PERINATAL OUTCOMES FOLLOWING EXPECTANT MANAGEMENT OF SEVERE PREECLAMPSIA AT MTRH, ELDORET, KENYA

BY

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DECLARATIONS

Declaration by the student

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DEDICATION

This study is dedicated to all expectant mothers to whom this work aspires to bring hope and fulfill their aspirations for successful pregnancy.

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ABSTRACT

Background: Preeclampsia occurs in about 5 to 12% of all pregnancies. Early severe preeclampsia accounts for 25% of all cases of preeclampsia. PET is the leading cause of maternal and perinatal morbidity and mortality. The only known treatment for preeclampsia is delivery, yet an early preterm delivery increases the risk for adverse neonatal outcomes. Despite its significance both nationally and at the Moi Teaching and Referral Hospital, there is paucity of information on the perinatal outcomes of severe preeclampsia managed conservatively remote from term. Further, there are no local studies to define the appropriate gestational age at which to initiate conservative management of severe pre-eclampsia remote from term by way of perinatal outcomes. In this regard, research was carried out in Moi Teaching and Referral Hospital Eldoret, Uasin Gishu County, Kenya to examine perinatal outcomes of expectant management of severe preeclampsia among women managed conservatively remote from term at MTRH's maternity unit in Eldoret- Kenya

Objective: To investigate the perinatal outcomes of severe preeclampsia among women managed conservatively at the Moi Teaching and Referral Hospital maternity unit in Eldoret, Kenya.

Methods: This was a prospective study done at MTRH.

A total of 72 women from 28 weeks gestation to 34 weeks gestation with severe preeclampsia were enrolled from admission to delivery and followed up for 7 days post delivery with outcomes evaluated. Expectant management was given whenever there was no indication for immediate delivery as per the hospital severe preeclampsia treatment protocol. The perinatal outcome of this expectant management was recorded and appropriate statistical analysis was carried out. Relevant data was collected using a semi structured questionnaires, entered into a computer access database, cleaned and analyzed using SPSS. Association between categorical variables was conducted using Pearson's Chi Square test and Fishers exact test. Descriptive data was summarized and presented using tables and graphs. Inferential statistics were presented using odd ratios and tabulated showing their P value ($p < 0.05$). Outcomes of interest included pregnancy prolongation, intrauterine fetal death, and birth weight, Apgar score at 5 minutes, newborn unit admission, and newborn status on day 7. **Results:** The mean age was 27.9+/- 6.6 years (range 16-43 years).The median pregnancy prolongation was 7 days. The majority (93%) of newborns had a birth weight less than 2500 grams. There were 24 perinatal deaths. Apgar score below 7 occurred in 8 (11.1%) newborns. More than half of newborns (51.4%) were admitted to the newborn unit. More than two thirds of babies (66.7%) were alive on day 7.

Conclusion: There was a mean pregnancy prolongation of a week with expectant management of early severe preeclampsia.

Recommendations: More studies are recommended in the area of early severe preeclampsia since the disease contributes to high mortality and morbidity in our setup. Pediatric follow up of newborns to document long term effect if any after expectant management of early severe PET. `

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LIST OF ABBREVIATION

ACE	Angiotensinogen Converting Enzyme
ACOG	American College of Obstetricians and Gynecologists
ASIP	American Society for Investigation Pathology
BMI	Body Mass Index
DNA	Deoxyribonucleic acid
HELLP	Hemolysis, Elevated Liver Enzymes, Low Platelets
IUGR	Intra Uterine Growth Restriction
IREC	Institutional Research and ethics Committee
MTRH	Moi Teaching and Referral Hospital
NHBPEDG	National High Blood Pressure Education Working Group Report
RNA	Ribonucleic Acid
SPE	Severe preeclampsia
WHO	World Health Organization

GLOSSARY OF TERMS

Neonatal Outcome Fate of newborn baby from birth to seven days post delivery

Perinatal Outcome Fate of fetus from 28 weeks gestation to 34 completed weeks and seven days post-delivery.

Remote from term Period of gestation from 28 completed weeks to 34 completed weeks

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CHAPTER ONE

1.0 BACKGROUND

1.1 Background to the study

Every tenth pregnancy is affected by hypertension, one of the most common complications and leading causes of maternal death worldwide (Khan, Wojdyla, Say, Gülmezoglu, & Van Look, 2006).

Hypertensive disorders in pregnancy include preexisting chronic hypertension, pregnancy induced hypertension and preeclampsia (PE). Preeclampsia is a multisystem pregnancy disorder characterized by *de novo* hypertension (>140/90 mmHg) and proteinuria at ≥ 20 weeks gestational age (i.e. the second half of pregnancy) in a previously normotensive woman (ACOG, 2002; Chaiworapongsa, Chaemsaithong, Yeo, & Romero, 2014; Lie et al., 1998). It is characterized by marked vascular, metabolic and inflammatory changes leading to generalized endothelial dysfunction and end organ damage (Kalk *et al.*, 2004).

In some cases, it manifests symptoms including intrauterine growth restriction, or reduced amniotic fluid volume (Khan et al., 2006)

Preeclampsia remains a potentially life threatening disease for both the mother and baby (BM Sibai, 2005). The World Health Organization (WHO) estimate that about 1.4 million women (about 10%) are affected by preeclampsia each year, resulting in an annual mortality of about 65,000 women worldwide (Hauth et al., 2000; Högberg, 2005; Roberts & Cooper, 2001; Zeisler *et al.*, 2016; Zhang, Meikle, & Trumble, 2003) but may be higher in resource limited settings or areas of the world which reflects inequities in access to health services (Onah, Okaro, Umeh, & Chigbu, 2005; B. M. Sibai, 2003). Although extensive research efforts have been aimed at

unraveling its pathogenesis, the etiology of preeclampsia remains to be elucidated. Most likely, preeclampsia is a result of interplay between maternal constitution, placental factors and inappropriate adaptive changes to pregnancy predominantly involving the cardiovascular and inflammatory system (Beste et al., 2005; Kalk et al., 2004).

There is wide variation in the incidence of preeclampsia between the developed and developing countries (Duley, 2009). WHO estimates the incidence of preeclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%)(WHO, 2005). The incidence of preeclampsia in the developed countries of North America and Europe is similar and estimated to be about 5–7 cases per 10,000 deliveries (Ronsmans, Graham, & group, 2006). On the other hand, incidence of preeclampsia in developing nations such as in Africa varies widely, ranging from 1 case per 100 pregnancies to 1 case per 1700 pregnancies (WHO, 1997). The incidence is high and the severity worse in developing countries due to malnutrition, hypoproteinemia, and poor obstetric care facilities (Olopade & Lawoyin, 2008). Rates from African countries such as South Africa, Egypt, Tanzania, Nigeria, Kenya and Ethiopia vary from 1.8% to 7.1% (Kimbally *et al.*, 2006; Mahaba, Ismail, El Damaty, & Kamel, 2000; Teklu & Gaym, 2006; Thiam *et al.*, 2003)

Typically, preeclampsia is classified by its severity into mild and severe types based on the woman's blood pressure , proteinuria , and symptoms or signs of a severe disease (Luealon & Phupong, 2010). Distinguishing between mild and severe preeclampsia is important because the management strategies are very different. Preeclampsia is classified as mild preeclampsia when the systolic blood pressure of >140 mmHg or a diastolic blood pressure >90 mmHg in combination with 300 mg of

protein collected in urine over 24 hours (Kenny *et al.,* 2010). Severe preeclampsia (SPE) is a more serious problem and is diagnosed if there are more severe elevations of blood pressure or evidence of other end organ dysfunction. Diagnosis of severe preeclampsia requires the basic features of mild preeclampsia as well as some indication of additional problems with either the mother or the baby. According to ACOG Committee on Practice Bulletins Obstetrics, (2002), one of the following findings is also necessary for a diagnosis of severe preeclampsia: signs of central nervous system problems (severe headache, blurry vision, altered mental status); signs of liver problems (nausea and/or vomiting with abdominal pain; elevated transaminases); at least twice the production of some liver enzymes on blood test; very high blood pressure (>160 systolic or 110 diastolic); thrombocytopenia; >500 gm of protein in a 24-hour urine sample; very low urine output (<500 ml in 24 hours); signs of respiratory problems (pulmonary edema, bluish tint to the skin); decreased glomerular filtration rate which may progress to Oliguria and acute renal failure and severe fetal growth restriction.

A triad of elevated liver enzymes, low platelets, and haemolysis is referred to as HELLP syndrome and its occurrence is associated with very poor prognosis for the mother and the fetus.

Severe preeclampsia causes multisystem deterioration that may be gradual or fulminant. Obstetric complications include IUGR, abruption, and fetal and maternal demise.

RISK FACTORS

The risk factors for preeclampsia can be divided into comorbid conditions, maternal demographics, and obstetric history (Hutcheon, Lisonkova, & Joseph, 2011; Luealon & Phupong, 2010). Women with diabetes, chronic hypertension, autoimmune

diseases, antiphospholipid antibody syndrome, chronic renal insufficiency, Angiotensinogen converting enzyme DD (ACE-DD) polymorphism, protein C deficiency, or protein S deficiency are among those at highest risk for preeclampsia (Alfirevic, Roberts, & Martlew, 2002; Dudding *et al.,* 2008; Jones & Hayslett, 1996; Landon, 2007; Mello *et al.,* 2003; Sanders & Lucas, 2001; Yamada *et al.,* 2000). Nevertheless, demographic factors such as obesity, and extremes of maternal age and obstetric characteristics such as nulliparity, multifetal gestation, prior history of preeclampsia and /or hydatidiform mole also increase risk (Duckitt & Harrington, 2005).

MANAGEMENT OF SEVERE PET

Effective management of preeclampsia is important as it will significantly contribute toward achievement of Sustainable Development Goal 3 which aims at ensuring healthy lives and promote wellbeing for all at all ages . Target 3.1 aimed at reducing global maternal mortality ratio to less than 70 per 100,000 live births while target 3.2 focuses on ending preventable deaths of newborns and under-fives by 2030 (UN, 2015).

Preeclampsia is progressive disease and management has been largely based on expert opinion with few prospective and retrospective studies that have addressed expectant management remote from term. Traditional management of preeclampsia has included immediate (and often) pre-term delivery aimed at preventing potential end-organ effects. However, this is usually associated with increased perinatal morbidity, mortality and prolonged hospitalization in the neonatal intensive care unit because of prematurity and therefore not in the best interest of the fetus.

On the contrary, attempts to prolong pregnancy with expectant management may result in fetal death or asphyxia related growth restriction in utero, and increased maternal morbidity (B. M. Sibai & Barton, 2007). Yet expectant management of preeclampsia remote from term has been shown to be beneficial to fetus and safe to the mother at the same time (Haddad *et al.*, 2004; Vigil-De Gracia, Montufar-Rueda, & Ruiz, 2003)

This highlights the importance of balancing the risks between maternal and perinatal outcomes. Management of severe preeclampsia protocol at Moi Teaching and Referral Hospital (MTRH) involves the following; 1) admitting the patient, 2) Control and prevention of seizures by giving magnesium sulphate, 3) Lowering of blood pressure using anti hypertensives, and 4) to expedite delivery by a delivery method safest to the mother and the baby based on a decision that takes into account disease severity and fetal maturity. There is however, lack of information on the outcome of such management regimen on preeclampsia. Therefore, this study assessed the maternal and perinatal outcomes of preeclampsia among women managed conservatively remote from term at MTRH maternity unit, Eldoret - Kenya.

1.2 Problem Statement

Approximately 2–7% of pregnancies are complicated by preeclampsia, depending on population and diagnostic criteria (Baha Sibai, Dekker, & Kupferminc, 2005). Among these, severe preeclampsia (SPE) is diagnosed in only 0.6% to 1.2% (Catov, Ness, Kip, & Olsen, 2007; Haddad *et al.*, 2004; Zhang *et al.*, 2003). Thus preeclampsia in both mild and severe form is an important health concern in developing countries where the incidence and rates of adverse outcomes are high against a background of limited medical facilities and resources.

Perinatal outcomes of expectant management of severe preeclampsia has not been determined in Kenya recently.

Several studies have focused on expectant management of severe pre-eclampsia syndrome before 28 weeks. For instance, (Bombrys, Barton, Habli, & Sibai, 2009) found eight such studies that included nearly 200 women with severe pre-eclampsia with an onset at less than 26 completed weeks. Maternal complications were common and owing to there being no neonatal survivors in women presenting before 23 weeks, the Task Force of the ACOG recommended pregnancy termination. The decision is less clear for women with slightly more advanced pregnancies. For example, at 23 weeks gestation, the perinatal survival rate was 18%, but long term perinatal morbidity is yet unknown.

1.3 Justification of Study

Preeclampsia continues to affect about 2-7 % of pregnant women and contributes 15% of maternal deaths. Management of preeclampsia requires skilled personnel, well established guidelines and premises equipped with the necessary instruments.

Little has been documented about perinatal outcomes of severe preeclampsia managed expectantly remote from term in Sub Saharan Africa, and few studies have examined perinatal outcomes of severe preeclampsia managed expectantly remote from term. Current Kenyan figures are unavailable but the morbidity report for the Moi Teaching and Referral Hospital in Eldoret the second national tertiary referral facility indicates that hypertensive disorders have replaced post-partum hemorrhage as the leading cause of maternal morbidity as well as contributing significantly to adverse fetal outcomes (Yego, D'Este, Byles, Nyongesa, & Williams, 2014).

Despite its significance both nationally and at the Moi Teaching and Referral Hospital, there is paucity of information on the perinatal outcomes of severe preeclampsia managed conservatively remote from term. Further, there are no local studies to define the appropriate gestational age at which to initiate conservative management of severe pre-eclampsia remote from term by way of perinatal outcomes. In this regard, research was carried out in Moi Teaching and Referral Hospital Eldoret, Uasin Gishu County, Kenya to examine perinatal outcomes of expectant management of severe preeclampsia among women managed conservatively remote from term at MTRH's maternity unit in Eldoret- Kenya.

1.4 Research Questions

The study was guided by the following research questions:

1. What are the characteristics of women with severe preeclampsia at MTRH's maternity unit?
2. Does expectant management of severe preeclampsia prior to 34 weeks of gestation result in improved perinatal outcome?
3. What are the perinatal outcomes of women with severe preeclampsia managed conservatively at MTRH's maternity unit?

