		(n=23) 12 (52.2%)
Duration (min)		(n=9)

		1440 (1124-10800; 350-17280)

† No Labetalol or Hydralazine at referring centre

There were 18 (78.3%) referrals, 9 (50%) from level 1, 8 (44.41%) from level 2 and 1 (5.6%) from level 3 facilities. The median SBP and DBP at referring centres were suggestive of acute severe hypertension. All patients referred had proteinuria and thus were presumed to have pre-eclampsia. The most common sign of severity was an acute severe BP reading. Other common symptoms of severity were symptoms of imminent eclampsia (60%) and seizures (20%). Long acting anti-hypertensives were given to 9 (50%) patients. There were 9 patients that were not given any long acting antihypertensive treatment at the referring centre. Nifedipine was given to 6 (33.3%) patients. There were 5 patients with acute severe BP readings that were referred without receiving a short acting anti-hypertensive. A loading dose of MgSO4 was given to 10 (66.7%) patients and 7(46.7%) were given intramuscular MgSO4 maintenance before transfer. There were 8 patients referred that required but were not given any MgSO4 and 2 patients were loaded with MgSO4 but not given maintenance for transfer.

The median interval between referral and arrival time was 117.5 minutes with the longest interval being 672 minutes. Only one patient arrived at CMJAH within in 30 minutes of referral and 6 patients arrived more than 120 minutes after referral. The median SBP and DBP at admission to CMJAH were respectively 149.5 mmHg and 103.5mmHg. These values are lower than those at the referring centres. Symptoms or signs of severity were detected in 16 (69.6%) patients of which 10 (62.5%) had an acute severe BP. The GCS was less than 15 in 7 (43.8%) patients. Symptoms of imminent eclampsia were present in 11 (68.7%) patients and 6 (37.5%) had seizures.

There were 18 (78.3%) patients admitted to maternity HCA with a median duration of admission of 870 minutes and 12 (52.2%) admitted to ICU with a median duration of 1440 minutes. A stat dose of Nifedipine was given to six (26.1%) patients while seven (30.4%) received Labetalol during their admission. A loading dose of MgSO4 was given to nine (29.1%) patients and 11 (47.8%) had maintenance MgSO4. Anti-hypertensives were initiated for 15 (65.2%) patients. Intravenous Labetalol was given to five (33.3%) patients as their first line therapy and 4 (26.7%) patients received an additional agent.

The most common complication was renal dysfunction with 17 (77.3%) patients presenting with elevated urea and creatinine levels; this was followed by HELLP Syndrome (65.2%), eclampsia (39.1%), intracranial haemorrhage (17.4%), pulmonary oedema (13%) and sub-capsular haematoma (8.7%). Table 3 shows the outcomes of patients at CMJAH.

Table 3: Outcomes at CMJAH

Description	**n (%) or median (IQR; range)**
EGA at delivery (n=20)	32 (29.3-36; 20-39)
Mode of delivery (n=20)	
NVD	4 (20%)
Caesarean Section	16 (80%)
Maternal Complications of HDP (n=23)	23 (100%)
Renal failure	17 (73.9%)
HELLP Syndrome	15 (65.2%)
Eclampsia	9 (39.1%)
Intracranial haemorrhage	4 (17.4%)
Pulmonary oedema	3 (13.0%)
Sub-capsular hematoma	2 (8.7%)
Acute Fatty Liver	1 (4.3%)
Abruptio Placenta	1(4.3%)
PPCMO	1(4.3%)
HHD	1 (4.3%)
Cerebral oedema	0 (0)
Post mortem (n=23)	
Done	2 (8.7%)
Not done	21 (91.3%)
Place of death (n=23)	
General ward/admissions	4 (17.4%)
Maternity HCA	7 (30.4%)
ICU	12 (52.2%)
Day of death post delivery (n=20)	4 (1-8; 0-16)

