ANTENATAL FACTORS ASSOCIATED WITH PERINATAL MORTALITY AMONG WOMEN WITH HYPERTENSION DISORDERS IN PREGNANCY AT A REGIONAL HOSPITAL IN KWAZULU-NATAL PROVINCE IN SOUTH AFRICA

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A mini thesis submitted in partial fulfilment of the requirements for the degree of Master of Public Health at the School of Public Health, University of the Western Cape

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KEYWORDS:

Blood pressure, hypertension disorders, ultrasound, gestational age, perinatal deaths, pregnancy and labour monitoring, antenatal, preeclampsia, eclampsia, gestational hypertension

1 Abstract

1.1Background

According to World Health Organisation (WHO), hypertension disorders in pregnancy are the leading maternal medical condition associated with high perinatal mortality in many parts of the world. Saving babies report-a triannual report in South Africa focusing on perinatal mortality also puts hypertension as the leading maternal condition associated with high perinatal mortality in South Africa. As per National Institute of Health (NIH) in United States of America (USA), aetiological processes involved in the development of hypertension in a pregnant woman are not well understood. This poses a challenge to predicting and preventing the onset of hypertension in a pregnant woman. It is against this background that proper antenatal management and monitoring of women with hypertension disorders and their unborn babies becomes crucial to reduce perinatal mortality. The aim of this study was to determine the antenatal factors associated with perinatal mortality in women with hypertension disorders in pregnancy at one of the regional hospitals in KwaZulu-Natal province in South Africa.

1.2 Methods

This was a retrospective cross-sectional analytical study. The study had 246 participants meeting the inclusion criteria out of the required 384 as per sample size calculation. All participants meeting the inclusion criteria were included so as to increase the power of the study. The inclusion criteria were that the participant must have been diagnosed with hypertension in pregnancy and had a perinatal mortality between 1 January 2019 and 31 December 2021. Data was extracted from participants' hospital records including files and registers. The researcher developed and used a data extraction sheet to extract data from the files and registers. Logistic regression was used to assess association between participants' sociodemographic characteristics, maternal factors as well as patient care on one hand and perinatal mortality on the other.

1.3 Results

Frequencies

A total of 246 files of participants were reviewed in this study. The average age of participants was 26.4 with a standard deviation of 6.9 years. There were only 12 (4.8%) participants who were married and 18 (7.3%) who were formally employed. Perinatal mortality was grouped into Macerated Stillbirths (MSBs), Fresh Stillbirths (FSBs) and Early Neonatal Deaths

(ENNDs). MSBs were in majority 194 (78.9%). There were 161 (65.5%) participants who completed between 1 to 4 Antenatal Clinic (ANC) visits and 85 (34.6%) had 5 or more ANC visits. As for High-Risk Clinic (HRC) visits 145 (58.9%) had 1 to 4 visits while 51 (20.7%) had 5 or more visits. Most of the participants were within para one to four 137 (55.7%). A total of 160 (65%) of the participants had routine ultrasound done and 34 (13.8%) had foetal monitoring ultrasound done. Blood tests were done in 74 (30.1%) and Blood Pressure (BP) was controlled in only 98 (38.2%) of the participants. Majority of the participants 137 (55.7%) booked ANC within 12 to 24 weeks of pregnancy. The commonest initial diagnosis was Gestational Hypertension (GHPT) with 96 (39.0%) and the commonest final diagnosis was Severe Preeclampsia (SPET) with 96 (39.0%). The least diagnosed condition was Imminent Eclampsia (IE) with 3 (1.2%) at initial diagnosis and 8 (3.3%) at final diagnosis.

Bivariate analysis

Age and employment status were not associated with perinatal mortality. No significant association noted between ANC or HRC attendance with perinatal mortality. Women within para 1 and 4 were less likely to have MSB (OR=0.51; 95% CI= 0.26-0.99; p= 0.048). No significant association noted between doing either a routine or foetal monitoring ultrasound with perinatal mortality. Doing blood test also not associated with perinatal mortality. Women whose BP was controlled were less likely to have FSB (OR= 0.31; 95% CI 0.13-0.75; p= 0.009) but marginally increased likelihood of having MSB (OR= 1.90; 95% CI 0.97-3.75; p= 0.062). Booking ANC within 12-24 weeks was marginally associated with reduced odds of MSBs (OR= 0.51; 95% CI 0.23-1.23; p= 0.098). Women who were diagnosed with GHPT and Preeclampsia (PET) were more likely to have MSB than those with other diagnoses (OR= 16.27; 95% CI 2.82-93-93.87; p= 0.002) and (OR= 8.67; 95% CI 1.54-48.70; p= 0.014) respectively.

Multivariate analysis

On multivariate analysis, married women were less likely to have MSB (OR= 0.22; 95% CI 0.05-0.89; p= 0.033). Women whose BP was controlled had significantly reduced odds of having FSB (OR= 0.18; 95% CI 0.06-0.55; p= 0.003) however significantly associated with increased odds of MSB (2.49; 95% CI 1.10-5.61; p= 0.028). Women who were diagnosed with GHPT were more likely to have MSB compared to those with Chronic Hypertension (CHPT) (OR= 22.62; 95% CI 3.49-146.87; p= 0.001). Similary women diagnosed with PET, Imminent Eclampsia (IE) and SPET were all more likely to have MSB compared to those with CHPT (OR= 12.14; 95% CI 1.90-77.44; p= 0.008), (OR= 20.90; 95% CI 1.37-318.43; p= 0.029), (OR= 5.44; 95% CI 0.98-3.35; p= 0.008) respectively.

Conclusion.

Patient related factors and poor monitoring of pregnant women with hypertension disorders in pregnancy contribute significantly to high levels of perinatal mortality at this regional hospital. There is need for community outreach programs to sensitise the community about hypertension disorders in pregnancy. The hospital needs to focus on hypertension through creation of a specialist hypertension clinic and review of the current guidelines.

DECLARATION

Full Name: Lyson Stembridge Gwesele

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Title of mini-thesis: Antenatal factors associated with perinatal mortality among women with hypertension disorders in pregnancy at a regional hospital in KwaZulu-Natal province in South Africa

I declare that this mini-thesis is my work, has not been submitted for any degree or examination at any other university, and that all the sources I have used have been indicated in text the and acknowledged in the references section.

Signature

Date: 09 June 2023

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Firstly, I would like to express my profound gratitude to the Almighty God for the paramount gift of life. In a special way I am grateful to God for giving me knowledge, skills and above all wisdom to realise that all is possible if I have faith in him.

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DEDICATION

I would like to dedicate this thesis to all women of reproductive age in the catchment area of the hospital under study

I would also like to dedicate this thesis to my late mother Naomi Gwesele for instilling in me the belief that all is possible with God and that in her own vision my future was bright.

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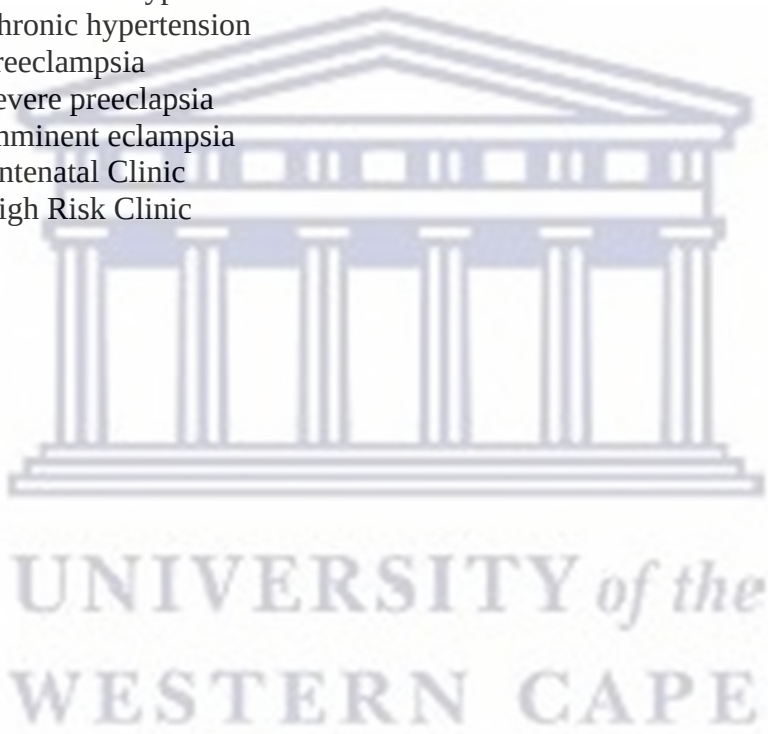
ACRONYMS AND ABBREVIATIONS

WHO	World Health Organisation
BP	Blood Pressure
USS	Ultrasound
ARR	Annual Reduction Rate
CDC	Centre for Diseases Control and Prevention
KZN	KwaZulu-Natal
AFI	Amniotic Fluid Index
RI	Resistance Index
EFW	Estimated Fetal Weight
FSB	Fresh Stillbirth
MSB	Macerated Stillbirth
ENND	Early Neonatal Death
GHPT	Gestational hypertension
CHPT	Chronic hypertension
PET	Preeclampsia
SPET	Severe preeclapsia
IE	Imminent eclampsia
ANC	Antenatal Clinic
HRC	High Risk Clinic



KEY DEFINITIONS

Hypertension: Hypertension is a cardiovascular disease diagnosed by a rise in blood pressure above 140/90 mmHg measured on two occasions separated by 4 hours (Alexander, 2019)

Chronic hypertension: Chronic hypertension refers to hypertension which is diagnosed in a pregnant woman before the woman is 20 weeks pregnant. (Leeman, Dregang, & Fontain, 2016)

Gestational hypertension: Gestational hypertension is defined as hypertension occurring after 20 weeks of gestation without any protein in the urine of that pregnant woman or any other features of preeclampsia (Leeman *et al*, 2016).

Preeclampsia: Preeclampsia is a hypertension disorder in pregnancy occurring after 20 weeks of gestation with either proteinuria (protein in the urine), thrombocytopenia (platelets below 100), impaired liver function tests, pulmonary oedema, cerebral or visual impairment (Leeman *et al*, 2016)

Chronic hypertension with superimposed preeclampsia: This is when a pregnant woman known to have chronic hypertension starts showing features of preeclampsia (Leeman *et al*, 2016)

Eclampsia: Eclampsia is a condition in which a woman diagnosed with hypertension in pregnancy suffers a generalised tonic-clonic seizures (Leeman *et al*, 2016)

Perinatal death: The death of a foetus (stillbirths) after 28 weeks of pregnancy and the death of a baby within 7 days of life (WHO, 2020)

CHAPTER ONE: INTRODUCTION

In the first chapter, the study's background and problem statement are explained, outlining the specific issue at the hospital that is the subject of the investigation. The aim and objectives of the study are presented next then finally the purpose of the study is explained.

1.1 Background

Worldwide there are 2.6 million stillbirths every year, and 98% of these occur in low and middle-income countries (WHO, 2021). Three-quarters of the stillbirths occur in sub-Saharan Africa and South Asia, and 60% occur in rural areas (WHO, 2021). Despite the fact that stillbirths have decreased between 2000 and 2015, the decline has not been significant compared to maternal mortality and under-five mortality. For example, between 2000 and 2015 Annual Reduction Rate (ARR) for stillbirths was 2% compared to 2.4%, 3% and 3.9% for neonatal, maternal and under-five mortalities respectively (WHO, 2021).

According to WHO, perinatal mortality is the death of a foetus (stillbirths) after 28 weeks of pregnancy and the death of a baby within the first 7 days of life (WHO, 2020). The mark of 28 weeks is considered because that is when the foetus is deemed viable in many parts of the world (WHO, 2020). Perinatal mortality rates within sub-Saharan Africa have varied widely, with a pooled rate of 34.7 perinatal deaths per 1000 births for the region (Akombi & Renzaho, 2019). In Southern Africa, there were 30.3 perinatal deaths per 1000 births, and Lesotho was on top of the list with 49.6 perinatal deaths per 1000 births (Akombi & Renzaho, 2019).

In South Africa, there was a notable increase of perinatal deaths from 13020 in 1997 to 25389 in 2009, followed by a downward trend to 18683 in 2016 (STATS SA, 2018). Overall, perinatal mortality declined from 2009 to 2016 in South Africa. Similar rise and fall were noted for stillbirths. There was an increase in stillbirths from 5982 in 1997 to 15851 in 2004, which subsequently declined to 11961 in 2016 (STATS SA, 2018). Provincially Gauteng and KwaZulu-Natal contribute about 47% of perinatal mortalities, with the rest shared among the other provinces. Northern Cape has the lowest proportion of perinatal deaths at about 3% (STATS SA, 2018). According to Saving Babies Report, Perinatal mortality in South Africa is about 36/1000 births in metropolitan areas and around 50/1000 births in rural areas (Bettercare, 2021)

Statistics in South Africa show that many of the perinatal deaths are associated with maternal medical conditions and complications of pregnancy (STATS SA, 2018). Maternal medical conditions are those conditions or diseases in the mother that may complicate the pregnancy leading to bad outcomes for the foetus, mother, or both (CDC, 2020). Some of these maternal medical conditions include hypertension, diabetes, cardiac diseases, and some respiratory diseases. Improvement of maternal health and avoidance of complications of pregnancy can prevent many deaths (WHO, 2021). Poor maternal medical conditions also lead to low birthweight (birthweight below 2500g) for most of the perinatal deaths (WHO, 2021). About 50% of stillbirths in South Africa were of low birthweight in 2016 and significant proportion (17.8 %) were born with weights lower than 1000g (STATS SA, 2018).

According to the Saving Babies Report of 2016, hypertension is the leading maternal medical condition causing perinatal mortality in South Africa (NAPEMMCO, 2016). The report shows that hypertension contributes 14.9% of perinatal deaths without adding its contribution through antepartum haemorrhage (bleeding before giving birth). A study in Mpumalanga, one of the provinces in South Africa showed that hypertensive disorders in pregnancy and intrapartum haemorrhage (bleeding during the time of giving birth) were associated with most of the perinatal deaths (Allanson, Muller & Pattinson, 2015). According to perinatal mortality statistics at the regional hospital under study, hypertension disorders in pregnancy were the single direct leading cause of perinatal deaths (QNRH, 2020). Therefore, knowledge of the issues surrounding hypertension disorders in pregnancy in the antenatal period may reduce perinatal mortality.

1.2 Problem statement

Worldwide, hypertension in pregnancy contribute 15% of all perinatal deaths (NIH, 2019). A multi country study in sub–Saharan Africa found that hypertension disorders were responsible for 5 to 13.6% of perinatal deaths without adding its contribution via antepartum haemorrhage (Aminu, Zeev, White, Mathai & Broek, 2019). A prospective observational study in South Africa reported that hypertension disorders of pregnancy accounted for 19% of all perinatal deaths and caused 90% of all perinatal deaths attributed to maternal medical conditions (Madhi, Briner, Maswine, Moses, Mlandu, Chawana et al, 2019).

Many studies done globally have investigated the factors associated with perinatal mortality in general but not specifically among women with hypertension disorders. A study in Brazil

focusing on perinatal mortality in general found that insufficient prenatal care was associated with more perinatal deaths than sufficient prenatal care (Gracia, Fernandes, & Trabert, 2018). A similar study in Pakistan looked at obstetric factors affecting perinatal mortality in general and found that antepartum haemorrhage, hypertension, and mechanical factors during labour were significantly associated with perinatal mortality. Even though the study in Pakistan had hypertension as one of the factors associated with perinatal mortality, it did not explore why only hypertension emerged as one of the leading factors for perinatal mortality among all medical conditions.