1.5 General Objective

The objective of this study was to investigate perinatal outcomes of severe preeclampsia among women managed conservatively at MTRH's maternity unit in Eldoret- Kenya.

1.6 Specific Objectives

1. To describe the characteristics of women with severe preeclampsia at MTRH
2. To determine if expectant management of severe preeclampsia prior to 34 weeks of gestation result in improved perinatal outcome
3. To determine the perinatal outcomes of severe preeclampsia among women managed conservatively at MTRH

1.7 Significance of the Study

This research is expected to add to the existing knowledge information regarding preeclampsia and its management outcomes among medical practitioners working in Kenyan hospitals. This will help to provide evidence for maternal counseling on expectations during conservative management of preeclampsia. The study may encourage further research on the subject to broaden the understanding of the problem.

Although the management of severe preeclampsia using non-stress tests, expectant management through daily monitoring, ultrasound for assessment of fetal growth etc, has allowed for conservative management, it is clear that studies on the pregnancy outcomes have received little attention to date in Kenya.

Many of the studies done in many countries related to reproductive health issues have focused more on postpartum hemorrhage and anemia, with less attention given to assess fetal and neonatal outcomes of severe preeclampsia among women. An intensive literature search isolated only few preeclampsia studies in Kenya therefore it is imperative to assess the current impact of the disease and find ways of reducing the accompanying perinatal morbidity and mortality.

The findings will be used to develop educational strategies and provide accurate and factual local information for counseling affected individuals on the possible outcomes of conservative management.

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

This chapter discusses the previous studies done to assess perinatal outcomes of severe Preeclampsia among women managed conservatively remote from term. The chapter acknowledges the contribution made by other scholars, publications (articles, seminar papers, government policy papers, conference proceedings, training manuals, legislature documents, research reports, medical journals, textbooks, newspapers, and periodicals). It identifies gaps in the current literature, and suggests ways in which these gaps can be filled among preeclampsia women managed conservatively remote from term at MTRH, Eldoret, Kenya. This chapter is structured into sub-sections under the following headings:

2.1 General overview of preeclampsia

Preeclampsia was derived from the Greek word ‘eklampsia’ which means sudden flashing. Preeclampsia which has been variably called PET is also called Preeclamptic toxemia, and is a disorder that occurs in some women during pregnancy. It is associated with an increased systemic inflammation, and is a leading cause of maternal and fetal morbidity worldwide. Preeclampsia is linked with shallow extra villous trophoblastic invasion of the decidua, leading to uteroplacental flow that is inadequate for the developing fetoplacental unit. It is noticeable during the second half of pregnancy. Preeclampsia affects at least 5 percent of all pregnancies, and is characterized by high blood pressure, swelling in the limbs or face, and protein in urine. According to current criteria, Preeclampsia is diagnosed in the presence of a systolic blood pressure of 140 mmHg or higher or a diastolic of 90 mmHg or higher on two occasions at least six hours apart, and proteinuria, defined as an excretion of at

least 0.3 gram protein during 24 hours (ACOG, 2002; Turner, 2010). The symptoms can occur at any time after 20 weeks gestation, but early debut is usually more serious, and suggestions have been made to divide Preeclampsia into an early- and late-onset syndrome (Von Dadelszen, Magee, & Roberts, 2003) Placental pathology is reported to be more frequent and severe in early gestational age (Moldenhauer *et al.*, 2003).

As a medical condition in which hypertension arises in pregnancy, preeclampsia has an association with significant amounts of protein in the urine. It appears likely that there are substances from the placenta that can cause endothelial dysfunction in the maternal blood vessels of susceptible women. While blood pressure elevation is the most visible sign of disease, it involves generalized damage to the maternal endothelium, kidney and liver, with the release of vasoconstrictive factors being secondary to the original damage. Preeclampsia may develop from 20 weeks gestation and its rate of progress differs among patients; most cases are diagnosed pre-term. It may also occur up to six weeks post-partum. Apart from delivery, there is no other known definitive cure.

To develop effective treatment and prevention strategies one needs to be able to start treatment in early stages of the disease. Similarly, a study conducted by Jai Prakash, (2010) reported that preeclampsia was made using two cardinal features of the disease after 20 weeks of gestation in previously normotensive and non proteinuric women Preeclampsia was diagnosed in 106 (5.87%) patients (Prakash *et al.*, 2010). Primiparity constituted 53.77% of total patients. Hypertension and proteinuria were observed in all patients.

2.2 Epidemiology of severe preeclampsia

Preeclampsia is clinically divided into a mild and a severe form. Severe Preeclampsia is diagnosed in the presence of even higher blood pressure, proteinuria, fetal growth restriction or maternal complications and presence of symptoms. The signs and symptoms of severe preeclampsia included: Systolic blood pressure ≥ 160 mmHg, Diastolic blood pressure ≥ 110 mmHg, Proteinuria ≥ 5 g/24 hour, Oliguria <500 mL/24 hour, Cerebral or visual disturbances, Pulmonary edema or cyanosis, Epigastric or right upper-quadrant pain, Impaired liver function, Thrombocytopenia, and Fetal growth restriction (ACOG, 2002). If not treated, Preeclampsia can progress to eclampsia, defined as the development of convulsions or coma in Preeclampsia patients (Cipolla & Kraig, 2011). Preeclampsia affects approximately 2-7 % of pregnant women worldwide and is associated with both maternal and fetal mortality and morbidity. Although outcome is better in the developed world, Preeclampsia accounts for 15-20% of maternal mortality (BM Sibai, 2005). Along with hemorrhage and infection, hypertension is the major maternal complication in pregnancy. In three quarter of the cases, the syndrome starts near term, but it can also begin as early as in gestational week 20. Preterm delivery is reported in 15-67% and fetal growth restriction in 10-25% of pregnancies complicated by preeclampsia (Kattah & Garovic, 2013).

In developed countries, severe preeclampsia remote from term accounts for 1-2 % of maternal deaths while in developing countries preeclampsia /eclampsia account for more than 10% of maternal deaths, with some areas in sub-Saharan Africa e.g. Nigeria registering up to 40% maternal deaths from eclampsia.

Similarly there is a geographical variation in the prevalence of severe preeclampsia .For example, in Nepal, South Asia the preeclampsia prevalence rate was found to be

0.3 % while a study in Enugu Nigeria in 2012 observed a preeclampsia prevalence rate of 3.3 %. Another study by Osungbade in Nigeria showed a prevalence rates ranging from 2% to 16.7% (Osungbade & Ige, 2011).

A study conducted at Pumwani maternity hospital, Nairobi, Kenya and published in the East African medical journal 1985 analyzed a total of 23,084 deliveries for 1 year and reported an overall incidence of 3.7% cases of preeclampsia with an overall predominance in primi gravida. Almost 22.6% of babies born of preeclamptic mothers had an Apgar score of less than 8 at 5 minutes. Furthermore, the rate of stillbirths was directly proportional to the degree of severity of preeclampsia based on blood pressures and proteinuria.

Another severe complication of Preeclampsia is HELLP syndrome (acronym for hemolysis, elevated liver enzymes and low platelets). In addition to hypertension and proteinuria, typical symptoms in HELLP syndrome are malaise, upper quadrant tenderness, nausea and vomiting. Diagnosis of HELLP is based on laboratory findings and subjective symptoms such as epigastric pain.

Hypertension and proteinuria is absent in 10-15% of women with HELLP syndrome, suggesting a possible heterogeneity within this disease entity (Haram, Svendsen, & Abildgaard, 2009).

2.3 Etiology of preeclampsia

Preeclampsia complicates up to 2 to 7% of pregnancies and its main predisposing factors are family history of hypertension, extremes of reproductive age, primigravida, renal disease, hypertension prior to pregnancy , and obesity (Mustafa, Ahmed, Gupta, & Venuto, 2012). The protective effect of long-term sperm exposure could also provide explanation for the frequency of preeclampsia in teenage pregnancy. As all women do not develop preeclampsia maternal response

is believed to play a decisive factor in the development of preeclampsia (Sadat, Kalahroudi, & Saberi, 2012). Initial diagnosis is clinical and the severity of the disease is mainly based on blood pressure and proteinuria. However Liver function, Full Blood Count, platelet count and uric acid levels are important in determining the severity of the disease (Gupte & Wagh, 2014).

The cardinal requirements for the management of preeclampsia are early diagnosis, close supervision and timely delivery.

The mode of treating preeclampsia includes anti hypertension drugs, anticonvulsants drugs for control and prevention of seizures, and termination of the pregnancy. In early gestation prolongation of pregnancy with close monitoring could be indicated, however in case of imminent eclampsia or multi-organ dysfunction or fetal distress or sever preeclampsia after 34 weeks of gestation prompt delivery is indicated. However care needs to be taken, as immediate caesarean delivery might not always benefit the woman and her baby (Townsend, O'Brien, & Khalil, 2016). Considering expectant management, especially in cases of mild preeclampsia would prevent prematurity and associated complications in the neonate. In the management of severe preeclampsia or eclampsia, magnesium sulphate was found to be more effective than diazepam and Phenytoin. It is also cost effective and could be used in countries that are resource poor. It is important to note however that systematic Cochrane reviews show no improvement in neonatal outcome with magnesium sulphate use (Duley & Henderson-Smart, 2003).

The benefit of anti-oxidants and anti-platelets has also been reported in different studies with an observed decrease the incidence of prematurity in the neonate and development of eclampsia in the mother. However, substantial evidence is required

for their routine use during antenatal care or for the high-risk patients who might develop preeclampsia.

2.4 The Pathogenesis and risk factors for severe preeclampsia

The following are associated with pathophysiology of preeclampsia: Genetic predisposition (maternal, paternal, thrombophilias), Immunologic phenomena, Abnormal placental implantation (defects in trophoblasts and spiral arterioles), Vascular endothelial damage, Angiogenic factors (low level of placental growth factor), Platelet activation, cardiovascular maladaptation and vasoconstriction. As the speculations have been many, Preeclampsia has been described as the disease of theories. One of the leading theories at the moment is that there is a maternal immunological response to the fetal immune system, resulting in abnormal transformation of the spiral arteries, giving rise to some of the pathology described above. The absence of transformed spiral arteries leads to a high-resistance blood flow to the placenta. The turbulence of the blood flow and hypoxia in the placenta then give rise to a destruction of placental tissue and release of factors, such as soluble vascular endothelial growth factor receptor-1 (sFlt-1), syncytiotrophoblast membrane micro particles, fetal ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), which might injure maternal endothelium and be responsible for the maternal symptoms (Brosens et al., 2011; Redman & Sargent, 2000; BM Sibai, 2005).

Nulliparity, Maternal age greater than 40, Multiple gestations, Preeclampsia in a prior pregnancy (particularly if severe or prior to 32 weeks) or family history of preeclampsia, Interdelivery interval of more than 10 years ,Chronic hypertension, Chronic renal disease, Antiphospholipid syndrome, Elevated body mass index more than 35 kg/m2, Diabetes mellitus , and gestational trophoblastic disease and fetal triploidy.

Poor trophoblast invasion in PE causes impaired spiral artery remodeling following by placental ischemia/reperfusion and inflammation. Within the trophoblast cell, oxidative stress from unbalanced free radical formation is formed from different sources like XO, eNOS uncoupling, NADPH oxidase, and mitochondria. Ultimately, the reunion of all these events lead to peroxynitrite formation, lipid peroxidation, protein modification, MMP activation and DNA damage, contributing to endothelial dysfunction (Sánchez-Aranguren, Prada, Riaño-Medina, & Lopez, 2014).

Previously young maternal age was considered a risk factor, but this was not supported by a systematic review (Abalos, Duley, Steyn, & Henderson-Smart, 2007).

Several risk factors have been identified that would support the idea of an adaptation and development of a tolerance towards the paternal antigens. Robillard *et al* found that the time of cohabitation before conception was inversely related to the risk of pregnancy induced hypertension. Also, others have shown an increased risk for Preeclampsia after short cohabitation and after use of barrier contraception as well as a decreased risk for Preeclampsia if the couple had practiced oral sex before the pregnancy (Einarsson *et al.*, 2003; Koelman *et al.*, 2000; Robillard *et al.*, 1994). The risk for Preeclampsia is also higher in the first pregnancy than in the proceeding and both previous abortions and healthy pregnancies are protective against Preeclampsia (Trogstad, Magnus, Skjaerven, & Stoltenberg, 2008).

However, with change of partner, the protective effect of a previous pregnancy or abortion is lost (Dekker & Sibai, 2001; Saftlas et al., 2003).

2.5 Prenatal prevention of severe preeclampsia

Randomized controlled trials fail to support a role for routine prenatal supplementation with calcium, magnesium, Omega three fatty acids, or antioxidant vitamins E and C to prevent preeclampsia (BM Sibai, 1989). Calcium

supplementation has, however, been shown to reduce the risk of hypertension and preeclampsia for women at high risk and for women with low dietary calcium intakes. Calcium supplementation also reduces the incidence of neonatal mortality in healthy nulliparous normotensive women. Prevention is aimed at reducing progression from pregnancy induced hypertension or from mild preeclampsia to severe preeclampsia.

Prevention of preeclampsia should focus on the intervention and correction of pathophysiological changes (Dekker & Sibai, 2001). Currently there are no well-established measures for prevention of preeclampsia (Wagner, 2004) , however low dose aspirin, calcium and anti-oxidants are believed to be used as effective and inexpensive preventive measures to reduce the risk of preeclampsia (Dekker & Sibai, 2001).

2.6 Definitive Management of Severe Preeclampsia

Despite the high cost to families and health service sources, there is no effective management strategy other than elective delivery and no therapeutic intervention has been proven to prevent or delay the onset of the disease (Dekker & Sibai, 2001). Early diagnosis, close medical supervision and timely delivery are the cardinal requirements of the management of preeclampsia. Once the diagnosis is established, subsequent management should be based on the initial evaluation of maternal and fetal well-being. On the basis of the results of this evaluation a decision is then made regarding hospitalization, expectant management, or delivery. Irrespective of the management strategy chosen, the ultimate goal must first be the safety of the mother and, second the delivery of a live infant who will not require intensive and prolonged neonatal care. Even though delivery is the ultimate cure for pre-eclampsia, management aimed at

benefiting the mother may be detrimental to the fetus because premature birth is a significant cause of infant morbidity and mortality.