Cause of death (n=23)	
Eclampsia	6 (26.1%)
HELLP Syndrome	5 (21.7%)
Intracranial bleed	4 (17.4%)
Pulmonary Embolism	2 (8.7%)
Pneumocystis carinii pneumonia (PCP)	1 (4.3%)
Cryptococcal meningitis	1 (4.3%)
Renal failure	1 (4.3%)
Acute Fatty Liver	1(4.3%)
Disseminated Intravascular Coagulopathy (DIC)	1(4.3%)
PPCMO	1(4.3%)
Cardio Pulmonary Resuscitation (CPR) performed (n=21)	16 (76.2%)

Eclampsia (26.1%) was the leading cause of death, followed by HELLP Syndrome (21.7%) and intracranial haemorrhage (17.4%). CPR was performed on 16 (76.2%) patients and was not performed in 5 (23.8%) cases. The prognosis was poor for 1 patient and another patient was established to be brain dead prior to demise. The reasons for not performing CPR are unclear in the other 3 cases. There were 20 (87%) post-partum deaths and three (13%) ante-partum deaths. Most patients died in ICU (52.2%). The median day of post-partum death was day 4.

Discussion

In this study women that died were young. The interquartile range for age was 23-31 which is not in keeping with the distribution of age generally associated with HDP. A study by Wang et al found that the age group of 25-29 years old had the lowest incidence rate of HDP, but higher rates were observed in oldest and youngest age groups [12]. According to the Saving Mother's report (2017-2019), the extremes of age had the greatest iMMR for HDP [2]. In a study done in Norway by Nyflot et al, women that had died from HDP were younger than those that had died from other causes [13]. A study in Western Saudi Arabia showed that

multigravid women more commonly had HDP which comprised 56.7% of cases in their study [12] but a similar study done in India, by Chaudry et al showed that 68% of cases were nulliparous [1]. It is accepted that nulliparity is a risk factor for pre-eclampsia. Our study only looked at patients that died at CMJAH during the study period and not all patients diagnosed with HDP, which may account for our findings that more patients were multiparous (73.9%) however the median parity was 1 which is a low parity.

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In this study most patients did not have risk factors for HDP. Risk factors for HDP were identified in only 10 patients. Only eight patients had the relevant information to calculate BMI in our study but the median BMI classified most of these patients as overweight to obese. A study, analysing temporal changes in MMR showed that increasing rates of obesity played a significant role in the changes in hypertension related MMR [14]. Emergency caesarean sections were performed in 80% of patients and 20% had a normal vaginal delivery. Chaudry et al found that the most common mode of delivery in patients with HDP was lower segment caesarean section in 59% of the cases [1].

Nyflot et al found that deaths from HDP in many cases were avoidable as they are associated with substandard care [13]. According to the last Saving Mothers Report, quality of care issues did play a role in most deaths related to HDP [5]. There were multiple issues identified with the management of patients in this study. Most patients had booked early at a median gestation of 15 weeks. The median number of ANC visits was 3 and 9 (56.3%) booked patients attended 4 or more visits. Frequent antenatal visits with regular follow up of patients are essential as it helps in the early diagnosis and management of preeclampsia and prevents the development of complications [1]. Studies have shown that low-dose aspirin among women with risk factors for preeclampsia is useful in preventing pre-eclampsia [14]. A South African guideline in 2019 by Moodley et al also advocates for initiation of aspirin as well as calcium carbonate to prevent HDP [7]. Women with risk factors for HDP in this study were not given aspirin.

While there are no specific guidelines for the appropriate time intervals for inter-hospital transfer, in many cases, the times from referral to transfer were over 120 minutes. Delays in referral and transfer result in delays in diagnosis and management. The acute management of severe hypertension includes the administration of 10mg of quick-acting Nifedipine which is to be repeated after 30 minutes if the blood pressure does not drop below 160/110 [7]. Only

6 of the 10 patients with acute severe blood pressure readings at the referral centres received a fast acting antihypertensive before transfer.

Long acting anti-hypertensives were only given to 9 (50%) patients. The mortality rate from eclampsia has decreased by 46% and the risk of eclampsia is reduced by half in patients receiving treatment with MgSO4 [15]. There were 8 patients referred that required but were not given any MgSO4 and 2 patients were loaded with MgSO4 but not given maintenance for transfer.