Likewise, the studies done in Africa have either focused on perinatal mortality in the general population of pregnant women or have just quantified the problem of perinatal mortality. Akombi and Renzaho in their multi-country study on perinatal mortality simply reported the rates of perinatal mortality in various countries within sub-Saharan Africa (Akombi & Renzaho, 2019). A study in Ethiopia looked at various factors contributing to perinatal mortality including; antenatal care, preterm delivery, grandmultiparity, antepartum haemorrhage and many other factors but all of these factors were investigated among pregnant women in general (Endeshaw & Berhan, 2015).

In South Africa, a few studies have been done on perinatal mortality but I did not find any study that focused on antenatal factors associated with high perinatal mortality among women with hypertension. A study in South Africa that examined hypertension in pregnancy among black South African women found that the most common form of hypertension in these women was Gestational Hypertension (GHPT) and perinatal mortality occurred in 5.9% of all preeclampsia (PET) women (Moodley, Onyangunga & Maharaji, 2016). Moodley and colleagues did not investigate the factors associated with perinatal mortality among these pregnant women and the study investigated primigravida women only. Another study in KwaZulu-Natal province in South Africa only investigated factors associated with perinatal mortality in the general population of pregnant women and not specifically among women with hypertension. The study found that predictors of neonatal mortality included; extreme low birthweight, male sex, and preterm delivery (Hoque, Haaq & Islam, 2011). Besides investigating factors associated with perinatal mortality in general population, the study did not look at maternal factors that could be contributing to the bad perinatal outcome. The studies done so far present partial insight into the factors associated with high perinatal mortality particularly among women with hypertension disorders in pregnancy. Therefore, this study

focused on investigating antenatal factors associated with perinatal mortality among pregnant women with hypertension disorders at a regional hospital in KwaZulu-Natal province in South Africa. This facility is experiencing high perinatal mortality among pregnant women with hypertension disorders in pregnancy based on perinatal statistics reports (QNRH, 2020).

1.3 Aim

To determine antenatal factors associated with perinatal mortality in women with hypertension disorders in pregnancy at a regional hospital in KwaZulu-Natal province in South Africa.

1.4 Objectives

- To document the antenatal care provided to women with hypertension disorders in pregnancy who had perinatal death at the regional hospital under study between 1 January 2019 to 31 December 2021.
- To describe socio-demographic characteristics of women with hypertension disorders in pregnancy who had perinatal death at the regional hospital under study between 1 January 2019 to 31 December 2021.
- To determine patient-related factors associated with perinatal mortality among women with hypertension disorders in pregnancy at the regional hospital under study between 1 January 2019 to 31 December 2021.

1.5 Purpose of the study

The purpose of this study was to unearth information that would help assess if the current antenatal management of women with hypertension in pregnancy is adequate or not. This information can be used to inform changes in the national guidelines for management of hypertension in pregnancy. The information could also be used to inform changes in the policy as well as standard operating procedures for management of hypertension disorders in pregnancy. The hospital under study can use this information to change the current practice in as far as management of hypertension in pregnant women is concerned. In addition, the information can form a basis for quality improvement initiatives in managing hypertension disorders in pregnancy or to re-enforce good practices that are already existing. Finally, the information can be used to lobby those in various leadership positions including health authorities, community leaders, civil society leaders and religious leaders to sensitise the community on various issues relating to hypertension and perinatal mortality.

CHAPTER TWO: LITERATURE REVIEW

Introduction

This chapter presents literature review on various topical issues relating to the study. The chapter begins by looking at perinatal mortality and various groups of factors associated with it including; Obstetric, maternal, socioeconomic, and geographical factors. Then the chapter talks about hypertension in pregnancy describing the factors associated with it like sociodemographic, economic, maternal, obstetric, maternal medical conditions, lifestyle, and environmental factors. The chapter also looks at antenatal care provided to women with hypertension disorders in pregnancy. Finally, management of various forms of hypertension in pregnancy is discussed.

2.1 Perinatal mortality

Perinatal mortality includes Early Neonatal Deaths (ENND) which is the death of a baby before the end of 7 days and stillbirths (WHO, 2020). International Classification of Diseases 10th revision (ICD-10) defines stillbirth as death before complete expulsion or extraction from its mother of a foetus that has reached a birthweight of 500g or a gestation age of 22 weeks (Patterson & Bose, 2019). Death is evidenced by the absence of signs of life including no heartbeat, no cord pulsation, no respiration, and definite movements of voluntary muscles (Patterson & Bose, 2019). Stillbirths can either be macerated or fresh. Maceration involves the autolytic changes that occur after the foetus has demised in-utero. The changes start to appear after 3 to 6 hours post demise and can be confirmed on delivery. Fresh stillbirths on the other hand are those that occur probably around the intrapartum (during labour) period and they do not show any autolytic changes. In summary therefore, perinatal mortality is the sum of ENND, Macerated Stillbirths (MSB) and Fresh Stillbirths (FSB) (Gold, Razak, Mumin & Lieberman, 2014).

It must be stated that in other health facilities birthweight is used other than gestational age to distinguish between a birth and a miscarriage. A birth weight of 500g or more would be considered a birth and anything below 500g is considered a miscarriage (MacDorman & Gregory, 2015). The challenge with using birthweight to determine perinatal death is that once the foetus dies, in-utero absorption processes take place such that by the time the foetus is born the weight may have significantly reduced. Besides this challenge, some of the causes of perinatal deaths especially stillbirths tend to affect the growth of the foetus even before the

foetus dies in-utero. This can lead to a stillbirth whose weight is below 500g but has lived in-utero for more than 28 weeks. The overall effect of these challenges is that perinatal mortalities are underreported (MacDorman & Gregory, 2015).

Perinatal deaths are associated with various factors that can be categorised as obstetric, maternal, sociodemographic, and geographic. I will now explore some of the factors in those categories

2.1.1 Obstetric factors associated with perinatal deaths

Obstetric factors also referred to as direct causes of perinatal deaths, have been extensively studied. They do vary from region to region and relate to the quality of care given to pregnant women. In a study in Pakistan to determine obstetric factors related to perinatal mortality it was found that the leading risk factors included, antepartum haemorrhage (abruptio placenta 18 % and placenta praevia 10.8%). Hypertension disorders in pregnancy contributed 26.7 %. Other group of obstetric contributors were the mechanical problems that occur during labour including obstructed labour, cord prolapse, malpresentation and ruptured uterus (Iqbal, Majid, Muhammed & Khan, 2014).

In another study in Ethiopia, obstructed labour alone contributed to one-third of all perinatal deaths (Bayon & Berhan, 2012). In the same study, it was also found that other independent predictors of perinatal deaths included hypertensive disorders in pregnancy, antepartum haemorrhage, malpresentation and preterm delivery (Bayon & Berhan, 2012). Thus, evidence from previous studies suggest hypertensive disorders in pregnancy is a crucial independent contributor to obstetric cuases of perinatal mortality in low-middle-income settings.

2.1.2 Maternal factors associated with perinatal deaths

Perinatal mortality is a multifaceted problem that requires an interdisciplinary approach to deal with. While there are obstetric factors that seem to be direct causes of perinatal deaths, there are other factors that tend to predispose a pregnant woman to perinatal deaths. These factors include; age, parity and health seeking behaviour. These factors are largely in the control of a woman hence categorised as maternal factors.

Age

Several studies have shown that perinatal deaths occur mostly in the extremes of maternal age. In a study in Ethiopia on perinatal outcomes in pregnant women with hypertension, it was found that significant proportion of perinatal deaths occurred in women above 35 years (Endeshaw & Berhan, 2015). While Endeshaw and Berhan found that older women were associated with high perinatal deaths, another study in Nigeria found that most of the very young age pregnant women did not attend antenatal clinic adequately and had higher proportion of perinatal mortality (Fasina, Oni, Azuh, & Oduaran, 2020). Similarly, a study in South Africa found that perinatal mortality was high among the teenagers and those women above 35 years (Malinga, Du Preez & Rabie, 2020)

Parity

A lot of evidence exists linking perinatal mortality to the number of births a woman has had before (parity). Most studies have shown that higher parity is associated with perinatal mortality. Endeshaw and Berhan found that multipara women were 1.6 times more likely to have perinatal deaths compared to those with lower parity. Their study further showed that grandmultiparity (parity ≥ 5) posed even greater risk of perinatal death than just multiparity (para 2 to para 4). Grand multipara women were 2.8 times more likely to have perinatal death compared to those with lower parity in Ethiopia (Endeshaw & Berhan, 2015). This finding is also corroborated by Malinga *et al* who found that most of the perinatal deaths occurred among multipara women at a district hospital in South Africa (Malinga *et al*, 2020).

Health seeking behaviour

Other maternal factors relate to health seeking behavioural problems. It has been observed that many women do not attend antenatal clinic adequately, putting their unborn children at risk of dying because their pregnancies are not closely monitored. Low antenatal clinic attendance is typically linked to perinatal mortality. In their study, Iqbal *et al* found that 88 % of those women with perinatal deaths were not booked at antenatal clinic (Iqbal, Majid, Muhammed & Khan, 2014). Similar findings were also found in a study in Brazil where it was found that women who had insufficient prenatal care had a 3.25 risk of perinatal death than those who had sufficient prenatal care (Garcia *et al*, 2018). The findings by Iqbal *et al* and those of Garcia *et al* are also corroborated by another study in India where it was found that 94% of perinatal deaths were among women who had either irregular or no antenatal care (Behal & Vinayak, 2015).

2.1.3 Socioeconomic and geographic factors associated with perinatal mortality

Perinatal mortality has its socioeconomic and geographical factors just like many other medical conditions seen in health institutions. Perinatal mortality and general health are typically impacted by such factors like education, income, occupation, and place of residence.

Education

Some studies have shown that education is associated with perinatal mortality. In a study in Nigeria, it was found that educated women from the level of high school completion and above were more likely to attend antenatal care and had lower proportions of perinatal mortality (Fasina, Oni, Azuh, & Oduaran, 2020). The findings of Fasina *et al* study were also corroborated by a related study in Malawi and Uganda where the researchers wanted to determine the causal effect of maternal education on child mortality. In this study it was found that one additional year of maternal education reduced the probability of child mortality by 10% in Malawi and 16.6% in Uganda (Adriano & Monden, 2019). Adriano & Monden also explored the pathways through which maternal education could affect child mortality. In this regard they found that maternal education confers financial ability to be able to afford health services, positively influence altitudes towards modern health services and that being educated, enhanced proximity to health facilities (Adriano & Monden, 2019). Even though the study of Adriano and Monden focused on child mortality same explanations on how education affects perinatal mortality could be applicable. While Fasina *et al* as well as Adriano and Monden noted this association between education and perinatal mortality, Garcia *et al* found that there was no any association between perinatal mortality and education (Garcia *et al*, 2018).

Income

Income has been shown to have some influence on perinatal mortality. Studies have shown that women with a better income have lower levels of perinatal mortality. Fasina et al found that higher income was associated with lower proportions of perinatal mortality (Fasina et al, 2020). Conversely, a study in Ethiopia found that women with lower income levels were 1.95 times more likely to have perinatal death than those with higher income (Woldeamanuel & Gelebo, 2019).

Low income can lead to high probability of perinatal mortality through a number of ways. Pregnant women with low income are at risk of poor and inadequate nutrition which eventually affects nutrition of their unborn babies. Malnutrition of the foetus may lead to small for

gestational age foetus and abnormalities like neural tube defects which increase the likelihood of dying in utero or immediately after being born (Doser, 2022). Besides, poverty is also associated with high levels of stress resulting from the need to pay bills, buy food, housing, and all sorts of expenses. High stress levels lead to high levels of cortisol hormone in the body. With high cortisol levels circulating in the body of a pregnant woman, the chances of preterm labour are high with resultant ENND due to severe prematurity (Doser, 2022).

Occupation

The impact of occupation on perinatal mortality seems to be related to the amount of income the woman gets from that occupation. In a study in India, it was found that perinatal mortality occurred more commonly among women with less paying jobs (Surekha & Kumar, 2012). Surekha and Kumar found that 46.73% and 35.86% of perinatal deaths occurred among women who were landless labourers and household workers respectively (Surekha & Kumar, 2012)

Occupation influences perinatal mortality through income that is earned. As in the findings of Doser, low levels of income are associated with poor nutrition as well as high levels of stress both of which are associated with bad pregnancy outcomes like perinatal deaths (Doser, 2022). Besides, some occupations also expose pregnant women to environmental hazards such as noise pollution. Studies have shown that high noise pollution is associated with small for gestational foetus also known as intrauterine growth restriction. A study in Sweden showed that women who were exposed to more than 85dBA of noise were 1.44 times at risk of intrauterine growth restriction than those exposed to lesser noise (Selander, Raylander, Albin, Rosenhall, Lewne and Gustavsson, 2019). National Institute for Occupational Safety and Health (NIOSH) in USA says noise pollution is associated with high levels of stress and that in pregnancy high levels of stress could lead to preterm birth with the babies dying of severe prematurity (NIOSH, 2022).

Geographical factors

Like with occupation, geographical differences in the proportions of perinatal mortality borders on the economic status of the location with rural areas having a bigger share of perinatal deaths since they are mostly economically disadvantaged than urban areas. Fasina *et al* found that poorer regions which happened to be rural areas in most cases had higher proportions of perinatal deaths than rich regions which happened to be mostly urban areas (Fasina *et al*, 2020). Similar results were also obtained by Surekha and Kumar where they found that 72.28% of

perinatal deaths occurred in rural areas as opposed to 27.71% of perinatal deaths which occurred in urban areas (Surekha & Kumar, 2012).

2.2 Hypertension in pregnancy

Hypertension in pregnancy is a cardiovascular disease diagnosed by a rise in blood pressure above 140/90 mmHg measured on two occasions separated by 4 hours (Alexander, 2019). Pregnant women are at risk of developing hypertension and its complications due to physiological changes that take place in their bodies. Hypertension is the most common medical problem encountered during pregnancy complicating up to 10 % of all pregnancies (Carson & Gibson, 2018).

One of the complications of hypertension in pregnancy is perinatal mortality. In a case control study in Ethiopia, Bayon and Berhan found that hypertension in pregnancy is the third single leading cause of perinatal mortality behind obstructed labour and antepartum haemorrhage (Bayon & Berhan, 2012). This finding also agrees with another study in Mpumalanga, South Africa which found that hypertension and antepartum haemorrhage were the leading causes of perinatal mortality (Allanson, Muller & Pattinson, 2015). Multi country survey done by WHO found that antepartum haemorrhage and hypertension were the factors associated with perinatal mortality (WHO, 2013).

Of note is that among the perinatal deaths attributed to antepartum haemorrhage most of them are associated with a condition called abruptio placenta defined as the early separation of the placenta from the lining of the uterus before the completion of second stage of labour (Schmidt, Skelly & Raines, 2022). Hypertension in pregnancy is a well-documented risk factor for abruptio placenta. In a retrospective study in Nigeria hypertension was a risk factor for abruptio placenta in 53.1 % of women of which 46.9 % had perinatal death (Akadri, Ogunsowo & Odelola, 2018). This implies that hypertension is probably the leading cause of perinatal deaths if one accounts for its direct and indirect (via abruptio placenta) association with perinatal deaths.

2.2.1 Factors associated with hypertension disorders in pregnancy

Literature has documented several risk factors for hypertension disorders in pregnancy. In a study at one of the hospitals in Ethiopia, it was found that factors including; residing in the

rural areas, prim gravidity (having the first pregnancy), family history of hypertension, multiple pregnancies, lack of antenatal follow ups and preexisting hypertension were significantly associated with hypertension disorders in pregnancy (Hinkosa, Tamene & Gabeyehu, 2020).