2.7 Neonatal outcomes of management of preeclampsia

The contributing factors to adverse outcomes include lack of ante-natal care, late presentation, and weak health system leading to poor quality emergency obstetric and newborn care. Social contributing factors to adverse fetal outcomes include poverty, poor reproductive health care-seeking behavior, and cultural perception of preeclampsia and lack of access to quality maternal services including intra-partum care (Backes *et al.*, 2011).

Delivery is the ultimate cure of preeclampsia and is always appropriate for the mother but may be responsible for neonatal adverse outcome particularly if it occurs at less than 34 weeks of gestation (Walker, 2000). The timing of delivery could also affect the outcome for mother as most maternal deaths occur at post-partum (Duley, Henderson-Smart, Walker, & Chou, 2010) A rushed delivery, especially a caesarean section in an unstable patient may add to her risk rather than lowering it. Decisions regarding the timing and mode of delivery are based on a combination of maternal and fetal factors.

Fetal factors include gestational age, evidence of lung maturity and signs of fetal compromise on antenatal assessment. Maternal factors include the degree to which the hypertension is controllable and any clinical or laboratory signs of impending decomposition. Patients with resistant severe hypertension or other signs of maternal or fetal deterioration must be delivered within 24 hours, irrespective of gestational age or lung maturity.

There is insufficient data to recommend an “interventionist” versus an “expectant management” approach for severe preeclampsia between 24 and 34 weeks (Churchill & Duley, 2002) Consultation is indicated (Odendaal *et al.*, 1990; BM Sibai, 1995).

An “interventionist” approach advocates induction or caesarean delivery 12 to 24 hours after corticosteroid administration. An “expectant” approach aims to give corticosteroids, stabilize the woman and fetus, and delay delivery even longer, if possible (Churchill & Duley, 2002),

Expectant management, with close monitoring of the mother and fetus, reduces neonatal complications and neonatal stay in the newborn intensive care nursery (Nicholson et al., 2008).

In a study, bed rest and close monitoring of women with gestation age between 28 and 32 weeks with preeclampsia prolonged pregnancy an average of 15 days, resulting in fewer cases of respiratory distress syndrome and necrotizing enterocolitis, without increasing maternal morbidity (Uzan, Carbonnel, Piconne, Asmar, & Ayoubi, 2011b).

Contraindications to expectant management of severe preeclampsia include persistent severe symptoms, multi organ dysfunction, severe IUGR (estimated fetal weight less than 5^{th} percentile), suspected placental abruption or non- reassuring fetal testing .

Attempted vaginal delivery is recommended for severe preeclampsia with no evidence of maternal or fetal compromise or other obstetric contraindication (NHBPE Program, 2000). Caesarean delivery in severe preeclampsia is indicated for some obstetric conditions e. g. status eclampticus or non-reassuring fetal heart rate pattern.

Reviewed current literature on fetal and neonatal outcomes of expectant management of preeclampsia prior to 34 weeks of gestation painted a mixed picture of the outcomes. Whereas some neonatal benefits are accrued, especially prolongation of

gestation, several have failed to demonstrate any improvement in morbidity or mortality. A number have reported worse outcomes in terms of mortality and morbidity as well as increased need for neonatal intensive care (Leite & Paravidino, 2018; Swamy, Patil, & Nageshu, 2012).The trend in these studies appears to be that the fetus gets more time to develop, hence escapes the complications of prematurity such as respiratory distress, but the benefits do not go very far beyond that.

Severe preeclampsia and Eclampsia have been associated with a number of fetal and neonatal complications. Multiple lines of evidence have implicated preeclampsia as a major cause of perinatal morbidity and death mostly due to premature delivery and uteroplacental insufficiency (Backes *et al.*, 2011). Preeclampsia, being a progressive disorder, may necessitate prompt delivery, being the definitive treatment for the good, especially, of the mother, but of the fetus as well (ACOG, 2002). As things stand however, optimal management guidelines for severe preeclampsia do not exist (Uzan, Carbonnel, Piconne, Asmar, & Ayoubi, 2011a). The need to deliver neonates with the capacity to adapt to the extra-uterine environment has necessitated a different approach, one of them being expectant management until the gestation is 34 weeks or more, which has been the subject of multiple studies (ACOG, 2008).

The potential benefits of expectant management have been reported in some studies that have suggested a significant reduction in neonatal respiratory complications, a benefit seen for each week increase in gestational age up to term (Backes et al., 2011). Similarly, one prospective case study to evaluate the perinatal outcome of expectant management in 340 women with severe

Preeclampsia of early onset reported that expectant management results in high perinatal and neonatal survival rates. On average, there was an increase in gestation by 11 days. This increase was found to be the only significant factor in determining neonatal outcome. There was a 94% rate of neonatal survival, and only 0.5% of the pregnancies ended in intrauterine death. Following delivery, 40.7% of them needed neonatal intensive care which lasted a median of six days, while among those who had complications; respiratory disease and sepsis were the main causes (Hall, Odendaal, Kirsten, Smith, & Grove, 2000).

A similar study to determine maternal and perinatal outcomes after expectant management of severe preeclampsia between 24 and 33 weeks' gestation analyzed increase in gestation by birth as well as perinatal morbidity according to the gestational age at time of expectant management: 24 to 28, 29 to 31, and 32 to 33 weeks. Pregnancy prolongation was found to be higher with earlier onset of expectant management. However, perinatal morbidity and neonatal morbidities had the reverse trend: being worse with earlier gestation at start of management (Haddad *et al.*, 2004).Similar results were reported in a retrospective analysis of outcome in patients with severe preeclampsia at <27 weeks which reported that outcome in the second trimester is dependent on gestation age at onset of expectant management and at delivery(Bombrys *et al.*, 2008). Its recommendation was termination after extensive counseling at <24 weeks due to very low perinatal survival in expectant management for this group.

In the MEXPRE Latin Study, a randomized, multicenter clinical trial (Vigil-De Gracia *et al.,* 2013) conducted in low-resource settings in Latin America, looked into

whether expectant management of severe preeclampsia prior to 34 weeks of gestation results in improved neonatal outcome. In the group under expectant management, a mean prolongation of pregnancy by 10.4 days was observed, compared to 2.2 in the group undergoing prompt delivery. There was no improvement in neonatal mortality or morbidity with expectant management, but this group suffered more placental abruption and tended to be born at an earlier gestation. Except for prolongation of gestation, there was no neonatal benefit.

These findings were more or less in agreement with a prior study where the effects of severe preeclampsia in low birth weight infants were observed in 35 pairs of infants with similar gestation. The effect of severe preeclampsia on the outcome of infants of very low birth weight was studied in a prospective case control study of 35 pairs of infants of comparable gestation. This study reported a significantly higher rate of delivery before the onset of labour and by caesarean section in the group with pre-eclampsia. This was associated with smaller babies and a similar profile of respiratory and infectious morbidities as well as higher rates of cardiovascular disease (patent ductus arteriosus and hypotension). The group with preeclampsia also required more intensive care: oxygen and mechanical ventilation. There was, however, no significant difference in the mean psychomotor developmental index or incidence of specific neurodevelopment impairment in the neonatal period (Szymonowicz & Yu, 2000)

Some studies, however, paint a picture of worse fetal-neonatal outcomes, especially with mortality. In one such study on preeclampsia in 26 pregnancies with an onset before 24 weeks' gestation, a median increase in gestation of 24 days was observed (range 3-46 days). However, the overall perinatal mortality was a high of 82%: 76% of these being fetal and the rest neonatal. There was a higher mortality in those

managed expectantly at an earlier gestation, similarly reported a high perinatal morbidity and mortality in gestational age < 28 weeks in severe preeclampsia (Jantasing & Tanawattanacharoen, 2009; Petra, 2006). A similar study by Attiya *et al* (Ayaz, Muhammad, Hussain, & Habib, 2009) on preeclampsia as a whole-without consideration of management- reported a perinatal mortality of 328 neonates per 1000 total births, resulting from still births and intrauterine fetal demise. A decrease in 5 minute Apgar score was observed as well.

2.7.1 Determination of gestational age

There are several ways available that can be used to determine the gestation age of a pregnancy**.** These include

1. The conceptional gestation age.

This is ideal and calculates the delivery date as 266 days or 38 weeks from conception. The limitation is that only few patients can determine the precise dates of conception including patients pregnant from ovulation induction, artificial insemination, and in vitro fertilization with a known date of embryo transfer.

2. Menstrual gestation age

This is based on the last normal monthly period and is more precise and practical. For it to be reliable the woman must have a definite last monthly period, a normal regular and predictable menstrual cycle that lasts from 21 to 35 days, and the pregnancy is planned. It assumes a 28 day cycle and that ovulation occurred on day 14 of the cycle and assumes the delivery date to be 280 days or 40 weeks from the last monthly period. Seven days are added for a 35 day cycle while 7 days are subtracted for a 21 day cycle to obtain the expected date of delivery i.e. 40 weeks gestation which can then be extrapolated to obtain the gestation of the pregnancy.

3. Naegele rule

The rule subtracts 3 months from the month and adds 7 days to the date of the last monthly period to obtain the expected delivery date.

4. Observing the basal body temperature to determine ovulation by inserting a thermometer in the vagina before arising out of bed and taking anything orally (Sakala, 2000).

5. Clinical landmarks

At 10-12 weeks fetal heart tones may be heard by a Doppler stethoscope.

At 18-20 weeks fetal heart tones may be heard with a Pinard fetoscope.

At 16-18 weeks quickening happens in a multigravida.

At 18-20 weeks quickening is reported in primigravida.

5. Fundal Height by pregnancy weeks.

After 20 weeks the weeks in gestation should approximate the centimeter measurement of the uterus size from the pubis to the fundus. This is valid for a single fetus.

A 2 to 3 cm variation from expected gestation is within the norm.

6. Ultra sound dating

An early pelvic ultrasound scan preferably done within the first trimester can be relied upon to accurately determine the gestation age . In the first trimester Crown- rump length measurement is used to determine the gestation age. In the second and third trimesters the biparietal diameter, head circumference, abdominal circumference and femur length are used to determine the composite gestation age based on normograms of the 4 parameters.

Its accuracy declines with advance in gestation by at least one, two and three weeks each for the first, second and third trimesters respectively. Thus the first and earliest scan is used for determining gestation age where available.

2.7.2 The Apgar score

In 1952, Dr Virginia Apgar devised a scoring system that was a rapid method of assessing the clinical status of the newborn infant at 1 minute of age and the need for prompt intervention to establish breathing.

The Apgar score provides an accepted standard method for reporting the status of the newborn infant immediately after birth and the response to resuscitation if needed.

Alone it cannot be considered to be evidence of or a consequence of asphyxia, does not predict individual neonatal mortality or neurologic outcome, and should not be used for that purpose.

It comprises five components:1)color, 2) heart rate, 3) reflexes, 4) muscle tone, and 5)respiration , each of which is given a score of 0 , 1 , or 2. Thus the Apgar score quantitates clinical signs of neonatal depression such as cyanosis or pallor , bradycardia, depressed reflex response to stimulation, hypotonia, and apnea or gasping respirations. The score is reported at 1 minute and 5 minutes after birth for all infants, and at 5 minute intervals thereafter until 20 minutes for babies with a score less than 7.

A score of 7 to 10 is defined as reassuring, a score of 4 to 6 as moderately abnormal, and a score of 0 to 3 as low in the term infant and late preterm infant. The low score at 5 minutes or more is a nonspecific sign of illness, which may be an early indicator of encephalopathy.

2.7.3 Limitations of Apgar score

The Apgar score is an expression of the infant's physiologic condition at one point in time, which includes subjective components.

Numerous factors can influence the Apgar score, including maternal sedation or anaesthesia, congenital malformations, gestational age, trauma, and inter observer variability.

The biochemical disturbance must also be significant before the score is affected.

Elements of the score such as tone, color, and reflex irritability can be subjective, and partially depend on the physiologic maturity of the infant.

Variations in normal transition may also affect the score.

The healthy preterm infant with no evidence of asphyxia may receive a low score only because of immaturity.

The incidence of low Apgar score is inversely related to birth weight, and a low score cannot predict morbidity or mortality for any individual infant.

It is inappropriate to use Apgar score alone to diagnose asphyxia.

2.7.4 Apgar score and Resuscitation

The 5 – minute Apgar score, and particularly a change in the score between 1 minute and 5 minutes, is a useful index of the response to resuscitation. If the Apgar score is less than 7 at 5 minutes, the Neonatal Resuscitation Program Guidelines states that the assessment should be repeated every 5 minutes for up to 20 minutes.

2.7.5 Apgar score and prediction of outcome

A 1- minute Apgar score of 0-3 does not predict any individual infant outcome. A 5-minute Apgar score of 0-3 correlates with neonatal mortality in large populations, but does not predict individual future neurologic dysfunction (Casey, McIntire, &

Leveno, 2001). However, a low 5-minute Apgar score clearly confers an increased relative risk of cerebral palsy, reported to be as high as 20-fold to 100-fold over that of infants with a 5- minute Apgar score of 7-10 (Kasdorf, Laptook, Azzopardi, Jacobs, & Perlman, 2015).

2.8 Summary of literature review

Preeclampsia is a disease that is not yet fully understood, however, with proper ANC and production of management guidelines suitable for different set-ups, its adverse effect to mothers and their offspring could be curtailed from the outset.

Sub-optimal clinical management of pre-eclampsia can have serious consequences thus it is necessary to formulate and implement clinical practice guidelines for Kenya. This study will help take the first step by assessing fetal and neonatal outcomes of severe Preeclampsia among women managed conservatively remote from term at MTRH in Eldoret- Kenya.

Hopefully thereafter, recommendations can be made for ways to improve that care and the development of appropriate clinical practice guidelines.

2.9 Conceptual Framework of the Study

This study sought to assess perinatal outcomes of severe preeclampsia among women managed conservatively at MTRH in Eldoret- Kenya. The study was based on the conceptual relationship between the independent variable and the dependent variable. The type of management of severe preeclampsia was itemized as independent variables which, included conservative or aggressive, and factors that influenced perinatal outcomes while outcomes i.e.; Fetal outcomes, neonatal outcomes, feto-perinatal outcomes and duration prolongation of pregnancy were itemized as

dependent variables. The conceptual framework was useful to the study in various ways. The study was based on the premise that types of management of severe preeclampsia were significant in determining perinatal outcomes. It was also significant in that perinatal outcomes of severe preeclampsia among women covered a variety of tasks whose effective operationalization positively affected preeclampsia women managed conservatively at MTRH's maternity unit, Eldoret- Kenya. Given the fact that the study sought to investigate perinatal outcomes of severe preeclampsia, the diagrammatic relationship between the independent and dependent variable is summarized in the figure 2.1 below.