The most common complication of HDP in this study was renal dysfunction. A retrospective cohort study in Canada suggests that this could be due to fluid restrictive protocols and antihypertensive treatment [16]. In a study from Ethiopia looking at predictors of maternal mortality, elevated creatinine levels were a strong and independent predictor of maternal death [17]. In a systematic review in Ethiopia, commonly reported complications with HDP included renal damage, pulmonary oedema, HELLP syndrome and placental abruption [18]. In this study 14 (63.6%) patients had HELLP syndrome, 10 (45.5%) had eclampsia and 4 (18.2%) patients had an intracranial haemorrhage. Chaudhary et al found that the most common maternal complication was eclampsia [1].

Schutte et al noted that cerebral haemorrhage was the leading cause of death in patients with HDP and most cases were associated with high SBP and low platelet counts [19]. In another study done in Norway, it was found that pulmonary oedema was as common as intracranial haemorrhage [13]. In this study, eclampsia was the leading cause of death; followed by HELLP syndrome and then intracranial haemorrhage.

In view of the devastating outcomes due to HDP we recommend that patients be educated regarding the importance of early booking and regular antenatal visits. Health care workers should be trained to screen for HDP and early referral is encouraged. Aspirin prophylaxis must be initiated early, which would imply nurse-initiated prescriptions. Guidelines should be accessible and followed by health care workers to reduce gaps in patient management.

Missing records and inadequate documentation were limitations related to this being a retrospective study. The database that documents the official cause of death did not have this information recorded for the years of this study and so it was taken from the death

notification forms filled out by registrars. The sample size was small, yielding information that is not statistically significant.

Conclusions

HDP remains a significant cause of maternal mortality. There were definite gaps in management. Most patients were young, booked early and did not have risk factors. Aspirin and antihypertensive treatment were not initiated appropriately. Early, quality antenatal care, early detection of disease, referral to the appropriate level of care and adequate treatment as well as timely delivery is necessary to reduce maternal deaths due to HDP. Management, treatment and referral guidelines are available at all levels of care and medical staff should be familiar with guidelines and trained in prompt and appropriate management of patients with HDP. Furthermore, large scale studies should be undertaken to assist in identifying areas of concern.

Declaration: This study was done in partial fulfillment of a MMed (Obs & Gynae) degree.

Author contributions: HLC and GMB conceptualized the study; ZLK developed the protocol with input from HLC and GMB. ZLK collected data. ZLK wrote the manuscript with input from HLC and GMB. All authors approved the manuscript for publication.

Ethics Considerations: Ethical approval from the human research ethics committee of the University of the Witwatersrand was obtained. Protocol number: M200765, Authorization from the CEO at CMJAH was obtained.

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Appendix A: Approved Research Protocol

Maternal deaths due to hypertensive disorders in pregnancy: A four-year review in a tertiary hospital

A research proposal presented to the

Human Research Ethics Committee, Faculty of Health Sciences, University of the Witwatersrand as a fulfilment for the degree of

MMed in Obstetrics and Gynaecology

Dr ZL Khan

Student Number: 306704

Supervisor: Dr HL Chauke

Co-Supervisor: Dr GM Balie

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INTRODUCTION

The World Health Organization (WHO) defines a maternal death as "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes". [1] Complications that arise from hypertensive disorders in pregnancy (HDP) are very large contributors of maternal death globally, accounting for about 30,000 deaths annually. [2, 3]

Approximately 18% of all admissions to King Edward VIII Hospital, Durban, consist of HDP [4] and hypertension was a complication in 12% of all pregnancies in the Durban metropolitan area. [5] According to Moodley (2007), it is therefore, not surprising that complications associated with HDP are common, not only in the province of KwaZulu-Natal, but also in the rest of the country. [6]