A systematic review of factors associated with hypertension disorders in pregnancy in sub–Saharan Africa found significant association between hypertension disorders in pregnancy and factors such as prim gravidity, family history of hypertension disorders, previous hypertension disorders in pregnancy and lower education levels (Meazaw, Chojenta, Muluneh & Loxton, 2020).

Factors associated with hypertension in pregnancy can be grouped into the following categories; socio-demographic, economic, maternal characteristics, underlying maternal medical conditions, and those related to lifestyle. I will now explore each category to highlight what is known.

2.2.2 Socio-demographic factors

While there is a genetic predisposition to hypertension disorders in pregnancy, the socio-demographic characteristics of the pregnant women play a role in the development and progression of the disease. In a study to determine factors associated with hypertension disorders in pregnancy in Cameroon, it was found that young participants between the ages of 14 and 24 accounted for 67.7 % of PET cases (Mbouemboue, Cellou, Tamanji, Blakga, Kamdji, Ngoufack & Youmbi, 2016). The association between hypertension disorders in pregnancy and age is on both ends. While Mbouemboue et al found significant association of hypertension and young age, other studies have shown that this association also exists with advanced maternal age (>35 years). In a study that analysed obstetric outcomes in women with hypertension disorders in pregnancy, it was shown that advanced maternal age was a significant factor in the development and progression of hypertension disorders in pregnancy (Onoh, Onyebuchi, Mamah, Anozie, Kenneth & Chidi, 2020).

Ageing is associated with low levels of nitric oxide and high oxidative stress which together affect negatively the relaxation of the endothelium (lining of the blood vessels). During pregnancy there is overall increase in cardiac output which means more blood needs to be accommodated within the blood vessels by relaxation of the blood vessels. If the blood vessels are stiff as it is in advanced maternal age then hypertension results (Diet & Farthmann, 2015).

This is how women with advanced maternal age tend to suffer from hypertension during pregnancy. The occurrence of hypertension in young pregnant women could be as a result of the same factors that play a role in development of hypertension in the general population. Factors like family history of hypertension, smoking, obesity, and diabetes. These factors coupled with high cardiac output as a result of increased blood volume in pregnancy could be the reason why young women suffer from hypertension during pregnancy (Jones, Iihaam, Esack, Mangena & Rayner, 2020).

In terms of education levels of the pregnant women, some studies have shown that even though there is an increase in the prevalence of hypertension disorders in pregnancy among those with less education, the association of education and hypertension disorders in pregnancy is not statistically significant (Singh, Ahmed, Egodu & Ikechukwu, 2014). In one case control study to determine sociodemographic factors associated with preeclampsia, it was found that there was no difference in literacy levels between the cases and the controls. Similarly, the study also found that literacy levels of the husbands of the cases and controls were similar (Ramesh, Gandhi & Rao, 2014). With respect to other sociodemographic factors including marital status, occupation and religion, there was no statistically significant association with hypertension disorders in pregnancy (Ramesh *et al*, 2014; Singh *et al*, 2014). On the contrary Meazaw *et al* found significant association between education and hypertension in their systematic review in sub–Saharan Africa (Meazaw *et al*, 2020). We know that education plays a role in the knowledge about hypertension in terms of its risk factors, prevention, and management therefore women with low education levels could be at risk of suffering from hypertension in pregnancy.

With regards to occupation, some studies seem to agree with findings of Ramesh *et al* that there is no association between occupation and hypertension disorders in pregnancy. A study in Taiwan to determine if long or short working hours has an impact on hypertension disorders in pregnancy found that there is no association between employment status and GHPT and PET (Chu, Hsieh, Chang, Liu & Chen, 2010). Chu *et al* also found that there is no association between maternal shift work or long hours with onset of GHPT or PET.

While Ramesh *et al* and Chu *et al* found no association between occupation and hypertension disorders in pregnancy, some studies have shown an association between some jobs and hypertension disorders in pregnancy. A systematic review in Italy found positive association

between job strain and hypertension disorders in pregnancy (Spadarella, Leso, Giordano, Fontana & Iavico, 2021). Similarly, a study in Texas USA found that occupations like business, management, legal, social services, teaching, healthcare, and counselling are associated with a significant risk of hypertensions in pregnancy (Bilhartz & Bilhartz, 2014). Bilhartz and Bilhartz also found that occupations in the category of supporting services like, house-keeping, food preparation, cosmetics, personal care, and unemployed women were associated with less hypertension disorders in pregnancy (Bilhartz & Bilhartz, 2014). Looking at the type of occupations associated with significant risk of hypertension, it is apparent to see that those occupations are relatively demanding and associated with more stress which in turn may lead to rise in blood pressure.

Some studies have shown association between hypertension in general (not in pregnancy only) with marital status. In a study in USA to compare dipping and nocturnal blood pressure among those who were married and not married, it was found that being married was associated with a 2.4 mmHg drop in blood pressure among married people (Causland, Sacks, & Forman, 2014). Causland *et al* also found that greater association was more between married men and blood pressure drop compared with married women and blood pressure drop (3.1 vs 1.7) (Causland *et al*, 2014).

2.2.3 Economic factors

The economic situation of the household particularly with regards to household income has shown significant association with onset and progression of hypertension disorders in pregnancy. In their study Ramesh *et al* found that pregnant women with household income of Rs4000 per month were 6.81 times more likely to develop PET than those with household income of above Rs4000 (Ramesh *et al*, 2014). Similar findings were also obtained in the study in Qatar to determine the impact of socioeconomic, lifestyle and obesity in the development of gestational hypertension. The study found that gestational hypertension was linearly associated with monthly household income. It was found that GHPT increases with each decrease of 5000QAR in monthly income (Bener & Saleh, 2013). Low income may limit the choice of foods that are healthy and prevent women from hypertension disorders hence low income found to be associated with hypertension disorders in pregnancy.

2.2.4 Maternal or obstetric characteristics

There is ample evidence on the association between various obstetric factors and hypertension in low and middle-income countries. Various studies seem to agree that there is association between factors like gravidity, parity, number of foetuses (single or multiple pregnancy), age at menachy, previous history of hypertension disorders in pregnancy, family history of hypertension and number of antenatal clinics a pregnant woman has attended. In their study, Mbouemboue *et al* found that primipara women were more likely to have PET than other levels of parity. They found that 65.8 % of all women with PET were primipara. In the same study they also found that twin pregnancy was associated with chronic hypertension (CHPT) (Mbouemboue *et al*, 2016). While Mbouemboue *et al* found an association between primiparity and hypertension disorders in pregnancy many studies have shown that this association exists between both low levels of parity and high levels of parity. In their study Singh *et al* found that both nulliparity and grandmultiparity are significantly associated with hypertension disorders in pregnancy (Singh *et al*, 2014).

Similar to hypertension in the general population, hypertension disorders in pregnancy has demostrated strong correlation with previous history and family history of the disease. Many women are more likely to experience hypertensive disorders in their index pregnancy if they have first-degree relatives who have experienced such diseases in the past or if they have themselves experienced such disorders in prior pregnancies. According to a study by Onoh *et al*, the second and third most significant risk factors for developing hypertension disorders during pregnancy, respectively, were prior history of such illnesses and familial history of hypertension (Onoh, Onyebuchi, Mamah, Anozie, Kenneth & Chidi, 2020).

In terms of antenatal clinic attendance, onset, and progression of hypertension disorders in pregnancy seem to be associated with less attendance of antenatal clinic. In one study in Ghana to determine perinatal outcomes among women with hypertension disorders, it was found that women who had PET and eclampsia completed less than 4 antenatal visits compared to those who had CHPT and GHPT (Dassah, Mensah, Morhe & Odoi, 2019). When a pregnant woman attends fewer than required number of antenatal visits, the likelihood is that the pregnancy will not be adequately monitored and the women will not get adequate education on how to prevent hypertension and other diseases in pregnancy.

2.2.5 Underlying maternal medical conditions

Similar to hypertension in the general population, hypertension in pregnancy is also associated with pre-existing medical conditions in the mother before conception. There is strong evidence that diabetes and hypertension disorders in pregnancy are related. Singh *et al*'s investigation revealed a strong correlation between hypertension disorders in pregnancy and gestational diabetes (GDM) (Singh *et al*, 2014). Besides the association between hypertension disorders in pregnancy and GDM, literature also show an association between hypertension disorders in pregnancy and chronic diabetes (CDM) (Mbouemboue *et al*, 2016).

While a lot of evidence has been found to link hypertension disorders in pregnancy with other cardiovascular diseases, a few studies have also shown that hypertension disorders in pregnancy has association with other conditions outside the cardiovascular domain. In one study it was found that pre-pregnancy depression and anxiety were significantly associated with hypertension disorders in pregnancy. In that study women with pre-pregnancy depression or anxiety symptoms were 2.7 to 3.5 times more likely to suffer from hypertension disorders in pregnancy than those who had no depression or anxiety symptoms. In the same study PET was followed by preterm delivery and seen to be significantly associated with lifetime history of depression (Thombre, Talge &Holzman, 2015).

2.2.6 Lifestyle factors

Hypertension in the general population is known to be largely a lifestyle disease meaning that modification of lifestyle including regular exercises and healthy diets tend to prevent one from developing the disease and for those who already have the disease such lifestyle modification can slow the progression of the disease (Sing, Shankar, and Prakash, 2017). Just like in the general population, hypertension disorders in pregnancy are also linked to lifestyle. Studies have shown that sedentary lifestyle which may lead to obesity predisposes women to hypertension disorders when they fall pregnant. In a study to assess the association between maternal obesity as well as blood pressure and risk of GHPT, it was found that the risk of GHPT was more than 4-fold higher among women with obesity (BMI 30 to 34.9) than those with normal weight (Romy, Eric, Albert & Vincent, 2011). Interestingly Romy *et al* also found that the degree of association between hypertension disorders in pregnancy and obesity varied based on the severity of obesity. Romy *et al* found that those women with morbid obesity (BMI $\geq$ 35) were 11.34 times more likely to suffer from GHPT than women with normal weight which is far higher than the 4.67 reported for those with non-morbid obesity (Romy *et al*, 2011). Romy *et al* also found that there was a difference in terms of how high the blood pressure rose

in those with morbid obesity and those with non-morbid obesity. Those with morbid obesity had far higher blood pressures than those with non-morbid obesity (Romy *et al*, 2011).

A retrospective study in South Africa found that 44% of women were either obese or morbidly obese (Basu, Jeketera & Basu, 2010). In the study Basu et al found that there was significant association between gestational diabetes, hypertension, failed induction of labour and urinary tract infection with obesity (Basu et al, 2010).

With regards to smoking, a survey in South Africa showed that overall, 5% of pregnant women smoked during their pregnancy and that a third of those who smoked also used alcohol (Mafuya, Peltzer & Pengpid, 2019). The same survey also showed that smoking during pregnancy was more common in urban areas than rural areas (Mafuya et al, 2019).

While smoking has been shown to be associated with many cardiovascular diseases including hypertension in the general population it is interesting to note that recent systematic review has shown that smoking is in fact protective for hypertension disorders in pregnancy. In the systematic review to consolidate evidence regarding association between smoking and hypertension disorders, it was found that women who smoke during pregnancy were protected from hypertension disorders in pregnancy (Wang, Yang, Xiao & Cao, 2022). In the same study, Wang *et al* found that while smoking seemed to be associated with hypertension in pregnancy in Asia, it was found that in Europe and North America smoking was protecting women from developing hypertension disorders in pregnancy. Neither quitting smoking before pregnancy nor quitting during pregnancy is associated with hypertension disorders in pregnancy (Wang *et al*, 2022).

In another study in Poland to determine the influence of various categories of smoking on the risk of GHPT various aspects of smoking were found to be associated with GHPT. For instance, the study found that being a smoker for longer period of time prior to pregnancy was associated with an increased risk of GHPT and PET compared to the number of cigarettes smoked in a day (Lewandowska & Wieckwska, 2020). Besides, the study also found that smoking ever before was associated with GHPT than never smoked before. Interestingly the study found that quitting smoking before a woman falls pregnant reduces the risk of GHPT while quitting smoking while the woman is already pregnant actually increases the risk of GHPT (Lewandowska & Wieckwska, 2020). The divergency on the findings regarding the association

between smoking and hypertension disorders in pregnancy may mean that more research is needed to find out other confounding factors that may be at play leading to either association or no association.

2.2.7 Environmental factors

Exposure to some environmental toxins has also been shown to be associated with hypertension disorders in pregnancy. Exposure to carbon monoxide and particulate matter in the first trimester were associated with hypertension disorders in pregnancy as found in the study to determine the association between hypertension disorders in pregnancy and ambient air pollution (Mobashar, Salam, Goodwin, Lurman, Ingles & Wilson, 2013). In the same study Mobashar *et al* also found that exposure to ozone in the second semester was associated with hypertension disorders in pregnancy (Mobashar *et al*, 2013).

2.3 Antenatal care

Antenatal care (ANC) is defined as the care provided by skilled healthcare professionals to pregnant women and adolescent girls in order to ensure the best health condition for both mother and baby during pregnancy (WHO, 2016). The main aim of ANC is to prevent bad outcomes for both the mother and the foetus through risk identification, prevention and prompt management of pregnancy related or any concurrent diseases (WHO, 2016). Besides, ANC also offers an opportunity for pregnant women to get health education and health promotion activities.

ANC has the potential to reduce both maternal mortality and morbidity as well as perinatal mortality and morbidity. Proper ANC can ensure early identification of diseases that can affect the pregnancy outcomes and therefore provide early and adequate treatment. Coupled with an efficient referral system, ANC can ensure timely referral of all high-risk pregnancies to a level where they can be properly managed (WHO, 2016).

Several studies done in developing countries have shown inefficient and ineffective ANC. The quality of the services rendered is substandard and often not adequate. A cross-sectional study to determine proportion of pregnant women screened for hypertension in Democratic Republic of Congo showed that only 26.7% of pregnant women were screened for hypertension (Nkamba, Ditenemena, Wembodinga & Bernard, 2019). In the same study, Nkamba *et al* also found incomplete provision of services hence making ANC ineffective. For example, Nkamba

et al found that while a good proportion (95.7%) of pregnant women had their blood pressure checked only 59.8% had their risk profile for hypertension assessed and 26.9% had their urine checked for proteinuria (Nkamba *et al*, 2019).

A national assessment of the quality of ANC in Zambia revealed that only about 47% of women received adequate antenatal care during pregnancy and that more than 50% of women received less than optimal care in the ANC facilities (Kyei, Chansa & Gabrysch, 2012). In the same study Kyei *et al* also found that 60% of pregnant women attended ANC at least 4 times even though in many of those attendances they were not attended by a skilled health provider (Kyei *et a*l, 2012).

Similarly, a cross-sectional study in Nigeria to analyse the quality of ANC found that all domains of quality scored poorly (Solomon, Ishaku, Kirk & Warren, 2019). In their study Solomon *et al* noted that except for interpersonal skills all other domains of quality including provider knowledge, technical skills and client satisfaction scored below 55%. The worst performance was registered in provider knowledge and technical skills with the score of 49.9% and 47.7% respectively (Solomon *et al,* 2019).

Attendance of ANC by pregnant women is very critical in ensuring effective antenatal clinic services. Even if antenatal services may be good but if women do not attend antenatal clinic the whole purpose of antenatal care is defeated. Several studies have pointed to several factors that influence attendance of ANC. A study in Ghana to determine factors associated with utilization of ANC found that predictors of increased number of antenatal clinic visits to be; better economic status, ownership of health insurance, education, age, religion, and region of residence (Amposah, Senadza & Arthur, 2013).