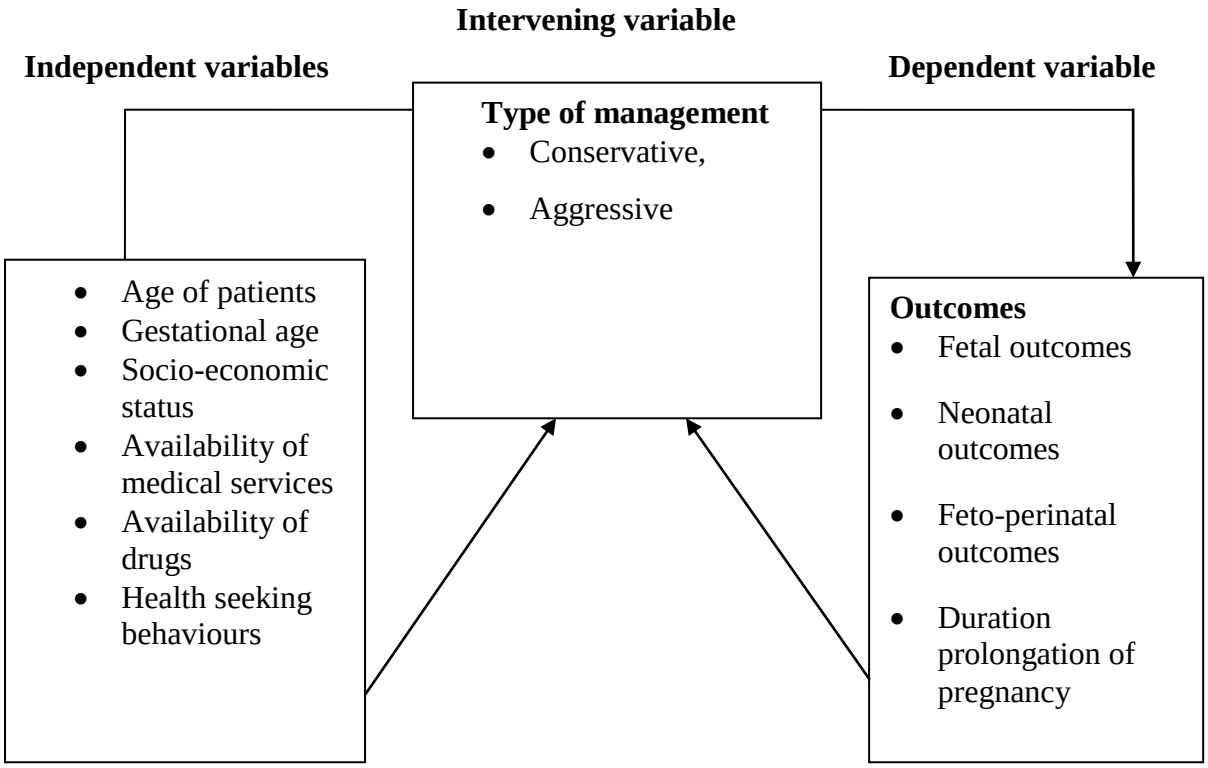

Figure 2: Study Conceptual Framework

The independent variable was the type of management of severe preeclampsia that influenced perinatal outcomes which was the dependent variable. However the intervening variables like age of patients, gestational age, socio-economic status,

availability of medical services, availability of drugs and maternal health seeking behaviors comes in between the independent and dependent variables. The intervening variables that influenced the dependent variables were the various degrees of severe preeclampsia, the age of patients, gestational age, socio-economic status, availability of medical services, availability of drugs and maternal health seeking behaviors.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Introduction

The chapter focuses on the study area, methodology and procedures and modalities in data collection. The study assessed perinatal outcomes of severe Preeclampsia among women managed conservatively at MTRH maternity unit in Eldoret, Kenya. This chapter describes the study design, study setting, study population, sample selection, sample size, data collection tool, data collection technique and ethical considerations.

3.2 Study Site

The study was conducted at the maternity wing of the Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. The hospital is located within the Uasin Gishu County. It is situated about 1km from the town centre on the south-eastern side along the Nandi road. The hospital is neighbored by the Uasin Gishu Memorial hospital, the faculty of health sciences, the student's hostel and Eldoret Medical Training College (MTC). MTRH is the largest and busiest national tertiary hospital in Rift Valley province of Kenya. The hospital was started as a district hospital and later on the mission of the hospital became clearly established as a treatment, teaching and research hospital. Since then there have been marked developments in the areas of research, clinical care and training of health personnel in the hospital. MTRH is the second largest referral facility in Kenya. It serves a catchment population of Western Kenya of approximately 3 million and also parts of Eastern Uganda, Southern South Sudan, Rwanda and Congo, an approximate population of 40 million.

The hospital currently has an 800 inpatient bed capacity and consists of several departments, including Obstetrics and Gynecology, Medicine, Surgery, Pediatrics, Orthopedics, Psychiatry, Casualty, Amenity, New born unit, Ophthalmology and Theatre. The Obstetrics and Gynecology department has an outpatient postnatal and family planning unit, which provides after delivery care, family planning and free immunizations of the new born babies.

MTRH has a constituent maternity hospital called Riley Mother and Baby Hospital with several antenatal, labour and postnatal wards. It is manned by consultants in obstetrics and gynecology, post graduate medical students of Obstetrics and gynecology (Registrars), and medical officer interns, as well as clinical and nursing/midwifery officers and students.

3.3 Study Design

The study was a prospective hospital based study. It involved a follow up of women diagnosed with severe preeclampsia and managed expectantly from between 28 and 34 weeks. The perinatal outcomes were then observed over and recorded from admission till 7 days post-delivery. This prospective study was carried out in MTRH in the period between November 2015 and April 2016. Information was obtained for variables such as age, parity, weeks of gestation, the presence of symptoms like headache, epigastric pain, blurring of vision, urine output and fetal movement. The study used a quantitative approach with the goal of creating a better understanding of perinatal outcomes of severe preeclampsia among women managed conservatively at MTRH.

3.4 Study Population

The study population was all expectant mothers with a confirmed diagnosis of severe hypertension in pregnancy who met the inclusion criteria. The accessible populations were those available in MTRH Eldoret during the time of study. The hospital recorded daily average of 30 deliveries and approximately 15% of all these had preeclampsia.

All women who gave birth within the study period were considered as source population. Women with preeclampsia were identified from all admissions and deliveries. The target population were women who were diagnosed with preeclampsia and met the inclusion criteria.

3.5 Inclusion and exclusion criteria

Inclusion criteria: Informed written consent, a confirmed diagnosis of severe preeclampsia, gestational age of 28 weeks to 33 weeks and 6 days, reassuring fetal testing, No suspected placental abruption, well controlled blood pressures.

Exclusion criteria: Persistent severe symptoms, multiorgan dysfunction, severe intrauterine growth restriction, suspected placental abruption, non-reassuring fetal testing, Thrombocytopenia, HELLP syndrome. The exclusion criteria may have led to bias but the hospital protocol and concern for patient safety prevailed in this decision.

3.6 Sampling technique

Since severe preeclampsia occurred infrequently, in order to reach the target sample size consecutive sampling was adopted. Non-probability sampling was used to identify the study participants whereby every patient presenting with severe preeclampsia at the RMBH wing and who met the study inclusion criteria was consecutively sampled and the relevant information obtained and entered into a data collection form. This was carried out until the desired sample size was attained.

The sample size required in order to be 95% sure that the proportion of fetal deaths that occurred as a result of preeclampsia women was within plus or minus 5% of the population proportion of 6.7% was estimated using the following formula (Cochran, 1963)

3.6.1 Sample size calculation

Thus the formula used to determine the sample size was as follows:

$$\begin{aligned} n &= \left(\frac{Z_{1-\alpha/2}}{\delta}\right)^2 P(1-P) \\ &= \left(\frac{1.96}{0.05}\right)^2 \times 0.067 \times 0.933 \\ &= 97 \end{aligned}$$

Where P=is the population proportion of fetal deaths (6.7%), including fresh still births and macerated still births

δ Is the margin of error equal to the 3% used in this case, and

$Z_{1-\alpha/2}$ is the $(1-\alpha/2)\times 100\%$ quantile of the standard normal distribution.

Adjusting this sample size for finite population gave us a minimum sample size of $\left(\frac{97}{1+97/279}\right) = 72$ participants. The prevalence of fetal death was obtained from (Michael, Ezem, & Ojiyi, 2002).

3.7 Data collection tools

Data was collected by means of descriptive survey using questionnaires, semi-structured interviews, observation and document examination (triangulation approach). Triangulation approach was chosen because it offered the use of different research techniques giving many advantages. A Phone call was made to those discharged home before day 7 after delivery to determine newborn status.

Questionnaires: Questionnaires were used to assess perinatal outcomes of severe Preeclampsia among women managed conservatively remote from term at MTRH's maternity unit.

A structured questionnaire was preferred for collecting data because in such a questionnaire, the questions, their wordings and sequence were fixed and identical for all respondents. According to Mugenda and Mugenda (2003), each item in the questionnaire is developed to address a specific objective and research question of the study. This was further augmented by questions in an interview schedule that addressed specific objectives of the study (Mugenda & Mugenda, 2003). The questionnaires contained various items that solicited for responses pertaining to research variables. Questionnaires were divided into two sections: section A: Socio-demographic data, section B: research questions. Samples of the questionnaire are provided as appendix B.

Interview Schedule: The study used the personal interview schedule to collect information from the patients.

The advantage of an interview was that the respondents provided in-depth information not possible to get using a questionnaire. The interviews were informally conducted through discussions using a set of structured questions (see appendix C).

Records were obtained from the health management information system and registry books designed to keep the records about the patients for the total number of antenatal attendees, deliveries and number of the patients with pre-eclampsia.

A pilot study, of about 10% of the estimated sample size, was carried out at Kapsabet county Hospital as a trial run to clarify the feasibility, validity and reliability of the objective of the study. It tested whether the research procedures, data collection tools,

statistical and analytic processes yielded consistent information needed to answer the research questions of the study.

3.7 Validity and reliability of the research instruments

3.7.1 Validity

In order to strengthen validity of the research instrument, the data abstraction tool was reviewed by an obstetric specialist for content validity. Data was pre-coded to reduce coding error. The tool was pre-tested on ten files of cases of preeclampsia in the county hospital at Kapsabet. The medical records at the MTRH were verified relatively and other sources of data were used to reduce potential information bias The information retrieved from the patients' files and record books was transferred to each individual abstraction tool.

In order to meet the construct validity, namely "establishing correct operational measures for the concepts being studied", established and validated scales were adopted. The data collection was carried out with the help of quantitative methods which gave better understanding of the phenomenon that was being investigated.

For meeting the internal validity, before conducting interviews a wide theoretical framework was worked out. The theoretical background determines the definitions and concepts to be used and ensures that the theoretical propositions and empirical results match. The external validity or "establishing the domain to which a study's findings can be generalized" was established through a comprehensive study design. Within the frames of the study, only the respondents possessing necessary experience and knowledge were chosen.

3.7.2 Reliability

The trustworthiness of the study is established through provisions of validity and reliability. The reliability of the research defined by Yin (1989) as "demonstrating that the operations of a study – such as the data collection procedures – can be repeated, with the same results," was met by thorough documenting of all interviews and developing a survey database. At the same time during personal interviews both the respondent and the interviewer can influence the process of conducting the interview. During the process of the study the interviewer would be asking, guiding and additional questions and sometimes explaining the meaning of the questions in order to eliminate misunderstandings and to achieve more comprehensive information. The quantitative data on the relationship quality were collected with the use of multi-item questions that allowed evaluating from different sides, and thus increased the reliability of the study. The questions for collecting quantitative data were derived from the literature; hence it indicates the reliability. The questions chosen for the present study adequately represent the domain of interest, and thus the content-related validation was observed(Tashakkori & Teddlie, 2010).

A test of reliability was conducted on the questionnaire. The result of the coefficient alphas indicated satisfactory reliability. According to DeVellis Reliability Guidelines (1991), a Cronbach alpha coefficient over 0.7 implies respectable reliability. In this study, Cronbach alpha coefficients of the questionnaire was 0.77. A value of over 0.7 is seen as an acceptable value for Cronbanch's alpha; a value substantially lower indicates an unreliable scale. In this study, the Cronbach alpha coefficient of the 5 scales was over 0.7 that was seen as a good indicator of their reliability and high acceptability.

3.8 Data management and analysis

The data to be collected for the purpose of the study was adopted and coded for completeness and accuracy. Statistical Package for Social Sciences (SPSS) version 22 Software and Microsoft Excel were used for all the data analysis and interpretation. The incidence of confirmed preeclampsia was deduced by dividing the number of preeclampsia cases who met the standard clinical definition for preeclampsia and presented in the inclusion criteria and who delivered within the study period divided by the total number of the cases who gave birth within the study period. The data was analyzed statistically using descriptive analysis techniques encompassing frequency distribution, percentages, mean, median and standard deviation.

Frequency and means for age, hospital stay, birth weight, different laboratory investigations for the different stages of preeclampsia were analyzed. The mode of delivery, indications for caesarean section and complication for each diagnostic (severity) group were also analyzed. Risk Ratio and P-value of confidence interval were analyzed to compare across groups of variables (age, parity, address, status, antenatal care, uric acid level). The variables were dichotomized as Caesarean section done (Yes) and not done (No), Age>34(Yes) and Age<34 (No), Antenatal care attended (Yes) and not attended (No), Primiparity (Yes) and multipara (No), MTRH (Yes) and Outside MTRH (No),

It also looked into whether the severity of the disease contributed to the high caesarean section rate, or to low vaginal birth rate. Relations between neonatal birth weight or gestational age or caesarean section or the severe preeclampsia to neonatal ICU admission was also analyzed in order to look into the general

management and possible implications. Inferential statistics were employed to examine the relationships between independent and dependent variables. Correlation coefficient analysis was conducted to determine the relationship between independent variable, and dependent variable.

Associations between categorical variables was assessed using Pearson's Chi Square test. Fishers' exact test was used when the Pearson's Chi square assumptions were violated. We reported the associated p-values $P \leq 0.05$

Results are presented using tables and graphs.