According to the latest Saving Mother's report, in South Africa, the overall maternal mortality rate for hypertension was 24.01/100 000 live births compared to a rate of 22.75/100 000 live births from 2011 to 2013. [7] When comparing the last three trienniums, the overall number of maternal deaths has reduced, however, those due to HDP have increased by 14% over that time period. [7]

In the latest triennium there were 661 maternal deaths associated with HDP. [7] Pulmonary oedema, renal failure, respiratory failure and intra-cranial haemorrhage were the final causes of deaths in most cases. The severe impact of pre-eclampsia on the brain was highlighted by the fact that additionally to intracranial haemorrhage, there were a number of deaths due to unspecified cerebral problems and cerebral coning secondary to cerebral oedema. [7] The most common final cause of hypertensive deaths were in fact cerebral complications. A report from the United Kingdom (UK), 'Why Mothers Die' reports that cerebral haemorrhage was also the most common cause of death. There was also a similar recommendation as the Saving Mother's Report, made with regards to the need to lower very high systolic blood pressures. [8]

Sixty-six per cent of all maternal deaths in the last triennium were found to have a significant avoidable factor. [7] Another significant contributor to maternal deaths was referral problems. In 19% of cases of those due to HDP, a delay in transport between facilities was found to be a contributing factor. Discharging of patients prematurely and not having adequate follow-up in the post partum period was found to be a major problem. In 34% of women who died due to HDP, a lack in skilled doctors was noted. [7\]

An avoidable factor that was noted in a previous Saving Mother's Report (1999-2001) was absence of monitoring in all phases of pregnancy, including the antenatal period, labour, and in particular, the postpartum period. [9] Research has emphasised that monitoring of vital signs should be done regularly at all times in the acute phase of the condition. Patient's need to be assessed thoroughly, having their pulse rate, respiratory rate, Glasgow coma scale, blood pressure, fluid balance, urinary output and blood coagulation parameters measured regularly. [4] Automatic blood pressure machines are used commonly in South Africa. They tend to underestimate blood pressure values and therefore need to be checked regularly. [10]

In the United States of America, an increasing number of women are experiencing HDP due to other factors. Delayed childbearing, the use of assisted reproductive technologies and the rising obesity epidemic are all contributors to this. Despite this however, there are declines in hypertension-related mortality. [11] Between 1998 and 2006, the number of hospitalisations for HDP increased from 67.2 per 1,000 deliveries to 81.4 per 1,000 deliveries. This increase was mostly related to chronic hypertension (50% increase). [12] There was a rise in preeclampsia/eclampsia from 9.4 to 12.4 per 1,000 deliveries. Severe forms of preeclampsia were related to 38% of hospitalizations for acute renal failure and 19% to 24% of hospitalizations with complications involving pulmonary dysfunction/oedema, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy (DIC) and cerebrovascular accidents. Death resulted from 14% of the hospitalizations. [11] Furthermore, according to a recent report from the Centers for Disease Control and Prevention, hypertensive disorders were responsible for 6.6% of deaths during pregnancy, 9.3% of deaths within 42 days of pregnancy and 5.4% of deaths happening between 42 days and 1 year. [13]

In South Africa, there is a limited epidemiological consensus regarding mortality rates emanating from hypertensive disorders among pregnant women. Based on the above debilitating statistics and considerations regarding mortality profiles of women arising from hypertensive related complications in pregnancy, causes and avoidable factors, further research in this area could assist clinicians in early identification and escalation of care for such women at risk. There is currently no study that has investigated patient cases at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) or within its cluster. As such, this research study aims to fill this research void by investigating maternal deaths arising from hypertension among pregnant women.

Aim and Objectives

The aim of this research study is to assess maternal deaths in a tertiary hospital due to complications arising from hypertension during pregnancy.