A similar study in South Africa to determine factors associated with late presentation to ANC facilities found that many of the women (51%) living in rural communities started ANC late compared to peri-urban women (28%) (Ebonwu, Mumbauer, Uys, Wainbers & Marino, 2018). In the same study Ebonwu *et al* found that in rural community late presentation was associated with being married, being employed, and reporting an unplanned pregnancy. As for the peri-urban communities, the study found that factors including; an unplanned pregnancy, being told to come later after presenting early and primigravida were factors associated with late presentation to ANC (Ebonwu *et al*, 2018).

In 2017 South Africa started rolling out implementation of the new antenatal care guidelines developed by WHO in 2016. As per these new guidelines the number of antenatal care visits required has been adjusted from 4 contact visits to 8 contact visits (WHO, 2016). The change has been necessitated by the observation that 4 or less ANC visits were not enough to detect and promptly manage the complications that arise in pregnancy. An analysis of the sample of maternity case records in 4 different provinces in South Africa showed that the average number of antenatal clinic visits by pregnant women has moved from 4.76 in 2017 to 5.9 in 2018 (Hlongwane, Boskurt, Barreix Pattinson, Gulmezoglu, Vannevel & Tunculp, 2021). In the same analysis Hlongwane *et al* also showed that the proportion of women with hypertension disorders who received appropriate treatment including urgent referral improved from 83.3% in 2017 to 100 % in 2018. Despite this seemingly well handling of hypertension as reported by Hlongwane *et a*l, the regional hospital in my study still registers very high numbers of perinatal deaths related to hypertension disorders in pregnancy (QNRH, 2020).

2.4 Management of hypertension disorders in pregnancy

Management of hypertension in pregnancy is very critical for the mother and the survival of the foetus. Management of hypertension is dependent on the type of hypertension disorder and the severity. The overall strategy is to prevent cardiovascular and cerebrovascular complications in the mother while at the same time not jeopardizing the well-being of the foetus (Snigdha & Jim, 2019).

2.4.1 Chronic Hypertension (CHPT)

CHPT refers to hypertension that is diagnosed in a pregnant woman before the woman is 20 weeks pregnant. It is assumed that the woman may have already been hypertensive at the time of conception (Leeman, Dregang, & Fontain, 2016). Most of the CHPT women with mild disease (BP less than 150/100) may require only non-pharmacological measures including, lifestyle and diet modification (Leeman *et al*, 2016). According to National Institute for health and Care Excellence (NICE) guidelines, pharmacological intervention is needed if BPs remain above 140/90 for a sustained period (NICE, 2019). The guidelines recommend weekly BP monitoring, monitoring of the foetus by ultrasound (USS) at least every 2 to 4 weeks if normal at diagnosis, checking for proteinuria at every visit and delivery of the baby at 37 weeks and above if BPs are controlled (NICE, 2019). The NICE guidelines are similar to the South African National guidelines of 2019, except that the blood tests including; haemoglobin, platelet,

creatinine, liver enzymes are mentioned in South African National guidelines but not so in the NICE guidelines (Moodley, Pillay, Buchmann & Pattinson, 2019).

2.4.2 Gestational Hypertension (GHPT)

GHPT is defined as hypertension occurring after 20 weeks of gestation without any protein in the urine of that pregnant woman or any other features of PET as explained below (Leeman *et al*, 2016). As per NICE guidelines, the management GHPT involves twice a week BP checking, doing blood tests weekly, giving antihypertensives if BP is above 140/90 for a sustained period, monitoring for onset of PET and USS monitoring of foetal wellbeing every 2 to 4 weeks if the initial ultrasound is normal (NICE, 2019). Much as the South African National guidelines are not very specific on the frequency of doing blood tests and also ultrasound for foetal monitoring these activities are mentioned as part of monitoring (Moodley et al, 2019).

2.4.3 Preeclampsia (PET)

PET is hypertension disorder in pregnancy occurring after 20 weeks of gestation with any of the following; proteinuria (protein in the urine), thrombocytopenia (platelets below 100), impaired liver function tests, pulmonary edema, cerebral or visual impairment (Leeman *et al*, 2016). The presence of proteinuria is not essential in the diagnosis of preeclampsia but may rather point to the severity of the disease (Thornton, Makris, Ogle, Tooher & Hennessy, 2010). In their study Thornton *et al* found that proteinuria was associated with higher blood pressure, earlier delivery, eclampsia (discussed later) and mostly operative delivery (Thornton et al, 2010).

PET can be grouped as severe or non-severe (mild to moderate) depending on the signs and symptoms presented by the pregnant woman. Features of severe preeclampsia (SPET) include BP of 160/110 or above, platelet of less than 100, blood liver enzymes of two times above the upper limit, doubling of serum creatine levels, right upper quadrant abdominal pain, pulmonary edema, visual or cerebral disturbances. Any of the features above suggests SPET and the absence of these feature suggests non-SPET (Leeman *et al*, 2016).

Women with SPET must be hospitalized and aggressive treatment needs to be instituted promptly to prevent further complications. Management principles involve stabilization through controlling of BP, fluid management to prevent pulmonary oedema, prevention of seizures by giving magnesium sulphate, and where applicable (if gestation age less than 34 weeks) administering steroids to mature the lungs of the foetus then delivery of the baby as

soon as possible. A small window of expectant management (delaying delivery) can be allowed with very close monitoring of the mother and foetus (Leeman *et al*, 2016).

For non-SPET, NICE guidelines recommend BP check every 48 hours, Blood tests every week, USS assessment of the foetus every 2weeks and monitoring for features of severe preeclampsia (NICE, 2019). If its SPET, NICE guidelines recommend BP check every 15 to 30 minutes until BP is less than 160/110, blood tests 3 times a week and USS every 2 weeks if the first one is normal.

2.4.4 Eclampsia

Eclampsia is a condition in which a woman diagnosed with hypertension in pregnancy suffers a generalised tonic-clonic seizures (Leeman *et al*, 2016). A generalised tonic-clonic seizure is a type of a fit where there is sudden stiffness of the body associated with loss of consciousness (tonic phase) followed by jerking of almost the whole body (clonic phase) (Kodankadath, Theodore & Samanta, 2022). Most (53%) of eclampsia occurs in the antepartum period (before delivery), 19% intrapartum (during delivery) and 28% post-partum (after delivery). It is commonly preceded by headaches and visual disturbances. In some instances, eclampsia can occur without signs of SPET and significant rise in BP (Leeman *et al*, 2016). Management of eclampsia is delivery of the baby regardless of gestational age, administration of magnesium sulphate to prevent further seizures. Thus, these women require prompt resuscitation including management of the airway, breathing and circulation. Fluid management is very critical and regular monitoring of end-organ damage should be done (Leeman *et al*, 2016).

The topic on risk factors associated with perinatal mortality has been well covered in literature. Most of the studies have reported on common antenatal risk factors for perinatal mortality and all studies seem to agree that among the common risk factors hypertension in pregnancy rank as the most common maternal medical condition associated with perinatal mortality. What is obviously lacking in the literature is the explanation of the discrepancy in the management of hypertension in pregnancy especially when it comes to antenatal monitoring of pregnant women with hypertension. The disparity in the management guidelines and also thorough following of guidelines could be the reason why there is a difference in the magnitude of the impact of hypertension on perinatal mortality.

CHAPTER THREE: METHODS

Introduction

This chapter details the methodology followed in this study. Issues discussed include; setting, study design, population and sampling, inclusion and exclusion criteria, sampling strategy, sample size, variables and operational definition, data collection, data analysis, validity, and reliability. The chapter ends with a section on ethical issues relating to this study and how they were addressed.

3.1 Setting

The study took place at a regional hospital in South Africa. This hospital is situated in KwaZulu-Natal province in the city of uMhlathuze. As of 2019 the city of uMhlathuze had a population of 384 444 people (SAHO, 2019). The regional hospital under study is a 369-bed hospital specialising in the care of women and children. The hospital conducts approximately 8000 delivery of babies and 2000 gynaecological operations in a year. The hospital receives patients from 16 district hospitals and all surrounding clinics.

3.1.1 Study design

A retrospective cross-sectional analytical study design was used. The retrospective cross-sectional analytical study design was employed to examine association between perinatal mortality and the risks factors. In this design both the exposure and the outcome are measured at the same time (SOPH, 2020). The study sought to establish if there was an association between perinatal mortality among women with hypertension disorders in pregnancy and some antenatal factors like inadequate antenatal visit, few ultrasounds done for foetal monitoring and few blood tests.

3.1.2 Population and Sampling

The study population were all women of reproductive age (15-49 years) diagnosed with hypertension in pregnancy who attend antenatal clinic at the regional hospital under study.

3.1.3 Inclusion criteria for the sample

The study included all women diagnosed with hypertension disorders in pregnancy between 01 January 2019 and 31 December 2021 and had perinatal death as the outcome of their pregnancy.

In addition, these women attended antenatal clinic at the regional hospital under study during the stated period and had delivered at that hospital during the same period.

3.1.4 Exclusion criteria for the sample

The study excluded those women diagnosed with hypertension disorders in pregnancy but their babies were antenatally diagnosed with a congenital abnormality not compatible with life. I also excluded those women with chronic hypertension with complications before conception, those whose diagnosis of hypertension was made during delivery because it meant that they had no hypertension antenatally or it was missed. Those with hypertension in pregnancy but had scanty information were also excluded. Women who had perinatal deaths but did not receive antenatal care from the hospital under study or its catchment area for the entire period of the pregnancy up to birth were also excluded .

3.1.5 Sampling strategy

Simple random sampling procedure was followed in selecting the patient files of eligible participants for inclusion in the study. This procedure was adopted to offer all eligible patients the chance of being part of the study.

3.1.6 Sample size

Since there is no documented prevalence of hypertension in pregnancy in the catchment area of the regional hospital under study, the formular below was used to calculate sample size

$n = Z^2Pq /e^2$ (Iduozee, 2016)

$= (1.96)^{2} * 0.5*0.5/0.5^{2} = 384$

The minimun sample size would have been 384. However, it was found from the health facility records that when the inclusion criteria was applied, only 246 files qualified to be part of the study. I therefore decided to include all the 246 files so as to increase the power of the study.

3.1.7 Variables and operational definitions

The main outcome variable in this study was perinatal death, defined in this study as stillbirths occurring after 26 weeks of pregnancy or any stillbirth with a weight of over 500g, plus the death of any neonate occurring before the end of 7 days, delivered by a woman known to have been diagnosed with hypertension in pregnancy.

There were four main exposure variables in this study and these included; blood pressure control entered in the data collection sheet as controlled or not controlled, foetal monitoring ultrasound entered as done or not done, blood tests entered as done or not done and antenatal visits entered as adequate or not adequate. Below are the definitions as per this study of the exposure variables. The four variables represent the objectives of this study. Control of blood pressure, doing of ultrasound and blood tests sought to assess the type of care accorded to the patients while number of visits made represent objective number three which sought to determine the patient related factors associated with perinatal mortality among women with hypertension disorders.

Blood pressure was deemed controlled if the BP was normal (below 140/90) in the 4 visits preceding delivery otherwise the BP was said to be uncontrolled if any of those visits recorded high BPs.

Ultrasound monitoring of the foetal wellbeing was considered to have been done if a woman with hypertension disease in pregnancy had an ultrasound done by a qualified sonographer at least once after the routine ultrasound that is done when the woman is 22 weeks pregnant. The ultrasound report had to show the following to qualify as a foetal monitoring scan; Amniotic Fluid Index (AFI), Resistance Index (RI), foetal biometry including Estimated Foetal Weight (EFW).

Monitoring of the complications of hypertension in a pregnant woman was measured by checking whether relevant blood tests were done or not. The blood tests expected to be done on all pregnant women with hypertension diseases include; a full blood count, renal function tests, and liver enzymes tests. Monitoring through these blood tests was said to have occurred if the tests were done at least once every two weeks from the time of diagnosis.

For a pregnancy that was 36 weeks and above at delivery, a minimum of 4 antenatal visits was considered adequate. Clinical judgement was made on the adequacy of antenatal visits for pregnancies delivered before 36 weeks.

Other patient related variables included; age defined as the number of years of participant, marital status defined as whether the participant was married or not, gestational age at booking defined as the number of weeks the women was pregnant at the time she came to start antenatal

clinic, gesational age at diagnosis defined as the number of weeks the woman was pregnant at the time she was diagnosed with hypertension, gestational age at delivery defined as the number of weeks the woman was pregnant at the time she gave birth, parity defined as the number of births the woman has given, gravidity defined as the number of pregnancies the woman has had, and coomorbidities like HIV and Diabetes.

3.1.8 Data collection

Data was collected using a data extraction table/sheet developed by the researcher himself. The researcher and two other people conducted data collection. Data was extracted from High-Risk Clinic (HRC) registers, labour ward registers, neonatal ward registers and from nurses and doctors progress notes in the patient files. All martenity hand books used by women during antenatal and delivery are kept at the point of delivery so in the case of this study all the information was withing the hospital under study. All covid -19 protocols were observed during data collection including sanitising, wearing of face masks and social distancing.

Primarily, the measurement of blood pressure is done using an automated blood pressure machine that is regularly calibrated to ensure consistent and accurate results. Ultrasound is done using an ultrasound machine operated by a trained and qualified sonographer. The blood tests are done using various laboratory machines, and any abnormal blood tests are repeated to ensure accurate results. When it comes to antenatal visits, all visits by pregnant women are recorded in the antenatal register in HRC on a daily basis from Monday to Friday.

3.1.9 Validity and Reliability

Validity of a study is influenced by two factors namely; selection bias and measurement bias. Selection bias comes in because of inappropriate sampling method, loss to follow up and also non-response to questionnaires by participants (Kesmodel, 2018). All the files whose patients met the inclusion criteria were included, and this helped to minimise the selection bias. Since this study used available data there was no loss to follow up as is the case in other studies.

Measurement bias was minimised by making sure that the data entered is accurate. In order to ensure accurancy of data collected, the other two data collectors were trained on how to extract data from the various sources mentioned above. At the end of each data collection day data collectors cross-checked each other to ensure that data entered was correct.

Reliability speaks to the consistency of the results obtained if the study is repeated several times (Kesmodel, 2018). As explained above we tried to make sure that the data captured is true and entered the same way. The study had clear definitions of variables as explained already and those collecting data were trained to ensure that they extract data correctly. The data extraction tool was made user friendly and was pretested. Inter-rater reliability was sought especially where clinical judgement was used in order to rate a certain variable.

3.2 Data analysis

IBM SPSS 28.0.0.0 was used to conduct data analysis. Analysis of data was done by first determining the frequncies and percentages of all variables. A frequency table showing percentages and actual figures was then drawn. I then conducted a bivariate analysis of all the variables with the aim of determing if there was any association between each of the variables mentioned and perinatal deaths. Perinatal mortality was split into Macerated Stillbirths (MSBs), Fresh Stillbirths (FSBs) and Early Neonatal Deaths (ENND) to weigh the association between each of the independent variables with each category of perinatal death. The rationale for splitting perinatal deaths into MSBs, FSBs and ENNDs is based on the implications for occurence of each of the category of perinatal death. For Instance, FSBs and ENNDs relate to intrapartum adverse events which are more commonly caused by either system failures or substandard management of patients. On the other hand, MSBs relate more to antenatal failures which may be poor monitoring of patients or broadly some health determinants like economic status of patients, education and accessbility to health facilities. MSBs are also more related to patient factors like poor clinic attendance. The significance level was set at 5% (0.05). P-values below 0.05 were considered significant while those between 0.05 and 0.10 inclusive were regarded as marginally significant. Further to that multivariate analysis was conducted on selected variables based on the findings from bivariate analysis. Three models were developed for the three Perinatal outcomes using backward elimination method (starting with a model with all the possibe predictors and systematically dropping the variables that are least significant till I arrived at the model with the least AIC (until I got to a model where all the variables had a p-value of atmost 0.15).