3.9 Ethical Considerations

Approval was sought from IREC before the study commenced. The permission to conduct the study was obtained from the management of Moi Teaching and Referral Hospital.

All the participants were notified about the purpose of the study and politely asked without any coercion, or force or pressure to give a signed written informed consent before participating. The culturally sensitive questions were designed to address the research objectives properly and respect the privacy and confidentiality of the participant. Data management practices that ensured adequate confidentiality were maintained and these included storing data in key locked cabinets, password coded databases and consenting in private consultation room. There was no direct financial benefit or compensation for participating in the study. Sound clinical judgment was involved in all stages and aspects of this research.

CHAPTER FOUR

4.0 RESULTS

4.1 Social demographic characteristics

There were a total of 7,763 deliveries during the five months study period.

Of the 644 patients with preeclampsia 72 had severe preeclampsia, met the inclusion criteria for the study, and were treated at Moi Teaching and referral Hospital. The severe PET prevalence was 0.92%.

The mean age (± SD) of the patients was 27.9 ± 6.6 years (range, 16–43 years). In terms of age distribution, majority of the women were aged 24 to 28 years followed by 28 to 32 years. Those below 21 years were fewest.

Majority of the women had college level of education (44.4%) followed by those with secondary education (27.8%) and primary (25%), while those without education were fewest at only 2.8%.

In terms of employment status, 55.6% of the women were unemployed followed by those who were formally employed (23.6%). Those self employed were the least at 20.8%.

Majority of the respondents were married (80%).

In terms of areas where the respondents came from, majority of the respondents were from the rural areas (87.5%).

Table 4. 1: Socio-demographic characteristics of 72 severe preeclampsia patients admitted and managed at the obstetric ward of Moi Teaching and Referral Hospital

Variables	Frequency	Percent
Age		
<21 yrs	6	8.3
21-24 yrs	14	19.4
24.1-28 yrs	20	27.8
28.1-32 yrs	18	25
>32 yrs	14	19.5
Levels of education		
None	2	2.8
Primary	18	25
Secondary	20	27.8
College	32	44.4
Occupation		
Employed	17	23.6
Unemployed	40	55.6
Self employed	15	20.8
Marital status		
Divorced	1	1.4
Married	58	80.6
Single	13	18.1
Residence		
Urban	9	12.5
Rural	63	87.5

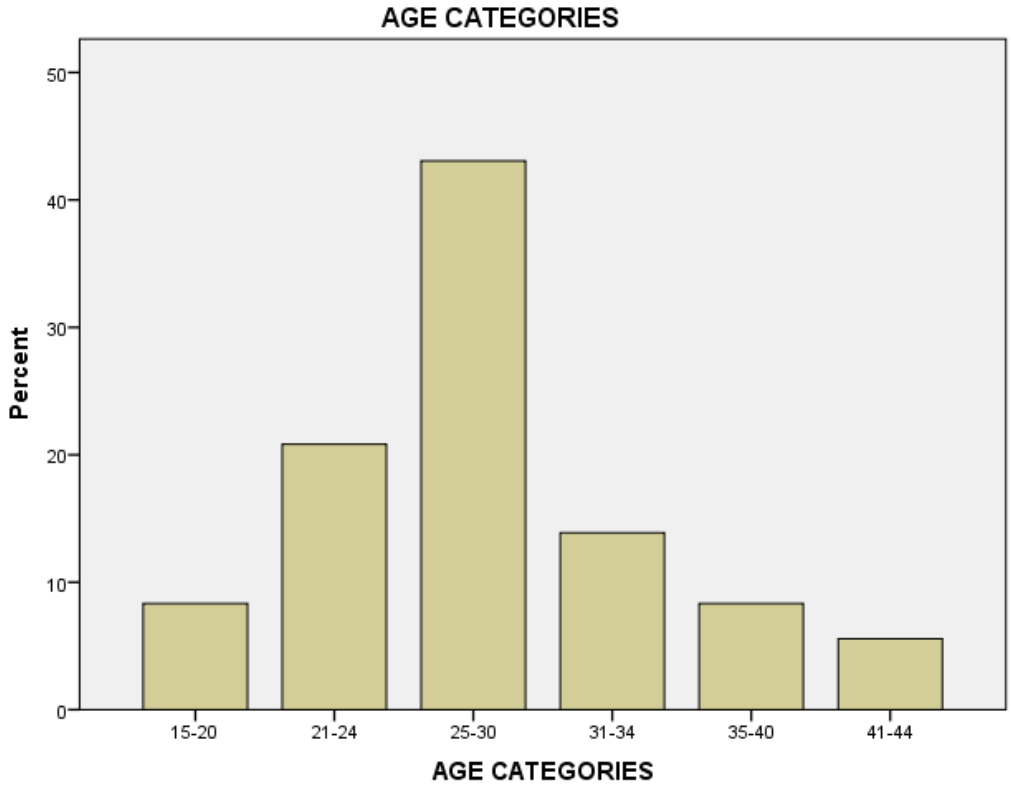

Figure 4. 1: Bar graph showing Age categories

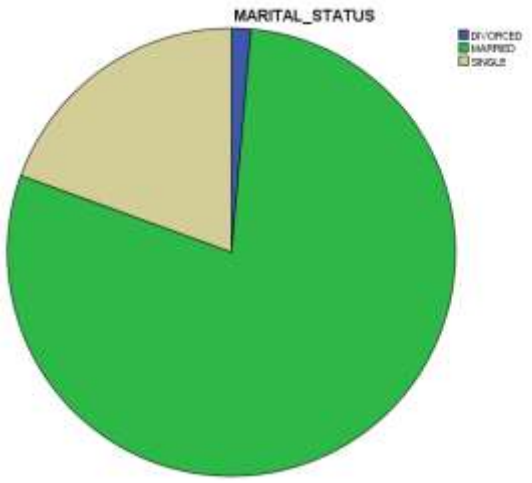

Figure 4. 2: Pie chart showing marital status

4.2 Biophysical Characteristics of women conservatively managed for severe preeclampsia at MTRH

The range of weights among the women was 54 to 117 kg while height ranged from 1.47 to 1.79 m.

The mean BMI was 30.2 kg /m^2 (21–47 kg/m^2).

In terms of distribution of BMI, majority of the women had BMI category 25-30 kg/m^2 (42%), followed by those with BMI ≥35 kg/m^2 (22%) while those with BMI <25 kg/m^2 was only 22%.

Based on these categories of BMI, 33% of the women had normal BMI, 25% were overweight, and 18% were obese while the remaining 24% were severely obese.

Proteinuria was found in all the women tested.

Table 4. 2: Maternal characteristics of 72 severe preeclampsia patients admitted and managed at the obstetric ward of Moi Teaching and Referral Hospital

Variables	Number	Percent
Preeclampsia history		
Yes	17	23.6
No	29	40.3
Not applicable	26	36.1
On preeclampsia treatment at admission		
Yes	21	29.2
No	51	70.8
Maternal weight (kg)[#]	76.6 ± 16.0	
Height (m)[#]	1.59 ± 0.06	
Body mass index (BMI)		
<25 kg/m^2	16	22.2
25-30 kg/m^2	30	41.7
31-35 kg/m^2	10	13.9
≥35 kg/m^2	16	22.2
Body mass index category (BMI)		
Normal	24	33.3
Overweight	18	25
Obese	13	18.1
Severely obese	17	23.6
Dipstick proteinuria		
Not done	1	1.4
+	21	29.2
++	50	69.4

[#]computation are means ± SD

4.3 Pregnancy Characteristics of women managed for severe preeclampsia

The majority of women (44.4%) was primigravida.

Those with an earlier pregnancy, regardless of outcome, were 20.8%.

Those who had at least two earlier pregnancies, regardless of whether these pregnancies were carried to term, were 34.8%.

4.4 Delivery Characteristics

Majority of the women (94.4%) stayed up to a week before delivery was necessary, followed by those between a week to two weeks with up to 5.6% .

The gestational age at admission for majority of the women was over 32 weeks followed by those of 30-32 weeks. The gestation age at delivery for 73 % of the respondents was over 32 weeks.

The most common mode of delivery for the women was vaginal (60%) while 40% underwent caesarean delivery.

Labour for most of the women was induced.

Most of the women were in their first trimester (55.6%) at their first antenatal clinic visit, followed by those in the second trimester (26.4%).

5.6 % of women had no prior antenatal clinic visit.

The indications for delivery were intrauterine fetal demise, attainment of 34 weeks gestation, and a non reassuring fetal status based on fetal heart tracing or formal obstetric scan report.

Table 4. 3: Pregnancy characteristics of 72 severe preeclamptic patients admitted and managed at the obstetric ward of Moi Teaching and Referral Hospital

Variables	Frequency	Percent
Gravida		
Nulligravida	32	44.4
Primigravida	15	20.8
Multigravida	25	34.8
Parity		
Nulliparous (0)	33	45.8
Primiparous (1)	15	20.8
Multiparous (2)	9	12.5
Grand multiparous (≥ 3)	15	20.9
Duration of stay before delivery(days)		
1-7	38	52.8
8-14	21	29.2
15 and above	13	18
Gestational age at admission		
< 30 weeks	12	16.7
30-32 weeks	23	31.9
≥32 weeks	37	51.4
Gestational age at delivery		
28 weeks < date of delivery < 32 weeks	19	26.4
Date of delivery ≥ 32 weeks	53	73.6
Mode of delivery		
Vaginal	43	59.7
Caesarean	29	40.3
Onset of labour		
Spontaneous	12	16.7
Induced	43	59.7
Caesarean	17	23.6
Trimester at first ANC visit		
No prior ANC visit	4	5.6
First trimester	40	55.6
Second trimester	19	26.4
Third trimester	9	12.5

Neonatal Outcomes

The neonatal outcomes of women admitted and managed at the obstetric ward of Moi Teaching and Referral Hospital after management of the preeclampsia are shown in Table 4.5. Outcomes of interest included newborn status at birth, the 5 minute Apgar score, new born unit admission, and newborn status at 7 days.

Indications for delivery included intrauterine fetal demise, attainment of 34 weeks, non reassuring fetal status based on CTG tracing and/ or obstetric ultrasound findings, and worsening maternal status.

The majority of women (87.5%) had Cephalic presentation at the time of delivery.

The majority of babies were delivered vaginally while 40.3 % were delivered by caesarean section.

Reasons for caesarean delivery included breech fetal presentation (12.5%), failed induction (16.7%) and non reassuring fetal status based on CTG monitoring (11.1%).

The birth weight of the babies delivered by most of the pre-eclamptic women was below 2500 g (93%) with only 7% recording a normal birth weight.

Most of the newborns were alive at birth while up to 18.1% were still births.

Of the live births 15.3% died within the first week of life which yielded a perinatal mortality rate of 152/1000 births. The main complications that resulted in neonatal mortality were prematurity–related and birth asphyxia (10), Meconium aspiration syndrome (3), and respiratory distress syndrome (13).N=13.

Of the thirteen newborns that died within the first week of life, only one had a normal birth weight.

Low Apgar score (defined as an Apgar score < 7 at 5 minutes) occurred in 70.8% of the live births.

Up to 51.4% of the newborns were admitted to special care unit at birth.

Up to 66.7 % of the newborns survived beyond the first week of life.

Table 4. 4: Neonatal outcomes of women admitted and managed at the obstetric ward of Moi Teaching and Referral Hospital after conservative management of the preeclampsia

Variables	Frequency	Percent
Birth weight		
<2500 g (LBW)	67	93.1
>2500 g (NBW)	5	6.9
Fetal mortality		
Dead	13	18.1
Alive	59	81.9
Preterm birth		
Date of delivery 28 to <32 weeks	16	22.2
Date of delivery ≥ 32 weeks	*56*	*77.8*
5 min Apgar score		
0-3	13	18.1
6-7	8	11.1
≥ 7	51	70.8
Neonate condition at birth		
Alive	59	81.9
Still birth	13	18.1
Fetal presentation at delivery		
Cephalic	63	87.5
Breech	9	12.5
Neonate admission to special care		
Yes	37	51.4
No	35	48.6

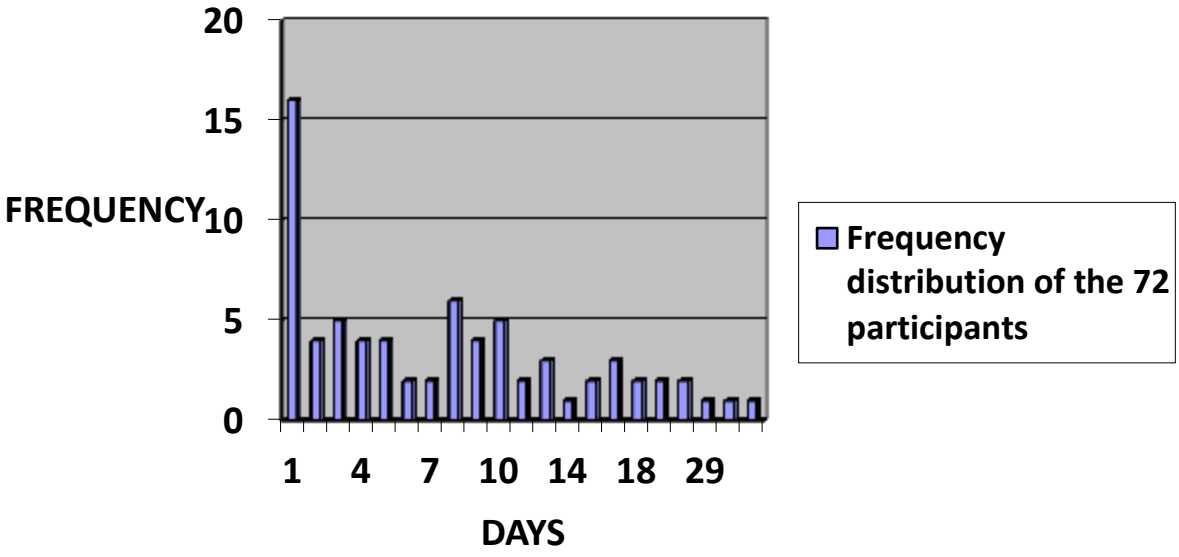

Figure 4. 3: Frequency Distribution of the 72 Participants

Table 4. 5: Wilcoxon two- sample test for duration of days stayed before delivery

Duration of stay before delivery	Total participants	**Dead**	**Alive**	**Total**	
	72	**3.0 (1.0,8.0)**	**7.5(2.0,13.0)**	**6.5(2.0,11.0)**	

Duration of stay before delivery. Median (IQR), Weeks: 6.5(IQR: 2.0, 11.0)

RELATIONSHIP BETWEEN LENGTH OF STAY BEFORE DELIVERY AND PERINATALOUTCOME.