Specifically, the aim is to investigate the following objectives:

1. To describe the maternal characteristics of women who died due to complications of HDP at CMJAH during the study period.
2. To determine the timing of these maternal deaths.
3. To describe medical and obstetric management of the women who had died.
4. To determine whether there were avoidable factors.
5. To determine the main complications arising from HDP

MATERIALS AND METHODS

Research Design and Site of Study

This is an epidemiological research study in which a retrospective review of patient records and files will be employed. A summary of each of the maternal deaths that took place at CMJAH which was discussed and recorded during the daily audit meetings, between January 2015 and December 2018, will be investigated and included in the review. The study site, CMJAH, is a central hospital. It has 1088 beds accommodating patient from the Gauteng province as well as the neighbouring provinces. It offers mainly level 3 and level 2 inpatient and specialist outpatient's services. It also serves as a referral hospital to over 10 other facilities and thus a vast number of patients are managed at CMJAH.

Study Population and Sampling

The target sample for this study will comprise of all the maternal deaths at CMJAH due to complications of hypertensive disorders in pregnancy which occurred between January 2015 and December 2018, regardless of age of the patient. Patients with incomplete patient files, data or records will be excluded from the study.

Procedure

The departmental maternal deaths data will be used to identify maternal deaths due to complications arising from hypertension. Patient's files will be retrieved from patient records

at the hospital. Maternal characteristics, causes of deaths, management of patients and avoidable factors will be collected into the data capturing form (Appendix A)

Data collection

The following demographical and medical information will be captured: age, gravidity, previous pregnancies and complications, medical and surgical history, social history, marital status, alcohol and smoking history. In addition, index pregnancy information will also be sourced which includes the following: The number of antenatal visits attended, timing of first visit, booking bloods, blood pressure at booking, presence of proteinuria, intervals between index pregnancy and the preceding one.

Furthermore, management data will also be captured: Referral /self-referral to CMJAH, location of initial management, management at the referring hospital/clinic, time from referral to arrival if available. The following information will be obtained from the patient's admission to CMJAH: Blood pressure, presence of proteinuria, haematology and biochemistry (Haemoglobin, platelet, aspartate aminotransferase or alanine transaminase and urea or creatinine) results, initiation and dosages of anti-hypertensive treatment, initiation and total dose of magnesium sulphate, high care or intensive care unit (ICU) admission, aetiology of deaths, timing of death and avoidable factors.

Data Analysis

The patient's data from files will be captured and exported on to a Microsoft Excel spreadsheet. Simple descriptive statistics will be used to describe the data set.

Limitations

This research study is retrospective in nature. As such, old files will be collected. It is possible that files may be missing or information needed may not be available from files sourced.

Ethical considerations

Data will be anonymous and the patient's details will not be recorded elsewhere. The study will still adhere to the ethical procedures enforced by the Human Research Ethics Committee at the University of the Witwatersrand. The study will be registered with the Human Resource Development Council. Only the researcher and supervisors will have access to it. The results will be written into a research report that will be assessed. All information pertaining to the study will be managed to ensure confidentiality of the attained information.

Timing

The expected time frame for the study is presented in the Gantt chart below.

	2019			2020											
	Oct	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Proposal development															
Departmental submission															
Ethic & HDC submission															
Data Collation															
Data analysis															
Writing dissertation															
Language editing															
Submission															

Budget

A breakdown of running costs for this study is presented in the table below:

Stationary	Cost
Paper	R 300
Printing	R1200
Total	R1500

LIST OF ABBREVIATIONS

ARDS: Acute Respiratory Distress Syndrome

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

DIC: Disseminated Intravascular Coagulopathy

HDP: Hypertensive Disorders in Pregnancy

ICU: Intensive Care Unit

WHO: World Health Organisation

Protocol References

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Appendix B: Data Capturing Form

Demographics

Age	
Gravidity	
Parity	

Past Medical History

Chronic Hypertension	NO	YES	
Diabetes	NO	YES	
Other	NO	YES	Specify:

Past Obstetric History

Year						
Caesarean Section						
Normal Vaginal Delivery						
Assisted Delivery						

Previous Gestational Hypertension	NO	YES	Specify:				
Proteinuria	NO	YES					
Maternal Complication of hypertensive disorder	NO	YES	Eclampisia	Cerebral oedema	Pulmonary Oedema	HELLP Syndrome	Other:

Foetal Complications of hypertensive disorder	NO	YES	Intra-uterine growth restriction	Intra-uterine foetal death	Pre-term delivery	Other

Index Pregnancy

Gestation at booking (weeks)	
Number of Antenatal Visits	
Rhesus	
RPR	
HIV status	
Haemoglobin (g/dl)	
Height (cm)	
Weight (kg)	
Mid upper arm circumference (cm)	

Gestation at diagnosis of hypertensive disorder							
Type of hypertensive disorder	Chronic Hypertension	Gestational Hypertension with proteinuria	Gestational Hypertension without proteinuria	Unclassified Hypertension	Other:		
Complications of hypertensive disorder	NO	YES	Eclampsia	Cerebral oedema	Pulmonary oedema	HELLP syndrome	Other

Referral to CMJAH

Referred	NO	YES	Referral centre:	Level:
Time and date				

of referral						
Systolic Blood Pressure						
Diastolic Blood pressure						
Proteinuria	NO	YES				
Symptoms of severity	NO	YES	Frontal headache	Epigastric pain	Visual Disturbances	Other
Nifedipine given	NO	YES	Dose:			
Labetalol given	NO	YES	Dose/Duration:			
Magnesium Sulphate given	NO	YES	Dose/Duration:			

Admission to CMJAH

Time and date of arrival			
Interval between referral and arrival			
Systolic blood pressure			
Diastolic Blood pressure			
Proteinuria	NO	YES	
Spot Urine PCR	NO	YES	Value:
24 hour Urine	NO	YES	Value:

collection for proteinuria						
Symptoms of severity	NO	YES	Frontal headache	Epigatric pain	Visual disturbances	Other
Nifedipine given	NO	YES	Dose			
Labetalol given	NO	YES	Dose/Duration			
Loaded with Magnesium sulphate	NO	YES				
Maintained on Magnesium Sulphate	NO	YES	Dose/Duration			
Anti-hypertensive initiated	NO	YES	First Line	Second Line:	Third line:	Other:
Maternity High Care Area Admission	NO	YES	Duration			
Intensive Care Unit Admission	NO	YES	Duration			

Blood results

Blood Test	Admission	Last Available
Haemoglobin		
Platelet Count		
Urea		
Creatinine		
Aspartate Amino Transferase		

Alanine transaminase		
Haptoglobin		
Lactate Dehydrogenase		

Maternal Death

Time of death							
Complications of hypertensive disorder	NO	YES	Eclampsia	Cerebral Oedema	Pulmonary Oedema	HELLP syndrome	Other :
Post Mortem done	NO	YES	Cause of death:				
Cardio-pulmonary Resuscitation performed	NO	YES					

Appendix C: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Zeenat Khan

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M200765

NAME: (Principal Investigator)	Dr Zeenat Khan
DEPARTMENT:	Obstetrics and Gynaecology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Maternal deaths due to hypertensive disorders in pregnancy: A four-year review in a tertiary hospital
DATE CONSIDERED:	31/07/2020
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr GM Balie and Prof HL Chauke
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	30/11/2020

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

Appendix D: Author Guidelines

Author Guidelines (SAJOG)

Article Processing Charges

All articles published in the South African Journal of Obstetrics & Gynaecology are open access and freely available online upon publication. This is made possible by applying a business model to offset the costs of peer review management, copyediting, design and production, by charging an article-processing charge (APC) of R2 730.50 (ex vat) for short articles and R5 787 (ex vat) for full-length articles published. The charge applies only to articles submitted after 1 Jan 2020. The APC is standard and does not vary based on length, colour, figures, or other elements.

When submitting a Research article to the SAJOG, the submitting author must agree to pay the APC should the article be accepted for publication. The APC is payable when your manuscript is editorially accepted and before production commences for publication. The submitting author will be notified that payment is due and given details on the available methods of payment. Prompt payment is advised; the article will not enter into production until payment is received.

Queries can be directed to claudian@samedical.org

Authorship

Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conceptualisation, design, analysis and interpretation of data; (ii) drafting or critical revision of important scientific content; or (iii) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an

article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Protection of rights to privacy

Research Participants

Information that would enable identification of individual research participants should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

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Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or

ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that it is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

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Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this requirement are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

• An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.

• Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.

• Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

• Manuscripts must be written in UK English (this includes spelling).

• The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.

• 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)'.
• 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.
SAJOG is a general specialist obstetrics and gynaecology journal, therefore for articles involving genetics, it is the responsibility of authors to apply the following:
- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.
** NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.
- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'
- Use the latest approved gene or protein symbol as appropriate:
o Human Gene Mapping Workshop (HGMW): genetic notations and symbols
o HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
o OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
o Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)
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 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. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. 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. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

• May include up to 3 illustrations or tables.

• A max of 20 - 25references

Structured abstract

• This should be no more than 250 words, with the following recommended headings:

o Background: why the study is being done and how it relates to other published work.

o Objectives: what the study intends to find out

o Methods: must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data.

o 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.

o Conclusion: must be supported by the data, include recommendations for further study/actions.

• Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.

• Do not include any references in the abstracts.

Here is an example of a good abstract.

Scientific letters/short reports

These are shorter length, scholarly research articles of no more than 1500 words, and include case reports.

Guideline word limit: 1 500 words

• Abstract: Structured, of about 150 words, with the following recommended headings: Background, Objectives, Methods, Results, and Conclusion.

• May include only one illustration or table

• A maximum of 8 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

• expert opinion

• personal clinical experience

• observational studies

• trials

• systematic reviews.

Review articles

Review articles should always be discussed with the Editor prior to submission.

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a précis of reviews published in the international literature

Please ensure that your article includes:

• Abstract: unstructured, of about 100-150 words, explaining the review and why it is important

• Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.

• When writing: clarify the evidence you used for key statements and the strength of the

evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.

• Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the SAJOG or to a topical issue of particular relevance to the journal's readership

• May include only one illustration or table

• Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

• If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.

• Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.

• Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).

• All images must be of high enough resolution/quality for print.

• All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.

• Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.

• Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

• Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.

• Embed/include each table in the manuscript Word file - do not provide separately as

supplementary files.

• Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.

• Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.

• Ensure each table has a concise title and column headings, and include units where necessary.

• Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for n and %:

Rather:

Combine into one column, n (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

References

NB: Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..

• Authors must verify references from original sources.

• Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]

• All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).

• Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.

• Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
• Volume and issue numbers should be given.
• First and last page, in full, should be given e.g.: 1215-1217 not 1215-17.
• Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
o On the Crossref homepage, paste the article title into the 'Metadata search' box.
o Look for the correct, matching article in the list of results.
o Click Actions > Cite
o Alongside 'url =' copy the URL between { }.
o Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

• Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx.doi.org/10.1000/hgjr.182
• Book references: Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
• Chapter/section in a book: Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
• Internet references: World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

• Legal references

• Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996. In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

• Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

• Acts:

South Africa. National Health Act No. 61 of 2003.

• Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

• Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

• Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

• Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

NOTE: no.after the v

• Other references (e.g. reports) should follow the same format: Author(s).Title. Publisher place: Publisher name, year; pages.

• Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.

• Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

Appendix E: Turnitin Plagiarism Report

Submission journal article.docx

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3	www.researchgate.net Internet Source	1%
4	Webber, Janine, Aimee Stewart, and Piet Becker. "The effect of a reminder diary on risk factors in patients with chronic hypertension attending a clinic at a hospital in Johannesburg, South Africa", African Journal of Primary Health Care & Family Medicine, 2013. Publication	<1%
5	discovery.ucl.ac.uk Internet Source	<1%

6	RC Pattinson, T M A G Hlongwane, V Vannevel. "Challenges to improve antenatal and intrapartum care in South Africa", South African Medical Journal, 2019 Publication	<1%

Exclude quotes	On	Exclude matches	< 8 words
Exclude bibliography	On		

Appendix F: Plagiarism declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Zeenat Lenina Khan (Student number: 306704) am a student registered for the degree of Mmed: Obstetrics and Gynaecology in the academic year 5.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature:  Date: 13 February 2023