3.2.1 Ethical considerations

This study used routinely collected data which is in the custody of the regional hospital under study. As such, ethical principles governing use of routinely collected data applied. In general, core ethical principles in clinical research include; informed consent, confidentiality,

independent ethical reviews and risk management (McCord *et al*, 2018). With regards to studies that are using routinely collected data like this study, confidentiality becomes much more important while issues to do with consent can be simplified. Privacy and confidentiality dominate ethical assessment of studies using routinely collected data like this study (McCord *et al*, 2018). While some guidelines do not recommend consent from the actual owners of the personal information but rather approval from the custodians of that information, other guidelines advocate for verbal consent on top of the approval from the custodians of that information (McCord *et al*, 2018). In the case of this study permission to use the data was sought from the custodians of this information which include the hospital under and department of health in KZN.

In this study no any identifying information was used. No patient names were used in the data. Instead, all participants had a unique number that corresponded to data extracted from them. All patients coming to this hospital are assigned what is called an outpatient number if they are not admitted or inpatient number if they are admitted. These inpatient and outpatient numbers were used to locate the files from the records office. Once the files were located each file was assigned a random number for identification and all the information in the file that would have led to identification of the patient was removed. In this way all participants were annonymised and no one was able to link the information to a specific participant.

Data extraction took place in one room which was under lock and key and that room was only accessed by the research team. All the data extracted were kept in a password protected computer to ensure no one except the research team could access the data. At the end of each data extraction day all files from which data had been extracted were returned back to the records office of the hospital for safe and secure keeping. Before commencing data collection, the proposal was approved by the ethics committee of the hospital, KwaZulu-Natal provincial health office and the Biomedical Research Ethics Committee (BMREC) of the University of Western Cape.

CHAPTER FOUR: RESULTS

Introduction

This chapter presents results of the study. The results are presented in narration form as well as in tables. The chapter begins with presenting descriptive statistics of all variables, then bivariate analysis and ends with multivariate analysis.

4.1 Participants sociodemographic, maternal characteristics and other factors

Descriptive statistics of various factors and perinatal death occurrences of participants in the study is described (Table 4.1). The average age of the participants was 26.4 years (standard deviation = 6.9 yrs) with median of 25 years and range 15-45 yrs. While 38 (15.5%) had FSB, 194 (78.9%) had MSB and only 14 5.7% had ENND. Only 12 (4.9%) of the participants were married; 33.3%, 58.3% and 8.3% of whom had FSB, MSB and ENND respectively. In addition, 18 (7.3%) were employed, out of which 16.7%, 72.2% and 11.1% had FSB, MSB and ENND respectively.

Of the participants, 116 (47.2%) were referred from clinics while 130 (52.8%) were from hospitals. Among those referred from the clinics, 85.3% had MSB, 11.2% had FSB, while only 3.5% had ENND. Among those referred from hospitals, 73.1% had MSB, 19.2% had FSB while 7.7% had ENND. Routine ultrasound (USS) was done to 160 (65%) of the participants while foetal monitoring USS was done to only 34 (13.8%) of the participants. MSB was observed in 77.5% of those who had Routine USS and 81.4% of those who didn't have Routine USS. Moreover, FSB and MSB cases were slighly lower among those who had foetal monitoring USS when compared to those who didn't have foetal monitoring USS (11.8% vs 16.0%) and (76.5% vs 79.3%) respectively. However, ENND was more common among those who had foetal monitoring USS when compared to those who didn't have (11.8% vs 4.7%).

Whereas 94 (38.2%) had their BP controlled, blood tests were done for 74 (30.1%) participants, 61 (24.8%) were positive for HIV and 3 (1.2%) were diabetic. FSB was more common among those who had their BP controlled compared to those whose BPs were never controlled (20.4% vs 7.5%) but both MSB and ENND were relatively common among those who had their BPs controlled compared to those whose BPs were not controlled (85.1% vs 75.0% and 7.5% vs 4.6%), respectively. FSB and MSB were less common among those who had blood tests when compared to those who had no blood test done (14.9% vs 15.7% and 75.7% vs 80.2%)

respectively but a reverse trend was observed for ENND (9.5% vs 4.1%). Moreover, MSB and ENND were more common among those with HIV bu this was not the case for FSB. FSB was only more common among those who were diabetic.

The commonest initial diagnosis was GHPT 96 (39.0%) and the commonest final diagnosis was SPET 96 (39.0%). Imminent Eclampsia (IE) was the rarest dignosis both at initial and final diagnosis 3 (1.2%) and 8 (3.3%) respectively. Most of the women booked clinic between 12-24 weeks 137 (55.7%) and many of them were diagnosed with hypertension between 25-30 weeks of gestation 83 (33.7%) whereas 95 (38.6%) delivered between 26-31 weeks of gestation. Majority of participants 137 (55.7%) were within para 1 to para 4 with only 3.3% of the participants being grandmultipara. Many of the partcipants 161 (65.5%) attended ANC between 1 and 4 times and 50 (20.3%) did not attend HRC even though they were supposed to.

Table 4.1. Descriptive statististics of the study population

Variable	Perinatal Outcomes			
	Overall, n(%)	FSB	MSB	ENND
Married				
Yes	12 (4.9)	4 (33.3)	7 (58.3)	1 (8.3)
No	234 (95.1)	34 (14.5)	187 (79.9)	13 (5.6)
Employed				
Yes	18 (7.3)	3 (16.7)	13 (72.2)	2 (11.1)
No	228 (92.7)	35 (15.4)	181 (79.4)	12 (5.3)
Facility Type				
Clinic	116 (47.2)	13 (11.2)	99 (85.3)	4 (3.5)
Hospital	130 (52.8)	25 (19.2)	95 (73.1)	10 (7.7)
Routine USS done				
Yes	160 (65.0)	25 (15.6)	124 (77.5)	11 (6.9)
No	86 (35.0)	13 (15.1)	70 (81.4)	3 (3.5)
Foetal monitoring USS done				
Yes	34 (13.8)	4 (11.8)	26 (76.5)	4 (11.8)
No	212 (86.2)	34 (16.0)	168 (79.3)	10 (4.7)
BP Controlled				
Yes	94 (38.2)	7 (7.5)	80 (85.1)	7 (7.5)
No	152 (61.8)	31 (20.4)	114 (75.0)	7 (4.6)
Blood test done				
Yes	74 (30.1)	11 (14.9)	56 (75.7)	7 (9.5)
No	172 (69.9)	27 (15.7)	138 (80.2)	7 (4.1)
HIV				
Positive	61 (24.8)	8 (13.1)	49 (80.3)	4 (6.6)
Negative	185 (75.2)	30 (16.2)	145 (78.4)	10 (5.4)

Diabetic				
Yes	3 (1.2)	1 (33.3)	2 (66.7)	0
No	243 (98.8)	37 (15.2)	192 (79.0)	14 (5.8)
Initial diagnosis				
CHPT	20 (8.1)	4 (20.0)	13 (65.0)	3 (15.0)
GHPT	96 (39.0)	10 (10.4)	81 (84.4)	5 (5.2)
PET	57 (23.2)	9 (15.8)	46 (80.7)	2 (3.5)
SPET	52 (21.1)	9 (17.3)	40 (76.9)	3 (5.8)
I.E	3 (1.2)	1 (33.3)	2 (66.7)	0
Eclampsia	18 (7.3)	5 (27.8)	12 (66.7)	1 (5.6)
Final diagnosis				
CHPT	7 (2.9)	3 (42.9)	3 (42.9)	1 (14.3)
GHPT	66 (26.8)	3 (4.6)	61 (92.4)	2 (3.0)
PET	45 (18.3)	6 (13.3)	39 (86.7)	0
SPET	96 (39.0)	18 (18.8)	69 (71.9)	9 (9.4)
I.E	8 (3.3)	1 (12.5)	7 (87.5)	0
Eclampsia	24 (9.8)	7 (29.2)	15 (62.5)	2 (8.3)
GA at booking (Weeks)				
<12	65 (26.4)	6 (9.2)	56 (86.2)	3 (4.6)
12-24	137 (55.7)	25 (18.3)	104 (75.9)	8 (5.8)
25+	44 (17.9)	7 (15.9)	34 (77.3)	3 (6.8)
GA at diagnosis (Weeks)				
<20	19 (7.7)	2 (10.5)	14 (73.7)	3 (15.8)
20-24	44 (17.9)	11 (25.0)	30 (68.2)	3 (6.8)
25-30	83 (33.7)	12 (14.5)	66 (79.5)	5 (6.0)
31-36	80 (32.5)	9 (11.3)	69 (86.3)	2 (2.5)
37+	20 (8.1)	4 (20.0)	15 (75.0)	1 (5.0)
GA at delivery (Weeks)				
20-25	35 (14.2)	8 (22.9)	25 (71.4)	2 (5.7)
26-31	95 (38.6)	13 (13.7)	77 (81.1)	5 (5.3)
32-37	93 (37.8)	13 (14.0)	74 (79.6)	6 (6.5)
38+	23 (9.4)	4 (17.4)	18 (78.3)	1 (4.4)
Parity				
0	101 (41.1)	10 (9.9)	86 (85.2)	5 (5.0)
1-4	137 (55.7)	27 (19.7)	102 (74.5)	8 (5.8)
5+	8 (3.3)	1 (12.5)	6 (75.0)	1 (12.5)
#. Of ANC visits				
0	0	0	0	0
1-4	161 (65.5)	28 (17.4)	123 (76.4)	10 (6.2)
5+	85 (34.6)	10 (11.8)	71 (83.5)	4 (4.7)
#. Of HRC visits				
0	50 (20.3)	6 (12.0)	43 (86.0)	1 (2.0)
1-4	145 (58.9)	23 (15.9)	116 (80.0)	6 (4.1)
5+	51 (20.7)	9 (17.7)	35 (68.6)	7 (13.7)

GA= Gestational age, HRC= High Risk Clinic, ANC= Antenatal clinic, CHPT= Chronic hypertension, GHPT= Gestation hypertension, PET= Preeclmpsia, SPET= Severe preeclampsia, IE= Imminent eclampsia, USS= Ultrasound

4.2 Bivariate analysis

Table 4.2 below shows the results of binary logistic regression for the association between the 3 perinatal outcomes and the various possible predictors. The table presents the n for each variable, Odds Ratio and the 95% Confidence Interval while p-values are indicated in the narrative below.

4.2.1 Sociodemographic characteristics of participants

Age was not significantly associated with FSB, MSB or ENND. Those who were married were more likely to have FSB than those who were not married (OR=2.94; 95% CI= 0.84-10.3; p=0.092) but less likely to have MSB than those who were not married (OR=0.35; 95% CI= 0.11-1.16; p=0.086) although these were only marginally significant. There was however no association between marital status and ENND. Employment status was not associated with FSB, MSB or ENND.

4.2.2 Type of care recieved, maternal characteristics, healthcare utilisation and diagnosis

Whether routine USS was done, whether foetal monitoring USS was done, whether blood tests were done, HIV status and diabetes status were all not significantly associated with FSB, MSB or ENND. Patients who were referred from clinics were less likely (marginally significant) to have FSB compared to those from the hospitals (OR=0.53; 95% CI= 0.28-1.09; p=0.085) but more likely to have MSB compared to those from the hospitals (OR=2.15; 95% CI= 1.13-4.09; p=0.020). However, facility type referred from was not associated with experiencing ENND. Participants who had their BPs controlled were less likely to have FSB compared to those who did not have their BPs controlled (OR=0.31; 95% CI= 0.13-0.75; p=0.009). Moreover, those whose BPs were controlled were more likely to have MSB compared to those whose BPs were not controlled although this was marginally significant (OR=1.90; 95% CI= 0.97-3.75; p=0.062). There was however no association between having BP controlled and experiencing ENND.

There was significant association between parity 1-4 and MSB (OR=0.51; 95% CI 0.26-0.99; p=0.048). Women who attended HRC 5 times or more were less likely to have MSB (OR= 0.36; 95% CI0.13-0.96; p=0.042) while ANC attendance was not associated with FSB, MSB,

or ENND. Except for Gestational age at booking 12-24 which was maginally associated with reduced MSBs (OR= 0.51; 95% CI 0.23-1.13; p=0.098), the other gestational ages at booking, diagnosis and delivery were not associated with FSB, MSB, or ENND. With respect to diagnosis, women who had an initial diagnosis of GHPT were more likely to have MSB (OR= 2.91; 95% CI 1.00-8.49; p=0.051). Similarly those who had a final diagnosis of GHPT were more likely to have MSB (OR= 16.27; 95% CI 2.82-93.87; p=0.002). Final diagnosis of PET was also significantly associated with MSB (OR= 8.07; 95% CI 1.54-48.70; p=0.014).

Table 4.2. Univariable logistic regression results

Variable		**Perinatal Outcomes**		
	n	**FSB**	**MSB**	**ENND**
		OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
Age (yrs)	246	1.03 (0.99-1.09)	0.97 (0.93-1.01)	1.02 (0.95-1.10)
Marital Status				
Married	12	2.94 (0.84-10.3)*	0.35 (0.11-1.16)*	1.55 (0.19-12.9)
Not Married	234	Ref	Ref	Ref
Employment Status				
Employed	18	1.10 (0.30-4.01)	0.68 (0.23-1.99)	2.25 (0.46-10.9)
Unemployed	228	Ref	Ref	Ref
Facility Type				
Clinic	116	0.53 (0.28-1.09)*	**2.15 (1.13-4.09)****	Ref
Hospital	130	Ref	Ref	**16.27 (2.82-93.87) *****
Routine USS				
Done	160	1.04 (0.50-2.15)	0.79 (0.41-1.52)	2.04 (0.55-7.52)
Not done	86	Ref	Ref	Ref
Faetal Monitoring USS				
Done	34	0.70 (0.23-2.11)	0.85 (0.36-2.01)	2.69 (0.79-9.13)
Not done	212	Ref	Ref	Ref
Blood Pressure				
Controlled	94	0.31 (0.13-0.75)*	1.90 (0.97-3.75)*	1.67 (0.57-4.91)
Not controlled	152	Ref	Ref	Ref
Blood test				
Done	74	0.94 (0.44-2.01)	0.77 (0.40-1.47)	2.46 (0.83-7.29)
Not Done	172	Ref	Ref	Ref
HIV status				
Positive	61	0.78 (0.34-1.81)	1.13 (0.55-2.32)	1.23 (0.37-4.07)
Negative	185	Ref	Ref	Ref
Diabetes Status				

Positive	3	2.78 (0.25-31.5)	0.53 (0.05-5.98)	-
Negative	243	Ref	Ref	
GA at delivery		0.97 (0.90-1.05)	1.02 (0.96-1.10)	0.99 (0.88-1.11)
Initial diagnosis				
CHPT	20	Ref	Ref	Ref
GHPT	96	0.47 (0.13-1.67)	2.91 (1.00-8.49) *	0.31 (0.07-1.43)
PET	57	0.75 (0.20-2.77)	2.25 (0.73-6.97)	0.21 (0.03-1.34) *
SPET	52	0.84 (0.23-3.10)	1.79 (0.58-5.52)	0.35 (0.06-1.89)
I.E	3	2.00 (0.14-27.99)	1.08 (0.08-14.08)	-
Eclampsia	18	1.54 (0.34-6.93)	1.08 (0.28-4.13)	0.33 (0.03-3.53)
Final diagnosis				
CHPT	7	Ref	Ref	Ref
GHPT	**66**	**0.06 (0.01-0.42) *** **	**16.27 (2.82-93.87) *** **	0.19 (0.01-2.38)
PET	45	0.21 (0.04-1.15) *	**8.67 (1.54-48.70) ** **	-
SPET	96	0.31 (0.06-1.50)	3.41 (0.71-16.24)	0.62 (0.07-5.74)
I.E	8	0.19 (0.01-2.50)	9.33 (0.71-122.57) *	-
Eclampsia	24	0.55 (0.10-3.12)	2.22 (0.40-12.29)	0.55 (0.04-7.09) *
GA at booking (weeks)				
<12	65	Ref	Ref	Ref
12-24	137	2.19 (0.85-5.65)	0.51 (0.23-1.13) *	1.28 (0.33-4.50)
25+	44	1.86 (0.58-5.97)	0.55 (0.20-1.48)	1.51 (0.29-7.86)
GA at diagnosis (weeks)				
<20	19	Ref	Ref	Ref
20-24	44	2.83 (0.56-14.26)	0.77 (0.23-2.54)	0.39 (0.07-2.14)
25-30	83	1.44 (0.29-7.03)	1.39 (0.44-4.39)	0.34 (0.07-1.58)
31-36	80	1.08 (0.21-5.45)	2.24 (0.67-7.46)	**0.14 (0.02-0.89) ** **
37+	20	2.12 (0.34-13.24)	1.07 (0.25-4.51)	0.28 (0.03-2.97)
GA at delivery (weeks)				
20-25	35	Ref	Ref	Ref
26-31	95	0.54 (0.20-1.43)	1.71 (0.70-4.19)	0.92 (0.17-4.96)
32-37	93	0.55 (0.21-1.47)	1.56 (0.64-3.79)	1.14 (0.22-5.92)
38+	23	0.71 (0.19-2.70)	1.44 (0.42-4.94)	0.75 (0.06-8.78)
Parity				
0	101	Ref	Ref	Ref
1-4	137	**2.23 (1.03-4.86) ** **	**0.51 (0.26-0.99) ** **	1.19 (0.38-3.75)
5+	8	1.30 (0.14-11.67)	0.52 (0.10-2.84)	2.74 (0.28-26.82)
Number Of ANC visits				
1-4	161	Ref	Ref	Ref
5+	85	0.63 (0.29-1.38)	1.57 (0.79-3.09)	0.75 (0.23-2.45)
Number Of HRC visits				
0	50	Ref	Ref	Ref

1-4	145	1.38 (0.53-3.62)	0.65 (0.27-1.60)	2.12 (0.25-18.01)
5+	51	1.57 (0.51-4.80)	**0.36 (0.13-0.96) ****	7.80 (0.92-65.89) *

OR (95% CI): Odds Ratios with 95% Confidence interval; * Significance at α=0.10; ** Significance at α=0.05; ***Significance at α=0.01; **In Bold**: p-value below 0.05

4.3 Multivariate analysis

Table 4.3 shows the results for the multivariate logistic regression models. As explained under data analysis, the resultant model for FSB and MSB had marital status, Facility type, whether BP was controlled or not and final diagnosis; ENND had facility type and number of HRC visits. Those who were married were more likely to have FSB than those who were not married (OR=6.40; 95% CI= 1.35-30.28; p=0.019) but were less likely to have MSB that those who were not married (OR=0.22; 95% CI= 0.05-0.89; p=0.033). Moreover, those who were referred from clinics were less likely to have FSB than those referred from hospitals (OR=0.49; 95% CI= 0.22-1.09; p=0.081) – (marginally significant); but were more likely to have MSB than those who were referred from hospitals (OR=2.29; 95% CI= 1.13-4.46; p=0.022). Those who had their BPs controlled were less likely to have FSB than those whose BPs were not controlled (OR=0.18; 95% CI= 0.06-0.55; p=0.003) but were more likely to have MSB compared to those whose BPs were controlled (OR=2.49; 95% CI= 1.10-5.61; p=0.028). Those who had atleast 5 HRC visits were associated with 8.02 times increased odds of experiencing ENND (OR=8.02; 95% CI= 0.94-68.25; p=0.057), although this was only marginally significant.

Compared to those who had CHPT as the final diagnosis, GHPT (OR=0.03; 95% CI= 0.00-0.26; p=0.001), PET (OR=0.10; 95% CI= 0.01-0.75; p=0.024), SPET (OR=0.12; 95% CI= 0.02-0.76; p=0.025) IE (OR=0.05; 95% CI= 0.00-0.88; p=0.041) were associated with reduced odds of FSB. On the other hand, compared to those who had CHPT as the final diagnosis, GHPT (OR=22.62; 95% CI= 3.49-146.87; p=0.001), PET (OR=12.14; 95% CI= 1.90-77.44; p=0.008), SPET (OR=5.44; 95% CI= 0.98-30.35; p=0.053) – (marginally significant) and IE (OR=20.90; 95% CI= 1.37-318.43; p=0.029) were associated with increased odds of MSB. However there was no significant difference in the odds of experiencing FSB or MSB between those who had CHPT and those who had Eclampsia.

Table 4.3. Multivariable logistic regression results

Variable	Perinatal Outcomes					
	FSB		MSB		ENND	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Married						
Yes	6.40 (1.35-30.28)	0.019	0.22 (0.05-0.89)	0.033		
No	Ref		Ref			
Facility Type						
Clinic	0.49 (0.22-1.09)	0.081	2.29 (1.13-4.66)	0.022	0.42 (0.12-1.39)	0.154
Hospital	Ref		Ref		Ref	
BP Controlled						
Yes	0.18 (0.06-0.55)	0.003	2.49 (1.10-5.61)	0.028		
No	Ref		Ref			
#. Of HRC visits						
0					Ref	
1-4					2.15 (0.25-18.38)	0.484
5+					8.02 (0.94-68.25)	0.057
Final diagnosis						
CHPT	Ref		Ref			
GHPT	0.03 (0.00-0.26)	0.001	22.62 (3.49-146.87)	0.001		
PET	0.10 (0.01-0.75)	0.024	12.14 (1.90-77.44)	0.008		
SPET	0.12 (0.02-0.76)	0.025	5.44 (0.98-30.35)	0.053		
I.E	0.05 (0.00-0.88)	0.041	20.90 (1.37-318.43)	0.029		
Eclampsia	0.20 (0.03-1.50)	0.117	4.04 (0.62-26.30)	0.143		

CHAPTER FIVE: DISCUSSION

This study aimed at finding the antenatal factors associated with high levels of perinatal mortality among women with hypertension disorders in pregnancy. Data was extracted from registers and files of patients who had suffered from hypertension while pregnant and ended up with a perinatal death as the outcome of their pregnancy between 1 January 2019 and 31 December 2021.

5.1 Sociodemogaphic factors

Age

The mean age of the participants in this study was 26.4 years with a median of 25. Many of the participants were below 30 years. This finding is in agreement with what is reported by Statistics South Africa (STATS SA, 2018). Acoording to STATS SA majority of the births occur between the ages 20-30 (STATS SA, 2018). It is not surprising to have the average age 26.4 because many people around that age have finished school and have probably started working or doing business to support the children they are ready to bear. Biologically both women and men are more likely to bear children below the age of 30 (Botha, Matsaseng & Kruger, 2016).

On bivariate analysis, this study did not find significant association between age and perinatal mortality. Contrary to the findings in this study, some studies have shown significant relationship between perinatal deaths and age. In a cross-sectional study in China to look at the association of maternal age at birth and neonatal mortality, it was found that younger age groups including 20-24, 16-19, and 12-15 were more likely to experience neonatal mortality compared to age group 25-29 (Wu, Zhao, Liang, Liu & Xi, 2020). Different from Wu *et al*, a study in Nigeria found that older women (more than 35 years) were more likely to have perinatal deaths than younger ones (Nwokoro, Dahiru, Olorukooba, Daam, Waziri, Adebowale, Waziri & Nguku, 2020). The reason why my study found no significant association between age and perinatal mortality as opposed to the findings by Wu *et al* and Nwokoro *et al* could be that my study focussed only on women with hypertension disorders in pregnancy while the two studies focussed on the general population of pregnant women and comparatively my study had smaller samples size. It is therefore recommended that further study be done to look at the association of age and perinatal mortality in the general pregnant women population.

Employment

Majority of the participants (92.7 %) were not formally employed meaning that they were either in the informal sector or they were literally not working. This finding is not surprising looking at the age of most of the mothers who participated (mostly young) and the rate of unemplyment among the youths in South Africa. According to the latest statistics, youth unemployment in South Africa is well above 40 % (STATS SA, 2022). Other studies have also reported high proportions of unemployed women experiencing perinatal deaths. A clinical observational study in india to determine socio-demographic factors associated with perinatal mortality found more than 80 % of the women who had perinatal deaths were not formally employed (Surekha & Kumar, 2012). This huge proportion of unemployed women may mean reduced household income resulting in most of the women not affording the cost of attending antenatal clinic, poor nutrition during pregnancy and high levels of stress, all of which can negatively affect the outcomes of their pregnancy. There is need for the local government in the area to look at ways of creating employment especially for the youth in general and women in particular.

After breaking down perinatal deaths into FSB, MSB and ENND, unexpectedly this study did not find any signifiant association between employment and FSB, MSB or ENND. The reason for finding no association between employment and perinatal mortality could be that the study looked at perinatal mortality in one group of patients namely; women with hypertension disorders in pregnancy. There is need to confirm this finding by conducting further research that will include perinatal deaths in all pregnancies.

Studies elsewhere have shown conflicting results. While some studies show a positive association between employment and perinatal deaths, other studies have shown that unemployment is actually associated with less perinatal deaths. In a study in Germany it was found that women who were unemployed and those who were housewives had a 2.58 and 2.06 risk respectively of having a stillbirth compared to those who were formally employed. Interestingly the study also found significant association between stillbirths and fathers who were not formally employed (Reime, Jacob & Wenzlaf, 2009). On the contrary, a study in rural India to find determinants of neonatal mortality, it was found that the odds of neonatal mortality were lower among unemployed women compared to those who were employed (Singh, Kumar & Kumar, 2013).

Unlike Reime *et al* who compared professional workers and unemployed women, Singh *et al* compared women who were working as labourers in factories and agriculture/farming sector. Looking at the nature of the jobs for labourers in the factories and agriculture, there might be some environmental factors like high levels of noise which may negatively affect the outcome of the pregnancies. A study in Sweden showed that women who are working in environments that have more than 85dBA of noise are at risk of preterm labour and preterm labour is one of the causes of perinatal deaths (Raylander, Albin, Rosenhall, Lewne, & Gsutsvsson, 2019). National Institute for Occupational Safety and Health (NIOSH) also found similar findings (NIOSH, 2022). NIOSH found that noise is associated with stress and then stress can lead to preterm labour which is one of the causes of perinatal mortality (NIOSH, 2022).

Marital status

In terms of marital status, this study found that 95.1 % of the participants were not married. This finding is not surprising because several households in KwaZulu-Natal province in South Africa are headed by women who are not married. According to STATS SA more than 46 % of households in KZN province are headed by women not married (STATS SA, 2011). Very low proportion of married women in this area could be because of exobitant financial cost of marrying as imposed by cultural norms practised in this area. In the multivariate analysis of this study, it was determined that married women were less likely to experience MSB than those not married. Notably, MSB accounted for a large proportion of all perinatal fatalities; therefore, it is possible that being married is associated with lower odds of perinatal mortality overall. The findings in this study are similar to the findings in other studies. In their study in Nigeria, Nwokoro *et al* found that majority of the perinatal deaths were experienced among women who were single. Nwokoro *et al* found that Single women were 11.9 times more likely to have perinatal deaths than those who were married (Nwokoro *et al*, 2020).

In another study in USA to evaluate the risk of stillbirths among women who are not married, it was found that unmarried women carried a 1.24 risk of stillbirths compared to the married women. Interestingly the study found that among those who were unmarried those 15 years and below plus those 40 years and above were at a much higher risk of stillbirths (Balayla, Azoulay & Abenhaim, 2014). High perinatal deaths for the very young and very old women could be as a result of other factors like poor antenatal clinic attendance among the very young women and congenital as well as other medical conditions associated with advanced maternal age as already alluded to. Lower odds of perinatal deaths among married women may be

beacuse married women are more likely to have close social support from their husbands besides financial support to attend antenatal clinic adequately. The findings in this study on marriage and perinatal mortality may help shape policy in the social services sector. There is need to lobby traditional leaders to help women who are single find social support from other family members including parents, siblings and other extended family members. These family members may help with social and financialsupport.

5.2 Patient related factors

The study also looked at patient related factors that could be associated with high perinatal mortality. Among the factors, the study focussed on ANC attendance, HRC attendnace, gestational age at booking, the number of visits a woman had before delivery and parity.

Antenatal clinic attendance

Majority of the participants (65.5%) had between one and four ANC visits and only 34.6% of the participants had 5 or more visits. With respect to HRC visits it is worth noting that above 20% of participants who should have attended high risk clinic did not attend the clinic and that majority of women attended between one and 4 times. According to the current WHO recommendation which South Africa is in the process of implementing, a minimum of eight contact visists are recommended (WHO, 2016). This implies that many participants in this study fall short of the recommended number of ANC visits. Besides possible socioeconomic and cultural reasons causing low ANC/HRC visits, the other reason has to do with the current guidelines being followed in South Africa which are yet to be updated. The guideline stipulates four visits for low risk pregnancies and for high risk pregnancies there is no stipulated minimum number of visits (NDOH, 2016). In a way this creates confusion and puts discretion solely on the healthcare provider on the number of visits a high risk pregnant woman can attend. Inadequate attendance of both ANC and HRC means that the monitoring of high risk pregnancies like those with hypertension is suboptimal and that may lead to adverse outcomes for both the mother and the foetus including perinatal and maternal mortality. The findings in this study may help to strengthen the need to review the current guidelines and expedite the implementation of the recommendation by WHO that pregnant women must have minimum of 8 visits for ANC.

Surprisingly on bivariate analysis it was noted that ANC attendance was not significantly associated with perinatal mortality . This finding is different from the findings in many other

studies. In a study in Kenya to assess effectiveness of antenatal clinic services in reducing neonatal mortality it was found that women who did not attend ANC were 4 times more likely to have neonatal death (Arunda, Emmelin & Asamoah, 2017). The findings in Kenya are also corroborated by a meta-analysis study in sub–Saharan Africa to determine the impact of antenatal clinic on neonatal mortality. In this meta-analysis they found that there was a significant association between ANC attendance and neonatal mortality (Tekelab, Jojenta, Smith & Loxton, 2019). Considering numerous studies that have shown low ANC visits being associated with high perinatal mortality, the reason why this study did not find similar results could be that this study did not compare ANC visits between the survivors (those who were hypertensive but did not have perinatal mortality) and those with perinatal deaths because all the participants had perinatal deaths. The other difference between my study and the studies by Arunda *et al* as well as Tekelab *et al* is that, my study only focused on women with hypertension and obviously the sample size was smaller compared to the two studies which looked at perinatal mortality in general. Because of this difference my study may not have adequately assessed the relatioship between ANC attendance and perinatal mortality. In that regard there is need for another study at the hospital to look at association between perinatal mortality in general and ANC attendance.

Nevertheless, a few studies do also corroborate with the findings in this study. For instance a hospital based study in Ethiopia found that number of ANC follow-ups was not associated with severity of the hypertension diosrder and perinatal deaths (Wolde, Segni, Woldie, 2011). This study was very much similar to my study in that the study also looked at perinatal mortality among pregnant women with hypertension only hence the findings are similar to my study.

These findings will strengthen the call for more community sensistisation on the need to encourage pregnant women to honour all antenatal clinic appointments. Community health practitioners need to work with traditional, political and religious leaders as well as civil society organisations to sensitise women to book early and attend clinic adequately when they fall pregnant.

Parity

Majority (96.8%) of the participants were of low parity (between para 0 and para 4) and only 8 participanats were grandmultipara (para 5 or more). On bivariate analysis, the study found that parity between 1 and 4 was associated with fewer MSB. This implies that women who

have had more births before are more likely to have MSB or perinatal mortality in general. The reason for this may be that women who have given births multiple times are more likely to be older and therefore prone to other conditions or factors associated with perinatal mortality including congenital abnomalities and maternal medical conditions like hypertension and diabetes. More attention should be given to mothers with high parity during consultation at clinics and hospitals to look for other factors that may be causing high perinatal mortality in this group.

Studies that have been done to test the association between parity and perinatal mortality have shown conflicting results. While some studies seem to agree with the findings in this study that lower parity is associated with reduced risk of perinatal mortality, some studies show that low parity is infact associated with high perinatal mortality. A study in Indonesia to assess the effect of parity on perinatal mortality found that women who were more than para 4 were 1.9 times more likely to have perinatal death than those with lower parity (Siahaan & Ariwan, 2021). Similarly, another study in eastern Uganda to determine neonatal mortality determinants found that grandmultiparity was associated with more perinatal deaths compared to women of lower parity. In that study it was found that grandmultipara women were 2.53 times more likely to have perinatal mortality than those with lower parity (Kananura, Tetui, Mutebi, Bua, Waiswa, Kiwanuka, Kiracho & Makambi, 2016).

On the other hand, a meta-analysis study to determine foetal and maternal factors for perinatal mortality, Berhan and Berhan in Ethiopia found that women who were para 0 were 1.5 times more likely to have perinatal mortality compared to those of higher parity (Berhan & Berhan, 2014). Another study in Ethiopia to determine perinatal outcomes among women with hypertension disorders in pregnancy found that parity between 2 and 4 was associated with 1.6 risk of perinatal mortality. With regards to parity most of the participants were of low parity. The study found that 68.7% of the participants were either nullipara or para 1. On bivariate analysis the study found significant association between para 0 as well as para 2 with perinatal mortality (Endeshaw & Berhan, 2015).

From the findings regarding perinatal mortality and parity, it is clear that both low and grandmultiparity could be associated with perinatal mortality and that the association could be mediated through other factors like maternal age. Women with low parity are more likely to be young and therefore issues related to inadequate antenatal clinic attendance leading to perinatal

mortality could be at play. On the other hand grandmaltiparity women are more likely advanced in terms of age and issues relating to congenital abnormalities and medical conditions like hypertension and diabetes could be leading to perinatal mortality among in this group.

5.3 Type of care

Among the objectives, this study wanted to document the type of care given to women with hypertension diosrders in pregnancy. Some of the parameters used to determine the type of care given were; use of ultrasound to monitor foetal wellbeing, blood tests perfomed to monitor complication in the pregnant woman and control of blood pressure.

Ultrasound

The study found that 65 % had routine ultrasound done while 35 % did not have any ultrasound done. With regards to foetal monitoring ultrasound, the study found that only 13.8 % of the participants had foetal monitoring ultrasound. Low levels of antenatal clinic visits coupled with inadequate resources in terms of ultrasound machines and skills to do ultrasound could explain such a low usage of ultrasound at the hospital under study. Besides, the national gudelines for management of hypertension in pregnancy in South Africa is not clear on the use of ultrasound durining antenatal care. For example, the national guideline does not specifically say how often an ultrasound can be done to monitor foetal well being (Moodley, Soma-Pillay, Buchmann & Pattinson, 2019). According to literature review and practice advice offered by experts in the management of hypertension in pregnancy, ultrsound should be done every 2-4 weeks and should include foetal biometry, umbilical dopplers and amniotic fluid index (Poon, Magee, Verlohren, Shennan, Dadelszen & Sheiner, 2021). Use of ultrasound to monitor foetal wellbeing is essential particularly for high-risk pregnancies. The findings in this study can be used to inform changes in the guidelines and standard operating procedures so as to clearly stipulate as to when ultrasound can be done for pregnant women especially those who are high risk including the ones with hypertesnion disorders.

Low usage of ultrsound during antenatal care is common particularly in developing countries. In a study in Ghana to determine Ghananian women experience and perception of ultrasound use during antenatal period, the mean number of ultrasound done was 2.2 (Mensah, Nkyekyer & Mensah, 2014). Similar results were also found in another study in Nigeria to determine altitudes of expectant mothers on the use of ultrasound where they found that only 58.7 % of women had ultrasound done in their previous pregnancies and 60.1 % cited cost as the reason

why ultrsound was not being done (Ikeako, Ezegwini, Onwudine & Enwereji, 2014). Contrary to my study, the studies by Mensah et al and Ikeako et al looked at the reasons why many women were not doing ultrasound. It is therefore important that my study is followed up with another study to look at why there is low ultrasound usage at the hospital where my study took place.

Even though the results show that doing USS does reduce the risk of perinatal mortality, they are not startistically significant. This finding is in agreement with a meta analysis study to determine if doppler ultrasound improve pregnancy outcomes. In that study it was found that no difference in both foetal and maternal clinical outcomes for those who had ultrasound done and those who did not (Stampalija, Gyte & Alfirevic, 2010). Contrary to the findings in this study, some studies have shown that doing ultrasound especially for high risk pregnancies like those with hypertension does reduce perinatal mortality. In their study looking at antepartum evaluation of the foetus and foetal wellbeing O'Neill and Thorp found that, while other monitoring activities showed no impact on perinatal mortality, doppler ultrasound for high risk pregnancies was associated with significant reduction in perinatal mortality (O'Neill & Thorp, 2012). Unlike in my study, O'Neil and Thorp looked at the use of ultrasound in both low and high risk pregnancies and compared the risk of perinatal deaths among the high risk pregnancies to that of low risk pregnancies and that could explain why my results and theirs are different. Therefore, there is need to do a similar study at the hospital where my study took place to assess the association between use ultrasound and perinatal mortality in low risk pregnancies and high risk pregnancies then compare the two in as far as perinatal mortality risk is concerned.

Blood tests

In terms of blood tests done, the study found that only 38.2% of the participants had their blood tests done. The study further found that doing blood tests was marginally associated with reduced risk of FSBs and MSBs. High number of participants who had no blood tests could be as a result of a number of factors. The national guidelines do not clearly stipulate as to how often blood tests can be done more particularly in women whose blood pressure is already controlled. Lack of clear guidelines means the frequency of blood tests to be done is at the discretion of the clinician seeing that client. Therefore if it happens that the clinician does not see the need to do blood tests that client will not have the tests done. The other reason could be related to poor ANC/HRC attendance on the part of pregnant women with hypertension. Most

of the women in this study did not attend clinic adequately. For most forms of hypertension in pregnancy blood tests including haemoglobin, platelets, renal function tests and liver function tests ought to be done almost every two weeks (Moodley et al, 2019). Regular blood tests help with picking up complications early and therefore prompt interventions to prevent adverse outcomes for both the mother and the foetus. Small proportion of women being done blood tests as found in this study will form the basis for review of the current guidelines to stipulate clearly when the blood tests can be done.

BP control

Majority of the participants (61.8%) had their blood pressure not controlled implying that their BPs were mostly above 140/90 in the preceeding four weeks to delivery. Blood pressure control was significantly associated with reduced risk of FSB but surprisingly it was marginally associated with increased risk of MSB. The increase in MSB could be as a result of overtreatment of hypertension compromising uteroplacental blood flow. Evidence has shown that treating blood pressure in the range of 140 to 155 systolic and 90 to 100 diastolic can be associated with adverse foetal outcomes including growth restriction and foetal demise (Magee, Abalos, Dadelszen, Sibai, Easterling & Walkinshaw, 2011). Since most of the patients did not attend HRC at the hospital meaning that they did no have a chance to be seen by the doctor prior to them giving birth, the management of their hypertension at ANC may have been suboptimal since they were seen by nurses only. It could be that the hypertension was prematurely treated with medication or else overtreated leading to lower blood pressures which ultimately leads to compromised utero-placenta flow then intrauterine foetal death. There is need for refresher course to remind nurses in the clinic to refer all women with hypertension disorders in pregnancy to the hospital for proper management.

The reduction in FSB with controlled BPs needs confirmation since this study had 38 FSB only therefore it may not be accurate to conclude that BP control is significantly associated with reduced FSB. The same applies to ENND, it may be inaccurate to conclude that BP control is associated with increased ENND as found in this study since there were only 14 ENND. Further study is required to evaluate the relationship between BP control and perinatal mortality. The study needs to have large sample size and have a fair representation of all categories of perinatal mortality.

5.4 Diagnosis

Diagnosis was split into two namely; initial diagnosis and final diagnosis. The reason was to see progression of the disease from less severe form at initial diagnosis to a more severe form at the time the woman gave birth. The diagnoses for both inital and final included; CHPT, GHPT, PET, SPET, IE and eclampsia.

From the results one can see that the commonest initial diagnosis was GHPT, followed by PET then SPET. In terms of the final diagnosis majority of the participants ended with SPET implying that hypertension disease had progressed from less severe forms including CHPT, GHPT and PET to SPET. This is important because it may point to poor control of hypertension as a result of inadequate monitoring resulting from poor antenatal clinic attendance or suboptimal treatment at the facility. Similar findings have also been found in other studies. A hospital based study in Ethiopia to determine maternal and foetal outcomes for women with hypertension disorders in pregnancy, SPET was found to be the commonest final diagnosis (Seyom, Abera, Tesfaye & Fentahun, 2015).

In terms of perinatal mortality, the study found that GHPT is significanly associated with MSB. As explained area, MSB was the majority type of perinatal mortality in this study, one can therefore say that overall GHPT is associated with perinatal mortality. This is very interesting because GHPT is a less severe form of hypertension disorders in pregnancy, therefore one would expect that it should not be associated with more risk of perinatal deaths as compared with SPET, IE and eclampsia. The explanation for this may be that there is less attention accorded to GHPT at this facility compared with SPET, IE and eclampsia. This is probably so because even the guidelines does not stipulate adequate monitoring for GHPT (Moodley et al, 2019). The hospital needs to review the guidelines for management of hypertension in pregnancy so as to accord enough attention to the less severe forms of hypertension in pregnancy. Prompt and optimal treatment of less severe hypertension will prevent progression of the disease to severe forms and may also reduce perinatal mortality.

Contrary to the findings in this study, a multicenter study in USA to determine the obstetric and perinatal outcomes among women with hypertension disorders in pregnancy found that GHPT was associated with the lowest risk of perinatal mortality (Meredith, Cruz, Gao and Hibbard, 2011). The findings in USA are corroborated with the findings in Ethiopia where a study to determine pattern and outcomes of pregnancies complicated with hypertension found

no perinatal deaths among women with GHPT while 16 perinatal deaths were recorded among women with SPET (Wolde, Abawollo & Woldie, 2011). Unlike my study, the participants in the study by Wolde *et al* had adequate antenatal care visits and more likely that the pregnancies were optimally monitored and managed. This then means those patients who presented with less severe hypertension like GHPT were promptly managed hence preventing perinatal mortality. Results in my study will help strengthen the basis for calling upon pregnant women to attend antenatal clinic adequately but also to alert clinicians and nurses to pay more attention to less severe forms of hypertension in pregnancy once they meet these women in their consultation.

5.5 Gestational age at booking, diagnosis and delivery

Majority of the participants booked in the second trimester which is considered late booking. Late booking also correlates with inadequency of antenatal care visits implying that part of the reason why participants attended ANC inadequately is because they booked late. Women who booked in the second trimester were marginally associated with reduced odds of MSBs otherwise no significant association was noted between all gestational ages at booking and perinatal mortality. Similar findings were obtained in a study in Cameroon to determine pregnancy outcomes for women who booked for ANC in the first trimester and those who booked later. In that study no significant association was noted between booking late and all adverse outcomes of pregnancy (Njim, 2016). The reason why this study and Njima's study found no difference in terms of perinatal mortality between those who booked early and those who booked late could be that other factors including inadequate antenatal visits and subptimal care affected the association between perinatal mortality and gestational age at booking. There is therefore need for further studies to look at the association between gestaional age at booking and perinatal mortality in the general pregnant women population other than just women with hypertension disorders in pregnancy.

With regards to the gestational age at the time diagnosis of hypertension was made, majority of the participants were diagnosed when they were between 25 and 36 weeks and very few were diagnosed with hypertension when they were 37 weeks and above. Gestational age group of 31-36 was significantly associated with ENND. The rest of the gestational age groups were not significantly associated with perinatal deaths. Some studies have shown that early onset of hypertension in pregnancy is associated with perinatal mortality. A study in India showed that early onset preeclampsia was associated with more perinatal deaths compared with late onset

(Heijst, Haan, Heijden, 2017). In the case of my study the reason why no significant association was found could be because I did not compare perinatal mortality with those who did not have hypertension in the same gestaional age categories. There is need for further study to compare perinatal mortality among women with hypertension in various gestational age groups and their counterparts without hypertension.

In terms of gestational age at delivery, the study found that majority of the participants delivered between 26-31 weeks followed by 32-37 weeks. In other words, most of the participants had preterm births. The reason why the study looked at the gestationa age at delivery was to see if it is necessary for pregnant women with hypertension disorders to be planned for an earlier delivery to prevent perinatal mortality. On bivariate analysis all gestational age groups did not show significant associationn with perinatal mortality. Preterm delivery has been shown to mediate the relatioship between hypertension in pregnancy and perinatal mortality. A cross-sectional study in USA to evaluate the impact of preterm delivery on the association between chronic hypertension in pregnancy and perinatal mortality found that most of the perinatal deaths occured were preterm. The study also noted that significant perinatal mortality would be prevented if delivery was planned at the early term stage in women with hypertension disorders in pregnancy (Brandt, Reddy and Ananth, 2021). Results in my study need to be confirmed by a followup study to compare perinatal mortality in various gestational age groups among those with hypertension in pregnancy and those without hypertension. Doing this comparison will help establish if indeed perinatal mortality is not associated with gestational age at delivery.

5.6 LIMITATIONS OF THE STUDY

Just as many studies, this study also had some limitations that may have impacted negatively on the results. The first limitation was the sample size which was small. As I planned in the proposal phase of this study, the sample size was supposed to be 384 but when I reviewed the files, I found 246 files that were meeting the inclusion criteria. There was discrepancy in the number of files entered in the register as women with hypertension disorders and perinatal deaths and the actual files that were being stored at the registry. I noted that there were fewer files compared to the number in the registers because many files were missing at the registry. As already explained, I had to use all the files (246) found in order to increase the power of the study.

The other limitation or challenge encountered was illegibility of the notes in some of the files. There were some files we were unable to extract adequate information because we could not read what was written. In some instances, we excluded the whole file because valuable information was illegible. There were 6 files which were completely excluded based on illegibility.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

In terms of the sociodemographic factors, this study found that majority of the participants were not educated and many of them were not married. Except for marriage which showed significant association with reduction in the risk for perinatal mortality, other sociodemographic factors did not show any significant association. With regards to patient related factors, many participants booked clinic late and had fewer than recommended visits for both ANC and HR. There was no statistically significant association between perinatal deaths and both ANC and HRC visits. Low parity was noted to be associated with reduced perinatal mortality. Finally in terms of type of care rendered to women with hypertension disorders in pregnancy, it was noted that most of the care was suboptimal as per guidelines even though no significant association was noted between type of care parameters and perinatal deaths. This study has therefore helped to find areas that may need improvements in order to reduce perinatal mortality at the hospital under study besides showing areas that need further research in order to understand fully the factors at play in as far as perinatal mortality is concerned at the hospital under study.

6.2 Recommendations

- Since this study only focused on pregnant women with hypertension disorders and that all of them had perinatal deaths, I recommend a follow-up study that will look at those women who had hypertension in pregnancy in the same period but their babies survived. This will help to generate evidence with regards to how much of influence the factors explored in this study have on perinatal mortality.

- Looking at patient related factors like ANC booking and attendance, I recommend that community education program be done to create awareness on the need for pregnant women to start clinic early and also honour all ANC appointments. Even though this study did not show significant association with perinatal mortality subject to follow-up studies on the same, the fact still remains that ANC is very important for holistic monitoring of pregnancies. The fact that majority of the pregnant women are not booking early and do not attend adequately ANC, clearly shows that majority are

missing out on the important services rendered at ANC apart from screening and monitoring of hypertension.

- I also recommend setting up a special clinic at the hospital under study that deals with pregnant women with hypertension in pregnancy only. As it is now, all pregnant women are attended at HRC which is often overcrowded with other pregnant women with other high-risk conditions. This clinic is mostly busy and usually understaffed leading to luck of focus on very important conditions like hypertension in pregnancy. If a clinic was to be set up to solely look at the number one cause of perinatal mortality at this hospital which is hypertension, I believe that perinatal mortality would be reduced significantly. I recommend that such a clinic be run by an obstetrician assisted by medical officers. Besides rendering high quality services, such a clinic would also be a teaching clinic for junior medical officers and nurses on the management of hypertension in pregnancy.

- I also recommend that the hospital come up with its own clear guidelines on the management of hypertension in pregnancy and these guidelines be sent to all clinics and hospitals that refer their patients to this hospital under study. As at now there are no clear guidelines such that most of the interventions are left at the discretion of the healthcare provider on whether to do them or not. Clear guidelines will not only improve management of hypertension in pregnancy but it will also reduce the number of unnecessary referrals to HRC run by this hospital.

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APPENDICES

APPENDIX 1 : INFORMATION SHEET (ENGLISH)-PARTICIPANT

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21 959 2809 Fax: 27 21 959 2872

E-mail: soph-comm@uwc.ac.za

INFORMATION SHEET

Project Title: ANTENATAL FACTORS ASSOCIATED WITH PERINATAL MORTALITY AMONG WOMEN WITH HYPERTENSION DISORDERS IN PREGNANCY AT A REGIONAL HOSPITAL IN KWAZULU-NATAL PROVINCE IN SOUTH AFRICA

What is this study about?

This is a research project conducted by Dr Lyson Stembridge Gwesele, a student at the University of Western Cape (UWC) pursuing Master in Public Health (MPH). The research is being conducted as part of the requirements for awarding of MPH. The research is being supervised by Prof Olagoke Akintola of UWC. You are being invited to participate in the study because you are a mother who was found to have high blood pressure in pregnancy between 1January 2019 and 31 December 2021 at the regional hospital under study and that you either delivered a still born or the baby died within 7 days of birth. The purpose of this study is to gather information that will help to assess whether the current management of women with hypertension in pregnancy is adequate or there are areas that need to be improved.

What will I be asked to do if I agree to participate?

You will be asked to allow the researcher to extract information from your file and other records at the regional hospital under study.

Would my participation in this study be kept confidential?

The researchers undertake to protect your identity and the nature of your contribution. To ensure your anonymity the researcher will not use your name on the data extracted or the final report of the research. Instead, the researcher will use an inpatient or outpatient number that will be linked to your information. All data extraction will be conducted in one room which will be accessed by the research team only. All the data extracted will be kept in a password

protected computer. After publishing the results of the study, the data extracted will be destroyed so that no one can access it.

What are the risks of this research?
Every research does carry some risks be it physical, psychological or emotional risks. By interacting with you through this information sheet your emotions and psychological impact of the loss of your baby might be aroused. As a research team we have tried to minimise this risk by using your records at the hospital other than taking you through that experience again by asking you questions regarding the loss. Should there be any emotional or psychological problem arising from participation into this study such participants will be appropriately referred to the hospital psychologist for treatment. The researcher commits to promptly minimise other risks that may be unforeseen at this point in time

What are the benefits of this research?
This study may not help you personally but the results may help inform the hospital under study the changes that are necessary to improve management of women with high blood pressure in pregnancy thereby reducing death of babies while in the womb of their mothers or a few days after birth.

Do I have to be in this research and may I stop participating at any time?
Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time by informing the researcher that your information should not be used anymore. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized or lose any benefits to which you otherwise qualify.

What if I have questions?
This research is being conducted by Dr Lyson Stembridge Gwesele at the University of the Western Cape. If you have any questions about the research study itself, please contact Dr Gwesele on +27606375146 or email 4001729@myuwc.ac.za. You can also contact the supervisor Prof Olagoke Akintola through email oakintola@myuwc.ac.za.

Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Prof Uta Lehmann
Head of Department: School of Public Health
University of the Western Cape
Private Bag X17
Bellville 7535
ulehmann@uwc.ac.za

Prof Anthea Rhoda
Dean: Faculty of Community and Health Sciences
University of the Western Cape
Private Bag X17
Bellville 7535
chs-deansoffice@uwc.ac.za

This research has been approved by the University of the Western Cape's Biomedical Research Ethics Committee (BMREC).
.

BMREC
University of the Western Cape
Private Bag X17
Bellville
7535
Tel 0219594111
E-mail research-ethics@uwc.ac.za

APPENDIX 2 : INFORMATION SHEET (ISIZULU)-PARTICIPANT

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa
Tel: +27 21 959 2809 Fax: 27 21 959 2872
E-mail: soph-comm@uwc.ac.za

IMININGWANE YOCWANINGO

Isihloko: Ucwaningo olwenziwa esibhedlela sesifundazwe saKwaZulu Natal olubheka imbangela yokushona kwezingane zomama abaphethwe iBP/ Hayi-hayi besakhulelwe.

Lumayelana nani lolucwaningo?

Lolucwaningo lwenziwa uDokotela uLyson Stembridge Gwesele, owenza izifundo zesiqu esiphezulu kwezenhlalakahle yomphakathi (Masters degree in Public Health) eNyuvesi yesifundazwe sase Western Cape (University of the Western Cape). Embambisene futhi ephethwe uProf Olagoke Akintola naye owaseNyuvesi yesifundazwe saseWestern Cape.
Uyamenywa ukuthi ube yingxenye yalolucwaningo ngoba ungowesifazane otholalakale ene BP/ Hayi-hayi esakhulelwe phakathi komhlaka 1 kuMasingane (January) 2019 nomhlaka 31 kuZibandlela (December) 2021 esibhedlela lapho khona kwenziwa lolucwaningo, futhi ubelethe umtwana osethule noma owashona esengaphansi kwezinsuku eziyisikhombisa. Lolucwaningo lubheka izimo zempatho yabesimame abatholakala beneBP besakhulelwe ngenhloso yokwenza ushintsho olungcono nokugwema ukushona kwezingane zalaba besimame

Yini engingayilindela noma engizoyenza uma ngivuma ukuba yingxenye yalolucwaningo?

Uma uvuma ukuba yingxenye yalolucwaningo uzobe uvumela abacwaningi (Dr Gwesele no Prof Akintola) ukuthi babuke imininingwane efayilini lakho lasesibhedlela owawusihamba futhi esenza lolucwaningo.

Engabe imininingwane yami izogcinwa iyimfihlo na?

Abacwaningi bahlose ukuvikela imininingwane yakho nabo bonke abavuma ukuba yingxenye yalolucwaningo. Lokhu bazokwenza ngokungasebenzisi igama noma inombolo kamazisi wakho uma sekuphuma imiphumela yocwaningo, esikhundleni salokho kuzosetshenziswa inombolo yakho yasesibhedlela exhumene nefayili lakho. Ukuhlaziywa kwemininingwane kuzokwenzelwa egumbini elilodwa ekungena abacwaningi kulo kuphela. Yonke imininingwane ezobe ihlaziwa izogcinwa eKhompyutheni ekhiyiwe (password-protected). Uma imiphumela yocwaningo isishicilelwe imininingwane yabahlanganyeli bocwaningo iyacinywa kuKhompyutha ukuze ingazukubonwa abangahlangene nocwaningo.

Engabe bukhona ubungozi ekuzibandakanyeni kwami kulolucwaningo?

Ukudalula imininingwane yakho ngezimo ezenzeka ukhulelwe kungavusa usizi nobuhlungu owabuzwa ngesikhathi ushonelwa yingane. Ukugwema lokho siyithimba labahlaziyi nabacwaningi sizobheka imininingwane efayilini lakho esikhundleni sokukubuza imibuzo siqu sakho. Uma kuvela obunye ubungozi esingabulindelanga, sizokwazisa ngokushesha.

Zithini izinzuzo (benefits) ekuzibandakanyeni kwami nalolucwaningo?

Imiphumela yalolucwaningo ingangesiza wena kodwa izoba nomthelela ekusizeni omunye okungenzeka abe sesimeni esifana nesakho. Lolucwaningo luzosiza isbhedlela owawunakekelwa kuso ukuthi sikwazi ukuphatha kangcono abesimame abaneBP bekhulelwe futhi sigweme nokushona kwezingane zabo labesimame.

Engabe ngiphoqelekile yini ukuba yingxenye yalolucwaningo futhi uma ngivuma ngingayeka nini ukuba umhlanganyeli?

Unelungelo lokuvuma noma ukunqaba ukuba yingxenye yalolucwaningo. Uma uthatha isinqumo sokuvuma ukuba umhlanganyeli kulolucwaningo ungasishintsha isinqumo sakho noma kunini ngaphandle kokusinikeza isizatho. Ungasitshela njengethimba labacwaningi ukuthi awusavumi ukuthi siqhubeke sisebenzise imininingwane yakho. Ayikho imiphumela emibi ezokuvelela.

Ngingenzenjani uma nginemibuzo?

Uma unemibuzo ungaxhumana nodokotela uGwesele owenza lolucwaningo ku +27606375146 noma uthumele i-email 4001729@myuwc.ac.za. Ungaxhumana nomphathi uProf Olagoke Akintola ngokuthumela i-email ku oakintola@myuwc.ac.za.

Uma unemibuzo ngenhloso yalolucwaningo noma ngamalungelo akho njengomhlanganyeli walolucwaningo noma ufisa ukubika izinkinga obhekane nazo ekuzibandakanyeni nalolucwaningo, xhumana nalaba abaphathi:

Prof Uta Lehmann
Head of Department: School of Public Health
University of the Western Cape
Private Bag X17
Bellville 7535
ulehmann@uwc.ac.za

Prof Anthea Rhoda
Dean: Faculty of Community and Health Sciences
University of the Western Cape
Private Bag X17
Bellville 7535
chs-deansoffice@uwc.ac.za

Lolucwaningo lugunyaziwe abezimiso zokuziphatha ngokuhlaziya nokucwaninga abaseNyuvesi yesifundazwe sase Western Cape (University of the Western Cape's Biomedical Research Ethics Committee)

Biomedical Research Ethics Committee
University of the Western Cape
Private Bag X17
Bellville
7535

APPENDIX 3 : CONSENT FORM (ENGLISH)

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa
Tel: +27 21-959 2809, Fax: 27 21-959 2872
E-mail: soph-comm@uwc.ac.za

Title of Research Project: ANTENATAL FACTORS ASSOCIATED WITH PERINATAL MORTALITY AMONG WOMEN WITH HYPERTENSION DISORDERS IN PREGNANCY AT A REGIONAL HOSPITAL IN KWAZULU-NATAL PROVINCE IN SOUTH AFRICA

The study has been described to me in language that I understand. My questions about the study have been answered. I understand what my participation will involve and I agree to participate of my own choice and free will. I understand that my identity will not be disclosed to anyone. I understand that I may withdraw from the study at any time without giving a reason and without fear of negative consequences or loss of benefits.

Participant's name……

Participant's signature……

Date……

APPENDIX 4: CONSENT FORM (ISUZULU)

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa
Tel: +27 21-959 2809, Fax: 27 21-959 2872
E-mail: soph-comm@uwc.ac.za

IFOMU LESIVUMELWANO

Isihloko: Ucwaningo olwenziwa esibhedlela sesifundazwe saKwaZulu Natal olubheka imbangela yokushona kwezingane zomama abaphethwe iBP/ Hayi-hayi besakhulelwe.

Ngichazelwe ngalolucwaningo ngolwimi engiluzwayo. Ngithole izimpendulo/ ingcazelo ngemibuzo ebenginayo. Ngichazelekile futhi ngizikhethela mina ngokwami ukuba yingxenye/ umhlanganyeli (participant) kuloluchwaningo. Ngichazelwe ukuthi imininingwane yami izogcinwa iyimfihlo. Ngichazelwe ngokuthi ngingakwazi ukuyeka ukuba yingxenye yocwaningo noma kunini ngaphandle kokubeka izizathu futhi ngaphandle kokwesaba imiphumela engalunganga.

Igama lomhlanganyeli:_____
Isignesha yomhlanganyeli:_____
Usuku (date):_____

UNIVERSITY of the WESTERN CAPE

Department of Institutional Advancement
University of the Western Cape
Robert Sobukwe Road
Bellville 7535
Republic of South Africa

06 December 2021

Dr L Gwesele
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM21/10/35

Project Title: Antenatal factors associated with perinatal mortality among women with hypertension disorders in pregnancy at a Regional Hospital in Kwazulu Natal Province in South Africa.

Approval Period: 06 December 2021 – 06 December 2024

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project and the requested amendment to the project.

Any further amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via:
https://sites.google.com/uwc.ac.za/permissionresearch/home

The permission letter must then be submitted to BMREC for record keeping purposes.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

APPENDIX 6: ETHICS CLEARANCE FROM THE HOSPITAL UNDER STUDY

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Queen Nandi Regional Hospital

Private Bag x 2005,Empangeni, 3880 29
Union Street, Empangeni, 3880
Tel.:035 907 7000, Fax.086 692 2075

Ethics Committee

10 February 2022

Dear Dr L Gwesele

RE: PERMISSION TO CONDUCT A RESEARCH AT QUEEN NANDI REGIONAL HOSPITAL

I have pleasure in informing you that consent has been given to you by Queen Nandi Regional Hospital Ethics Committee to conduct research on "Antenatal factors associated with perinatal mortality among women with hypertension disorders in pregnancy at a Regional
Hospital in KwaZuIu Natal Province in South Africa.

Yours sincerely

Dr Andrew J Grant (Ethics Committee Chair)

Dr M Samiowan (Medical Manager)

APPENDIX 7: Approval letter from Department of Health-KZN

Dear Dr L. Gwesele (OCT)

Approval of research

1. The research proposal titled 'Antenatal factors associated with perinatal mortality among women with hypertension disorders in pregnancy at a regional hospital in KwaZulu Natal province' was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby approved for research to be undertaken at Queen Nandi Regional Hospital.

2. You are requested to take note of the following:
   a. All research conducted in KwaZu/u-Nata/ must comply with government regulations relating to Covid- 19, These include but are not limited to: regulations concerning social distancing, the wearing of persona/ protective equipment, and limitations on meetings and social gatherings.
   b. Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of paüents attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.
   c. Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.
   d. Provide an interim progress report and final report (electronic and hard copies) when your research is complete to HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10102, PRIVATE BAG '(9051, PIETERMARITZBURG, 3200 and e-mail an electronic copy to hrkm@kznhealth.gov.za
   e. Please note that the Department of Health shall not be held liable for any injury that occurs as a result of this study.

For any additional information please contact Mr X, Xaba on 033-395 2805.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee
Date: 02/05/2022.

Fighting Disease, Fighting Poverty, Giving Hope