Table 4. 6: Length of Stay before Delivery and Newborn Status at Birth

Length of stay in days			
	New Born Status At Birth		
	ALIVE	**DEAD**	**% of Total**
1 -7	29 (76.3%)	9(23.7%)	52.8
8-14	18(85.7%)	3(14.3)	29.1
≥15	12(92.3%)	1(7.7%)	18.1

p-value=0.505

Table 4. 7: Length of Stay in Days and Newborn Status on Day 7

Length of stay in days	**New Born Status on Day 7**		**% of Total**
	ALIVE	**DEAD**	
1-7	22(73.3%)	8(26.7%)	50
8-14	17(94.4%)	1(5.6%)	30
≥15	9(92.3%)	3(25%)	20

P-value =0.148

Table 4. 8: Duration of Stay before Delivery and Five Minute Apgar Score

Duration of stay before delivery in days	**5 minute APGAR Score**		**% of Total**
	APGAR< 7	**APGAR≥ 7**	
1-7	16(53.3%)	14(46.7%)	50
8-14	8(44.4%)	10(55.6%)	30
≥15	8(66.7%)	4(33.3%)	20

P-value =0.614

Table 4. 9: Duration of Stay before Delivery and Newborn Unit Admission

Duration of stay before delivery in days	**New born unit admission**	**% of Total**
1-7	20(66.7%)	50
8-14	10(55.6%)	30
≥15	7(58.3%)	20

P-value =0.950

Table 4. 10: Cross tabulation between length of stay in hospital against Newborn condition at birth

		Newborn Condition at Birth			Value=0.505
		ALIVE	DEAD	TOTAL	
Length of stay before Delivery	1-7	29	9	38	
	8-14	18	3	21	
	15 and above	12	1	13	
Total		59	13	72	

A Fisher's examandera

ct test was done to determine the measure of association between Length of stay in hospital and Neonatal outcomes at birth and the P-Value was 0.505 which was not statistically significant at $p < 0.05$.

Table 4. 11: Cross tabulation between length of stay in hospital against Newborn condition on the 7th day

		NEWBORN STATUS AT DISCHARGE OR ON 7TH DAY			Value=0.148
		ALIVE	DEAD	TOTAL	
Length of stay before Delivery	1-7	21	16	38	
	8-14	17	5	21	
	15 and above	9	4	13	
Total		47	25	72	

A Fisher's exact test was done to determine the measure of association between Length of stay in hospital and newborn condition on the 7th day and the P-Value was 0.148 and this result was not statistically significant at $p < 0.05$.

Table 4. 12: Cross tabulation between length of stay in hospital against Apgar score at 5 minutes

		Apgar Score		Total	Value= 0.614
		Less Than 7	Greater than 7		
Length of stay before Delivery	1-7	13	25	38	
	8-14	4	17	21	
	15 and above	4	9	13	
Total		21	51	72	

A Fisher's exact test was done to determine the measure of association between Length of stay in hospital and Apgar score at 5 minutes and the P-Value was 0.614 and this result was not statistically significant at $p < 0.05$.

Table 4. 13: Cross tabulation between duration of hospital stay before delivery and newborn unit admission

Duration of stay before delivery	Newborn unit admission	% of Total	p- value =0.950
1-7	20 (66.7%)	50	
8-14	10(55.6%)	30	
≥15	7(58.3%)	20	

A Fisher's exact test was done to determine the measure of association between the duration of hospital stay before delivery and subsequent admission of the baby to the newborn unit. The P-value was o.950 which was not statistically significant at P<0.05.

CHAPTER FIVE

5.0 DISCUSSION

To the best of our knowledge, this was the first study of perinatal outcomes among severe preeclampsia patients undergoing management at the MTRH. There were three main findings from this study that were related to women with severe preeclampsia. First, patients with severe preeclampsia were more likely to extend their pregnancy by up to 7 days (one week) on conservative management. This is less than the average increase in gestation by 11 days reported by Odendaal et al in 2000.This increase was found to be the only significant factor in determining neonatal outcome with a 94% neonatal survival.

The MEXPRE Latin study of 2013 also reported a comparatively longer mean prolongation of pregnancy by 10.4 days and, except for prolongation of gestation, there was no neonatal benefit

Second, in terms of neonatal outcomes, Low birth Weight, Very Low Birth Weight and Extremely Low Birth Weight babies were found more often, which may be a result of the fetal indications that were refractory to control of maternal hypertension. This finding was consistent with the occurrence of preterm delivery.

Hall et al in 2000 reported only 0.5% of pregnancies ended in intrauterine death after conservative management, while 40.7% of babies required neonatal intensive care,

Third, two thirds of women managed conservatively for severe preeclampsia had a living child by day 7 post delivery. This is significantly less than the 94% neonatal survival reported by Hall in 2000.

Our study's findings of preeclampsia associated morbidities and their outcomes thus concur with the findings of several different studies from other parts of the world. Vaginal delivery was the leading mode of delivery at almost 60%, which is comparable to other studies.

The presence of preeclampsia alone was not an indication for caesarean delivery, but the decision to perform a caesarean delivery was based on multiple factors which included fetal gestational age, non reassuring fetal status, the fetal presentation and failed induction.

A major contributing factor to the significant perinatal morbidity and mortality was the significant number of extremely preterm infants. This study revealed that the major morbidities contributing to early neonatal deaths were severe birth asphyxia and prematurity. Other studies have reported similar findings. A significant number of low birth weight neonates correlated with the high number of preterm deliveries among the preeclamptic patients. Similar findings have been reported in the literature that links the incidence of low birth weight infants with preterm deliveries in preeclamptic patients.

Limitations of the Study

This research was restricted to perinatal outcomes of severe preeclampsia among women managed conservatively at MTRH as the core study patients.

The regional distribution of the patients did not exhaustively cover the entire country despite the assumption that the problems faced by these mothers are common.

The research area was limited to the maternity wing that handled mothers admitted with severe preeclampsia. The study was a hospital-based study and as a result

sampling and information bias may have occurred which may have limited its ability to examine rare events.

Even though a significant number of women in Kenya give birth in healthcare facilities , it is likely that some women with preeclampsia gave birth at home during the study period and thus were not be included in the study.

In addition, the lack of a control group of women without pre-eclampsia may have restricted the ability to examine risk factors for preeclampsia in general.

CHAPTER SIX

6.0 CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

This study has demonstrated that the incidence of preeclampsia at MTRH was 1.37% and that the proper management of preeclampsia at our hospital faces similar challenges as those at other hospitals in the developing world. Preeclampsia which was found to cause significant maternal morbidity also contributed significantly to high rates of perinatal morbidity and mortality.

It is feasible to continue offering conservative management for severe preeclampsia in eligible mothers.

The most common contributors of perinatal death were birth asphyxia and prematurity. Patient compliance was not shown to contribute significantly to the delayed management of preeclampsia as demonstrated by the high rates of antenatal clinic attendance. However, some women were not screened for preeclampsia during ANC visits and consequently presented late to our hospital, frequently with complications.

While factors such as limited resources and infrastructure are not within the control of the health care practitioner, attention to basic parameters such as blood pressure and urine screening for proteins is possible at antenatal clinics.

Our best chance for reducing maternal and perinatal morbidity and mortality due to preeclampsia may lie with the promotion of improvements in the quality of basic care provided by our antenatal clinics.

6.2 Recommendations

More studies with larger numbers are recommended in the area of early severe preeclampsia since the disease contributes to high morbidity and mortality in our setup.

Pediatric follow up of newborns to document long term effect if any after expectant management of early severe preeclampsia.

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APPENDICES

Appendix 1: Informed consent letter

Dear Madam

I am a Post graduate student of Moi University carrying out a research study on the "fetal and perinatal outcomes of expectant management of severe pre-eclampsia remote from term at MTRH, Eldoret, Kenya" in partial fulfillment of the requirement for the award of Degree of Masters of Medicine in Reproductive Health of Moi University. I kindly request you to answer the questions below. All responses will be handled confidentially and will be used only for this study.

Let me take this opportunity to thank you in advance for taking part in this study.

Yours sincerely,

Ben Jumba Locho

REG NO: SM/PGRH/06/11

Appendix 2: Informed consent form

CONSENT FORM

PROJECT TITLE: FETAL AND NEONATAL OUTCOMES OF EXPECTANT MANAGEMENT OF SEVERE PRE-ECLAMPSIA REMOTE FROM TERM AT MTRH, ELDORET, KENYA

Good morning/afternoon, Madam. My name is Dr. Locho Jumba. I am here today from Moi University, Eldoret to collect information and data for the study on fetal and neonatal outcomes of expectant management of severe pre-eclampsia remote from term at MTRH, Eldoret, Kenya.

I will be asking you regarding the outcomes of severe pre-eclampsia and this will include your demographic, laboratory and clinical related questions. I plan to sample 72 expectant mothers with severe pre-eclampsia at MTRH maternity wing. All information obtained will be kept highly confidential and will not be accessed by any unauthorized person except the principal investigator and the research assistants.

The Institutional Research and Ethics Committee (IREC) of Moi University have approved this research

Benefits

This is a research project and the findings will be beneficial in management of severe pre-eclampsia at MTRH and other setups

Risks

This is a minimal risk study and the psychological risks that may arise will be addressed through counseling.

May we proceed? Verbal consent: Yes…….No……..
Proxy consent: Signature …….
Date **…**……..

Thank you

Contacts for the research team,
Dr. Locho Ben Jumba
MOI UNIVERSITY, ELDORET P.O BOX 4606 -0100 Eldoret, Kenya
Phone; 0727991665**, E- Mail address**; julochoben@gmail.com

Appendix 3: Questionnaires for respondents

I am a Post graduate student of Moi University carrying out a research study on the "fetal and perinatal outcomes of expectant management of severe pre-eclampsia remote from term at MTRH, Eldoret, Kenya" in partial fulfillment of the requirement for the award of Masters of Medicine in Reproductive Health of Moi University. I kindly request you to answer the questions below. All responses will be handled confidentially and will be used only for this study. Your contributions are highly appreciated.

Thank you very much in advance.

Questionnaire Number…… Date of interview……..

Date of surgery …… Respondents identity ……..

Section A: Socio-demographic background

Identification/participant number.....

Date of hospital arrival..... Date of delivery.....

Duration of latency..... Date of discharge.....

Age in years..... Gestational age at admission.....

Number of pregnancies (including current delivery).....

Number of previous births (excluding current delivery).....

Number of previous Caesarean sections.....

Marital status.....Residence.....

Occupational status ☐ Employed ☐ Unemployed ☐ Self employed

Level of education: none ☐ primary ☐ Secondary ☐ College ☐

1. **Laboratory parameters**

Urine test results.....

Complete blood count -Hb level.....

-Total white cell count.....

-Platelet count.....

Liver function test results.....

Urea, Electrolytes and Creatinine.....

HIV status ☐ HIV Positive ☐ HIV Negative ☐

VDRL status ☐ Positive ☐ Negative ☐

Maternal blood group AB ☐ O ☐ A ☐ B ☐

Maternal rhesus ☐ Positive ☐ Negative ☐

Clinical Parameters

(a)Maternal

Weight ..... (Kgs)

Height..... (Meters)

BMI.....

Blood pressure on admission.....mm/Hg

(b)Fetal

Gestational age at delivery (based on LMP).....

Final mode of delivery -vaginal ☐

-Caesarean ☐

APGAR score at 5 minutes.....

Fetal growth restriction present –yes ☐ No ☐

Fetal demise present Yes ☐ No ☐

Total number of neonates delivered----------.

Birth order 1 ☐ 2 ☐ 3 ☐ > 3 ☐

Onset of labor

1. Spontaneous ☐
2. Induced ☐

Fetal Presentation at delivery

1. Cephalic ☐
2. Breech ☐
3. Other

Infant sex Male ☐

Female ☐

Birth weight in grams……

Neonatal condition at birth

(a)Vital status (1 = Alive 2=Fresh Still Birth 3=Macerated Still Birth

(b)Apgar score at 5 minutes

Was any neonatal complication identified? (1=Yes 2=No) .If yes, which one?.....

Admission to newborn special care unit (1=Yes 2=No).If yes, indication for admission……..

Newborn status at hospital discharge or on 7th day of life

1=Alive 2=Dead

Date of newborn hospital discharge or death.....

Appendix 4: Interview

1. Did you attended the antenatal clinic -Yes ☐ No ☐

2. If yes to question 1 above, at what month of your current pregnancy did you visit?

Month

(a) 1st trimester.....

(b) 2nd trimester.....

(c) 3rd trimester.....

Specify gestational age at first antenatal clinic visit----------

3. Previous history of pre-eclampsia- Yes.....No.....Not applicable (primigravida)

4. Whether on treatment for pre-eclampsia at time of presentation for admission

Yes.....No.....

If yes, what was the duration of treatment.....?

5. Reason for diagnosing severe pre-eclampsia

Appendix 5|: MTRH Department of Reproductive Health
Protocol for the Management of Preeclampsia and Eclampsia

I. Definitions

Chronic hypertension in pregnancy:
High blood pressure with systolic BP equal or more than 140 mmHg and/or diastolic BP equal or more than 90 mmHg with or without proteinuria before pregnancy, or prior to 20 weeks gestation.

Gestational hypertension:
New onset hypertension with systolic BP equal or more than 140 mmHg and/or diastolic BP equal or more than 90 mmHg after 20 weeks gestation without proteinuria.

Preeclampsia:
New onset hypertension with systolic BP equal or more than 140 mmHg or diastolic BP equal or more than 90 mmHg after 20 weeks gestation with at least 2 + proteinuria or urine protein to creatinine ratio greater than 0.6.

Signs and symptoms of severe preeclampsia:

- Systolic blood pressure above 160 and/or diastolic blood pressure above 110 mmHg.
- The presence of headache, visual changes, right upper quadrant pain or epigastric pain
- Intrauterine growth restriction
- Maternal end organ damage (elevated creatinine, oliguria, anuria, elevated AST/ALT at least three times normal, eclamptic seizure, stroke)
- HELLP syndrome

HELLP syndrome:
Evidence of hemolysis, elevated liver enzymes, and low platelets with or without elevated blood pressure.

Chronic hypertension with superimposed preeclampsia:
A rise in systolic BP by 30 mmHg above non pregnant level and/or a rise in the diastolic BP rise by 15 mmHg above non pregnant level accompanied by proteinuria beyond 20 weeks gestation.

Eclampsia:
A diagnosis of preeclampsia based on new onset hypertension with systolic BP equal or more than 140 mmHg or diastolic BP equal or more than 90 mmHg after 20 weeks gestation with at least 2 + proteinuria or urine protein to creatinine ratio greater than 0.6 accompanied by unexplained convulsions or coma.

II. Management of preeclampsia

The goals of the management of preeclampsia are to achieve optimal maternal and fetal outcome. Therefore management can vary depending on gestational age.

In general the aims of treatment are**:**

1. To stabilize the patient's blood pressure
2. To control or prevent eclamptic seizures
3. To monitor maternal well being, to prevent maternal complications such as pulmonary edema, liver failure, renal failure, and eye damage and stroke
4. To monitor fetal well being
5. To decide on appropriate timing of delivery
6. To choose of mode of delivery

1. Stabilize blood pressure

The goal is to stabilize the patient's BP between 120-140/70-90 using antihypertensive and non pharmacologic therapy.
BP must be taken with a validated device and the BP cuff must be the right size i.e. 1.5 times the circumference of the patients mid upper arm.

For hypertensive emergencies (diastolic ≥ 110 mmHg)/ (systolic ≥160 mmHg).
Give IV antihypertensive:

A. Start with Labetalol 20 mg IV bolus, 10 minutes later can give 40 mg; 10 min later can give 80 mg. To a maximum dose of 220 mg.
B. If BP still =/>160/110, give Hydralazine slow IV push over 2 minutes. Repeat 5 to 10 mg IV every 30 minutes to a maximum of 20 mg.
   OR
C. 40 mg Hydralazine in 500 ml of Normal Saline at 20 drops per minute titrated against diastolic BP by ± 5 drops till diastolic BP is 90-100 mmHg then maintain the number of drops per minute.

Monitor BP every 10-30 minutes and start concomitant oral therapy with <u>one</u> of the following. Only add a second oral agent if one agent is at maximum dose, or has adverse effects, and is unable to stabilize the BP.

A. Nifedipine 20g Retard BD (maximum dose: 90mg /day)
B. Methyldopa 500g TDS (maximum dose: 3grams /day)
C. Atenolol 100 mg OD (maximum dose: 100mg /day)

Non pharmacological therapy, such as bed rest and a quiet room can be used to lower BP and prevent worsening of disease.

2. Prevention and treatment of eclamptic seizures

Magnesium Sulfate is the drug of choice for both prevention and treatment of eclamptic seizures. It has been shown to be superior to other anti epileptics and anxiolytic medications. Midwives and medical officer interns and registrars can administer this drug when necessary for an eclamptic seizure or for severe preeclampsia in labour.

For seizure prophylaxis:

- Give 4 gm Magnesium Sulfate infusion over 10-15 minutes as loading dose followed with a maintenance dose of 1 gm/hour IV, continue until 24 hours postpartum.

For seizure treatment:

- Give 10 gm Magnesium Sulfate IM (5 gm in each buttock) then obtain IV access and start a maintenance dose of 1 gm/hour IV, continue until 24 hours postpartum.
  OR
- Give 4gm Magnesium Sulfate IV over 15 minutes and then continue a maintenance dose of 1 gm/hour IV, continue until 24 hours postpartum.

- For repeat seizures while on magnesium treat with 2 gms IV stat dose and maintain as 2 gm/hour until 24 hours postpartum.
- Turn patient on lateral side to protect airway from aspiration
- Provide one-on- one nursing and a guarded bed

Monitoring
While on Magnesium Sulfate, monitor the following:

- Respiratory rate (goal: ≥ 16/min)
- Pulmonary exam (goal: clear breath sounds)
- Urine output (goal: ≥ 30mls/hr)
- Patellar reflexes (goal: must be present)

NOTE: Only If Magnesium Sulfate is out of stock then use another anxiolytic such as Diazepam or Phenytoin.

It is not necessary to measure serum levels if patella reflexes and respiratory rate are normal. Serum level measurement is only necessary in patients with oliguria because renal clearance will be impaired. If patient is noted to have loss of DTRs, pulmonary edema, or respiratory depression then treat for Magnesium toxicity:

- Give IV Calcium Gluconate, 1-2gm (10-20 ml of 10% solution given slowly) until the respiratory rate improves.
- Check EKG to rule out cardiac toxicity.
  NB:
  After loading dose of Mg SO4 check BP before concomitant administration of antihypertensive.
  Give Mg SO4 IM stat only if IV access is not possible.
  In case of renal failure use either Phenytoin or diazepam instead of Magnesium sulphate.

3. Monitor maternal well being

Mild preeclampsia
The following bedside and lab monitoring is required for all **mild preeclamptic** patients admitted to MBH.

- Blood pressure measurement every ½ hr – 4hrs
- Input/output chart (bladder catheterization may be necessary)
- Urinalysis for protein at admission and daily to monitor for worsening disease
- Urea/Electrolytes/Creatinine at least weekly
- Liver function tests at least weekly
- Complete blood count (including platelet in) at least weekly

Severe preeclampsia
The following bedside and lab monitoring is required for all **severe preeclamptic** patients admitted to MBH.

- Blood pressure measurement every ½ hr – 4hrs
- Input/output chart (bladder catheterization may be necessary)
- Urinalysis for protein at admission and daily to monitor for worsening disease
- Urea/electrolytes/creatinine at least twice weekly
- Liver function tests at least twice weekly
- Complete blood count (including platelet in) at least twice weekly
- Coagulation panel on admission and daily if abnormal
- Peripheral blood smear on admission

4. Monitor fetal well being

The following bedside and ultra sonographic monitoring is required of all preeclamptic patients.

- Fetal heart rate monitoring with every BP measurement
- Fundal height monitoring at least weekly
- Daily fetal kick chart
- Outpatient NST for mild PET patients at least twice weekly and daily for inpatient severe PET if initial NST was not reassuring.
- Ultrasound biophysical profile with umbilical artery Doppler studies +/- MCA waveform at least weekly
- Full obstetrical US for fetal growth once every 2 weeks

5. Timing of delivery

Mild preeclampsia:
Mild preeclamptic patients should be delivered at 38 weeks gestation.

Severe preeclampsia:
Ideally severe preeclamptic patients should be delivered at 34 completed weeks unless if the patients status worsens. The patient should be delivered earlier if:

- The patient's blood pressure is unable to be controlled on the maximum doses of two antihypertensive agents

- The patient is experiencing persistent headache, visual changes or epigastric pain
- There is evidence of severe IUGR, BPP <4/8, absent end diastolic flow on umbilical Dopplers
- If the patient has been diagnosed with HELLP she should be delivered immediately

Eclampsia:
If the patient has had an eclamptic seizure she should be started on IV blood pressure medication (goal DBP: below 100), stop the seizure, and evaluate labs and plan for delivery immediately.
Corticosteroids administration

If the patient will need to be delivered prior to term gestation then maternal corticosteroids should be administered. Give either:

- Dexamethasone 6 mg every 12 hours for 4 doses
- Betamethasone 12 mg every 24 hours for 2 doses

6. Mode of delivery

Patients with mild preeclampsia, severe preeclampsia, HELLP and eclampsia may undergo induction of labour as per the RMBH protocol on induction of labour (No5). Cesarean Section should only be performed for obstetrical or fetal indications such as arrest of dilatation, arrest of descent or fetal distress.

NOTE: Eclamptic patients with a Bishops score greater than 5 can be induced. The goal is for delivery within 12 hours.

Special considerations during induction of labour for preeclamptic and eclamptic patients

The registrar on duty must review all eclamptic patients.

- Vital signs must be taken every 30 minutes.
- Fetal heart rate must be monitored every 15-30 minutes and after every contraction in the second stage.
- Complete blood count, UEC, liver function tests and coagulation studies must be monitored at least daily during the induction of labour.
- Platelet levels for patients in ICU or HDU with HELLP syndrome should be monitored at least twice daily.
- Urine Foley's catheter must be placed and strict intake and output must be recorded for all severe preeclamptic and eclamptic patients.
- All severe preeclamptic and eclamptic patients should be placed on Magnesium Sulfate during induction of labour and continued until 24 hours postpartum. Thus patients must be monitored for Magnesium toxicity during induction, labour, and 24 hours post partum.

- For patients on Magnesium Sulfate, the nursing and medical staff should be prepared for postpartum hemorrhage as per the RMBH protocol on PPH (No2) however Ergometrine is CONTRAINDICATED in hypertensive patients.

Recommendations for transfusion of platelets related to mode of delivery in HELLP

Platelet count	**Mode of delivery**	
	Caesarean	**Vaginal**
<20,000	Transfuse	Transfuse
20,000 to 49,000 rapidly	Transfuse	Consider if -excessive active bleeding -Known platelet dysfunction -Platelet count falling -Coagulopathy
=/> 50,000 known	Consider in presence of excessive active bleeding, Platelet dysfunction, platelet count falling rapidly and Coagulopathy.	

7. Immediate post partum management

Monitor blood pressure half-hourly for the first 2 hours post partum then 4 hourly for the next 24-48 hours then taper off drugs as per maternal improvement.

Continue therapy with:

- Magnesium Sulfate for at least 24 hours postpartum
- Monitor strict intake and output for at least 24 hours postpartum with a Foley's catheter in place

In case of end organ damage, refer for management in the specialized care units (Intensive Care Unit, the Renal Unit, and Ophthalmology Unit.)

8. Discharging antenatal patients preeclampsia

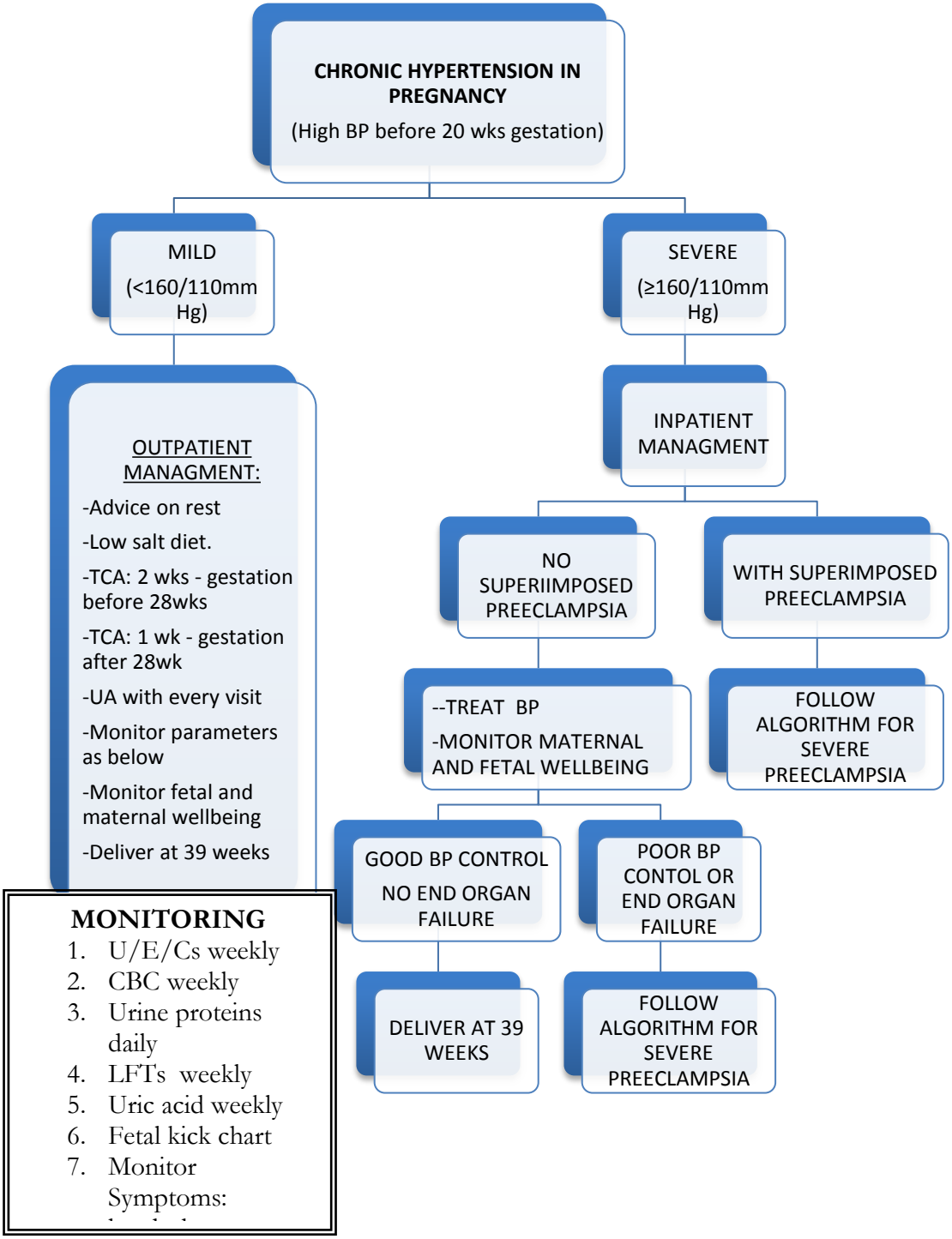
Patients with mild preeclampsia with no other co-morbidities or risk factors may be candidates for outpatient management. Patients should first be assessed for the severity of disease, once the patient's blood pressure has been stabilized and there is no evidence of severe preeclampsia, the patient may be discharged home with weekly follow up in High Risk OB clinic. Prior to discharge the patient must be educated to return to clinic for any of the following:

- Danger signs of preeclampsia
- Performance of Fetal kick chart for 10 movements in 12 hours and return for decreased movement
- Danger signs of labour
- Home bed rest

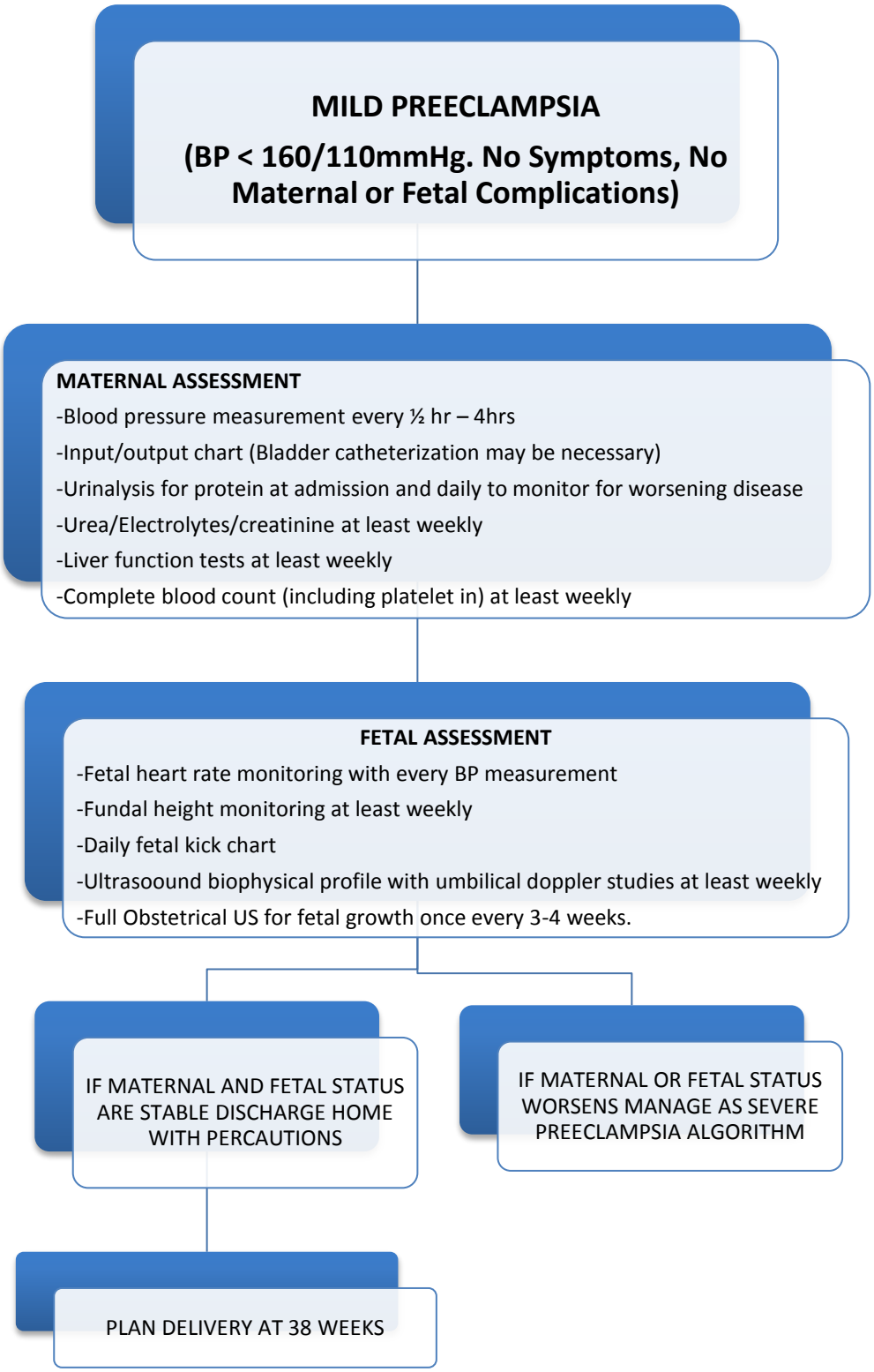
ALGORITHM FOR CHRONIC HYPERTENSION IN PREGNANCY

Aims:

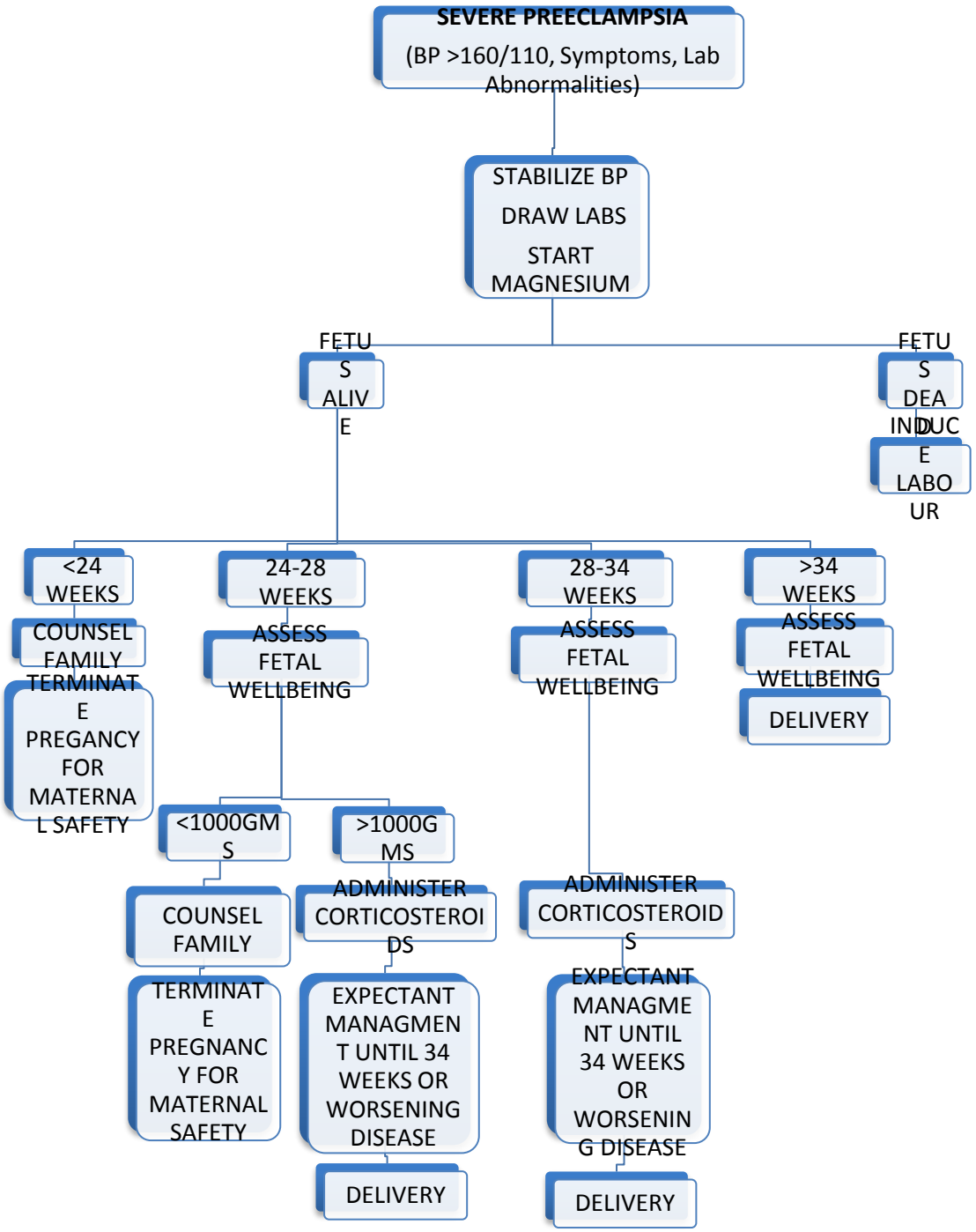
1. To stabilize the diastolic blood pressure to 90- 100 mmHg
2. To monitor for superimposed pre-eclampsia or eclampsia
3. To monitor maternal well being
4. To monitor fetal well being
5. Accomplish delivery at optimal time in maternal and fetal interests.



ALGORITHM FOR MILD PREECLAMPSIA

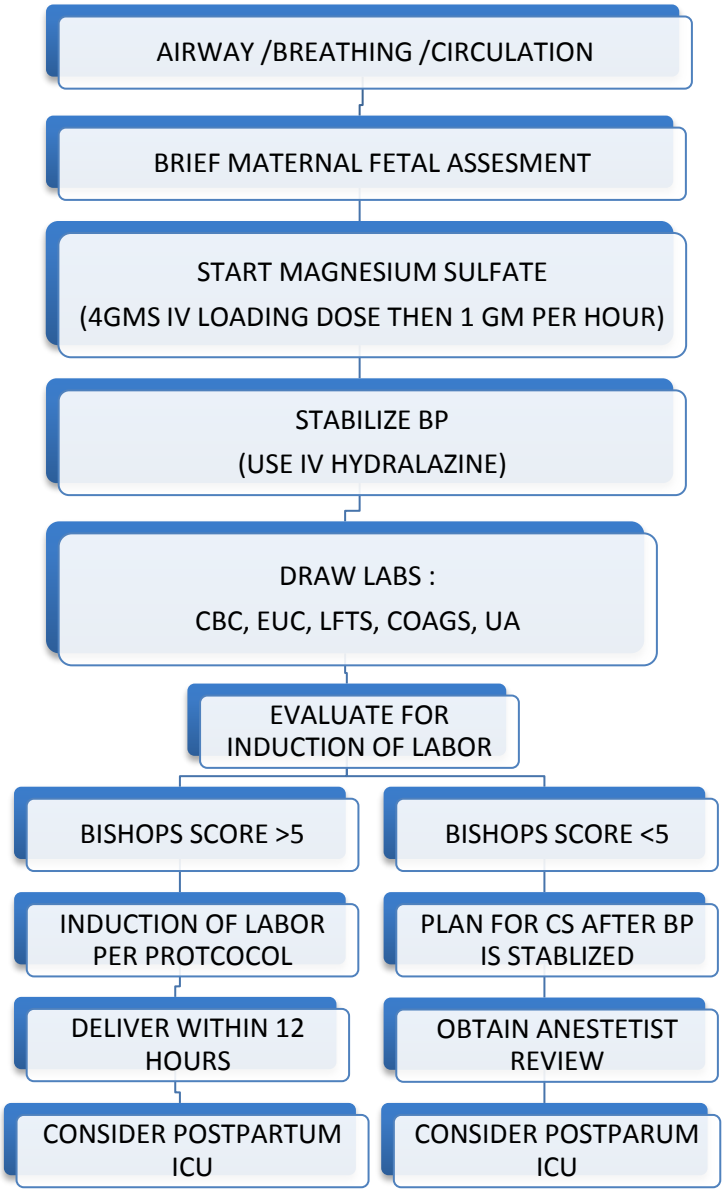


ALGORITHM FOR MANAGEMENT OF SEVERE PREECLAMPSIA



INDICATIONS FOR DELIVERY FOR SEVERE PREECLAMPSIA

MATERNAL	FETAL
34 completed weeks	IUGR
Uncontrolled BP on 2 agents at maximum doses	BPP 4/8
Platelets <100 000	Oligohydramnios/ Anhydramios
Liver enzymes 3 times normal	Dopplers with absent end diastolic flow
Deterioration in renal function (elevated creatinine, oliguria, anuria)	
Persistent severe headache or visual changes	
Persistent severe epigastric pain or nausea and vomiting	
Suspected abruption	

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**GENERAL CONSIDERATIONS:**

- **CALL FOR HELP FROM NURSE,REGISTRAR , CONSULTANT, ANESTHESIA**
- **PROTECT THE AIRWAY**
- **PLACE IN LEFT LATERAL DECUBITIS POSITION TO REDUCE RISK OF ASPIRATION**
- **GIVE SUPLIMENTAL OXYGEN**
- **FIX 2 IV LINES AS SOON AS POSSIBLE**
- **SEND BASELINE LABS (FHG, UEC, LFTS, COAGS, GXM, SMEAR, UA)**
- **MONITOR VITAL SIGNS EVERY 10-15 MINUTES**
- **CATHETERIZE BLADDER AND MONITOR STRICT INTAKE AND OUTPUT**
- **OBTAIN A GUARDED BED**
`````

DOSING GUIDE FOR IV MAGNESIUM SULFATE

	SEIZURE PROPHYLAXIS	SEIZURE TREATMENT	PRETERM LABOR
LOADING	**4 gm**	**4 gm**	**4 gm**
MAINTENANCE	**1 gm hourly**	**2 gm hourly**	**2 gm hourly**

MONITORING ON MAGNESIUM

- Respiratory rate (goal: ≥ 16/min)
- Pulmonary exam (goal: clear breath sounds)
- Foley's catheter to monitor urine output (goal: ≥ 30mls/hr)
- Patellar reflexes (goal: must be present)

MAGNESIUM TOXICITY

Symptom/Sign	Magnesium level
EKG changes	**5-10 mEq/ liter**
Loss if DTRS	**10 mEq/ liter**
Respiratory suppression	**15 mEq/ liter**
Cardiovascular collapse	**>25 mEq/ liter**

If a patient is noted to have loss of deep tendon reflexes, pulmonary edema, or respiratory depression then treat for Magnesium toxicity:

- Give IV Calcium Gluconate, 1gm IV(10-20 ml of 10% solution given slowly) until the respiratory rate improves
- Check and EKG to rule out cardiac toxicity

Fetal kick chart

	Week# _____						
Hours	M	T	W	Th	F	S	Su
:00							
:30							
:00							
:30							
:00							
:30							
:00							
:30							
:00							
:30							
:00							
:30							

You may notice many different kinds of movements: kicks, turns, flips or swishes. Starting at nine in the morning record each movement you feel into your fetal kick chart at the time that you feel it. After noting the tenth movement you can stop counting for the day and start again the following morning. Remember that your baby may move ten times in thirty minutes or in twelve hours.

Appendix 6: Approval to conduct Research at MTRH

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

25th June, 2015

Dr. Ben Jumba Locho,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Perinatal Outcomes of Expectant Management of Severe Preeclampsia Remote from Term at Moi Teaching and Referral Hospital, Eldoret".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. JOHN KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM

Appendix 7: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2015/110
Approval Number: 0001422

25th June, 2015

Dr. Ben Jumba Locho,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
25 JUN 2015
APPROVED
P.O. Box 4606-30100 ELDORET

Dear Dr. Jumba,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Perinatal Outcomes of Expectant Management of Severe Preeclampsia Remote from Term at Moi Teaching and Referral Hospital, Eldoret"

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1422*** on 25th June, 2015. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 24th June, 2016. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD