MATERNAL COMPLICATIONS (OUTCOMES) OF SEVERE PRE-ECLAMPSIA AT A TERTIARY LEVEL HOSPITAL IN ZAMBIA

BY

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A dissertation submitted to the University of Zambia in partial fulfilment of the Requirements of Degree of master of medicine in obstetrics and gynaecology

THE UNIVERSITY OF ZAMBIA

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DECLARATION

I declare that this dissertation is my original work and has never been presented or submitted anywhere for the award of any degree before. I therefore present it for the award of the degree of master of medicine in obstetrics and gynaecology of The University of Zambia, Lusaka, Zambia.

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This dissertation has been submitted for examination with the approval of the following supervisors

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ABSTRACT

Preeclampsia is a multi-systemic disorder typically unique to pregnancy and characterised by blood pressure above or equal to 140 systolic or 90 diastolic and proteinuria of 300g in a 24 hours urine sample collection. Preeclampsia complicates 3 - 8% of pregnancies and is a major cause of maternal mortality and morbidity. Although the etiology of preeclampsia is still unclear, some epidemiological findings support the hypothesis of a genetic and immunological etiology. The disease has a complex pathophysiology, the primary cause being abnormal placentation early in pregnancy. Without treatment the disorder leads to serious maternal and perinatal complications that includes; HELLP syndrome, abruption placentae, DIC, pulmonary oedema, renal failure, eclampsia, and death.

This descriptive study analysed cases of 175 women with Severe Preeclampsia admitted to the Mother and New Born Hospital between June and December 2017. Women meeting the criteria were identified antenatal and enrolled into the study after delivery to obtain data using the maternity record book and face-face interviews for clarification.

The data was analysed using SPSS to obtain frequency distributions of outcomes of interest that was illustrated in charts and tables.

The age range for the women was 15 - 41 years. Frequency of complications from SPE increased with advancing age towards 35 years and above. Unemployment and living in low cost housing was associated with higher risk of complication from SPE.

HELLP Syndrome occurred in 10.3% of women with SPE and so did placental abruption. IUFD was a complication in 28% of the pregnant women. Most women (34%) delivered through induction of labour. The 30-34 weeks was the peak gestation period associated with the most complications of SPE in the pregnant women.

SPE is a pregnancy condition with serious potential consequences for the mother and the fetus.

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ABBREVIATIONS AND ACRONYMS

CNS	Central nervous system
DIC	Disseminated intravascular coagulation
GIT	Gastrointestinal system
HELLP	haemolysis elevated liver enzymes and low platelets
IOL	Induction of Labour
IUFD	Intrauterine fetal death
IUGR	Intrauterine growth restriction
LMICs	Low and Middle Income Countries
MSB	Macerated stillbirth
NICU	Neonatal intensive care unit
PPH	Postpartum haemorrhage
RDS	Respiratory distress syndrome
SES	Social Economic Status
SPE	Severe pre-eclampsia
UTH	University Teaching Hospital

DEFINITION OF TERMS

Severe Pre-Eclampsia: Blood Pressure of equal to or less than 160/110 mm/Hg on two occasion at least 6 hours apart (not more than 1 week apart) and proteinuria of greater than 5g/24 hours sample or 3+ on 2 urine samples 6 hours apart (not more than 1 week).

Socio-economic status: - The standing of a person or group in a community or society based on education, occupation and income, which is often, used as a benchmark for investigating health inequalities.

CHAPTER ONE: STUDY BACKGROUND

1.1 Introduction

Preeclampsia is a multisystem disorder that complicates 3–8% of pregnancies and is a major source of morbidity and mortality worldwide (Lindheimer, 2009). This is a disease unique to pregnancy typically characterized by blood pressure ≥140/90 mmHg after 20 weeks gestation and associated with proteinuria ≥300 mg/24 h or ≥1+dipstick. About 10-15% of maternal deaths are directly associated with pre-eclampsia and eclampsia particularly in developing countries (Carty, 2010). Mounting evidence in recent years suggest that preeclampsia has important implications for future maternal health, in particular cardiovascular health.
Preeclampsia is characterized as mild or severe based on the degree of hypertension, proteinuria and the presence of symptoms resulting from involvement of systemic organs.

Although the etiology of preeclampsia is still unclear, the clinical phenotypes of preeclampsia have been demonstrated to be related to high circulating levels of anti-angiogenic proteins secreted by the placenta such as soluble Fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin, that cause impaired endothelial function (Carty, 2010). Endothelial dysfunction plays a central role in the pathogenesis of the maternal syndrome. Dysfunctional endothelial cells produce altered quantities of vasoactive mediators, which lead to a tip in the balance towards vasoconstriction (Baumwell S). An imbalance in circulating angiogenic factors is emerging as a prominent mechanism that mediates the endothelial dysfunction and the clinical signs and symptoms of preeclampsia.

Other research workers have demonstrated that Preeclampsia results from impaired trophoblastic differentiation and invasion in early pregnancy, which stimulates sustained oxidative stress and a systemic inflammatory response (Pijnenborg, 2006). Recent work has suggested that the pathology might be better viewed as resulting from extrinsic and intrinsic factors with abnormal placentation being considered an extrinsic cause that leads to early onset of preeclampsia. (Redman, 2014)Redman et al further suggested that late onset preeclampsia (≥34 weeks' gestation) may be triggered by a distinct, intrinsic pathology involving microvillus overcrowding

which is thought to occur as placental growth reaches its limits at term, with diminishing villous pore size impeding perfusion and increasing oxidative stress. This theory extends to suggest that oxidative stress proteins modulate the maternal response to developing preeclampsia through regulation of various growth factors. (Redman, 2014)

The National Institute for Health and Care Excellence (NICE), identifies many conditions and health risk behaviors, that are thought to predispose to preeclampsia; these include, among others, preexisting hypertension, chronic kidney disease, insulin-dependent diabetics, body mass index (BMI), age, and unfavorable levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides.

Left untreated the disorder often leads to serious maternal and perinatal complications. The common major maternal complications being the syndrome of haemolysis elevated liver enzymes and low platelets (HELLP syndrome), abruption placentae, disseminated intravascular coagulation (DIC), pulmonary edema, acute renal failure, eclampsia, and death.

Duley et al observed that most women with preeclampsia give birth without problems because of the prompt and adequate health care services they receive (Duley, 2009). However, severe pre-eclampsia can cause problems such as stroke, kidney failure, liver failure, and blood clotting. Though the disease has been known for many years, we still lack methods to predict and prevent pre-eclampsia and delivery appears to be the only definitive and curative treatment.

With increasing understanding of the disease process, the occurrence of maternal complications and mortalities have fallen over the last few decades in the developed countries (Ghulmiyyah, 2012). On the contrary, in under developed countries like Zambia, the rates of mortality and morbidity still remain very high (WHO, 2007). This is mainly due to the poor systematic follow up and early identification of pregnant mothers with risk factors for pre-eclampsia.

At the University Teaching Hospital (UTH) in Lusaka, Zambia, severe Pre-eclampsia (SPE) is one of the leading causes of emergency obstetric admissions. Anecdotal information from unpublished 1st quarter of 2016 inpatient main diagnosis data collection sheet indicated that, between January and March, 2016 not less than two pregnant women were admitted to the labour ward intensive care unit at UTH, with severe preeclampsia each day.

Numerous previous studies have investigated the causes of maternal morbidity and mortality at the University Teaching Hospital. Hickey MU and Kasonde (1976) JM, reviewed eighty maternal deaths occurring at the Hospital in Lusaka, from 1974-1976. The maternal mortality rate was 1.5 per 1000 births. (Hickey, 1977) The commonest causes of death were pre-eclampsia and eclampsia (23), septicemia (14), hemorrhage (13) and ruptured uterus.

In another study involving 162 women by Chisoko Ernest chipampe Preeclampsia: maternal and fetal outcomes according to symptomatology and proteinuria at university teaching hospital, Lusaka (Chisoko, 2013), Zambia, it also showed the large contribution of complicated hypertensive disorders of pregnancy to maternal morbidity and mortality.

There still remains a dearth of knowledge, today, of the impact of severe preeclampsia on maternal outcome at the UTH as the few cited studies given here analyzed all causes of maternal death and refer to the period over three decades ago. It is therefore necessary to audit maternal outcomes arising from sever preeclampsia at UTH in the recent time.

This study therefore audits the occurrence of severe preeclampsia in relation to specific maternal complications arising during pregnancy, child birth and puerperium.

In this dissertation, the Introduction will be presented in chapter One. Chapter two will present the review of literature highlighting relevant studies from different global and regional sites performed on a similar subject. The methodology of this study will then be discussed in chapter three and the results in chapter four. The discussion will be presented in Chapter five and finally the conclusion and recommendation in chapter six.

1.2 Problem Statement

World Health Organization indicates that in developing countries, a woman is seven times more likely to develop preeclampsia than a woman in a developed country, with 10 to 25% of these cases resulting in maternal death (WHO, 2007). The UTH records a high number of pregnant women admitted and treated for pre-eclampsia and eclampsia. The prevalence of pre-eclampsia at the UTH was 12% of all admissions (Chisoko, 2013). Unpublished data from the UTH labour

ward daily statistics register for the period January to December 2015, indicated that out of the 23,934 pregnant women admissions, 1 829 (7%) had hypertensive disorders and 579 (32%) of these had Severe Pre-Eclampsia (SPE) requiring high dependency and occasionally intensive care therapy, with fatal outcomes.

1.3 STUDY JUSTIFICATION

Though previous studies on pregnancy outcomes in pre-eclampsia in UTH have focused on prevalence and clinical characteristics of this condition, the epidemiological profile of patients with severe pre-eclampsia and the characteristics of their complications that this study seeks to explore will hopefully serve as a basis to influence investment in the clinical management of this hypertensive disorder. Additionally it will also help streamline the existing local checklists and/or protocols currently used in maternity units at UTH-MNH and other maternity centres across the country. The findings will further help heighten and improve clinical vigilance on patients with mild pre-eclampsia and gestational hypertension to avert disease progression to its complicated form. This will improve maternal survival by reducing morbidities and mortalities.

1.4 Main Objective

To describe the mode of delivery and maternal outcomes among women with SPE admitted to the UTH-WNH.

2.1.3 Specific Objectives

1. To study maternal outcomes in terms(relating to) of severity and complications of severe preeclampsia among the women admitted at the UTH-WNH from June to December 2017
2. To study distribution patterns of severe preeclampsia among women with different social economic characteristics with special reference to (age, education, parity, occupation and monthly household income.
3. To analyse delivery option in relation to disease severity.

CHAPTER TWO: LITERATURE REVIEW

Worldwide, complications of preeclampsia do arise in about 3 % of pregnancies, and all hypertensive disorders affect about 5–10 % of pregnancies (WHO, 2007). Hypertensive disorders are associated with higher rates of maternal, fetal, and infant mortality, and severe morbidity, especially in cases of severe pre-eclampsia, eclampsia, and haemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome (Hutcheon, 2011). The World Health Organization (WHO) estimates that at least 16% of maternal deaths in low and middle-income countries result from complications of severe pre-eclampsia and eclampsia (WHO, 2007). Globally several studies have been done to characterise these complications.

Generally, the incidences of complications are variable depending on the social economical settings and healthcare level of the hospital in which the study is conducted (Khan KS, 2006). This section reviews literature from various studies on the complications of hypertensive disorders associated with pregnancy.

2.1 Clinical Complications Of Sever Preeclampsia

2.1.1 Eclampsia

Refers to the occurrence of one or more generalized convulsions and/or coma in the setting of preeclampsia and in the absence of other neurologic conditions (ACOG, 1999). Till recently, this complication was thought to be the end result of preeclampsia, hence the nomenclature. However, it is now clear that seizures are only one of several clinical manifestation of severe pre-eclampsia. The cause of seizures in women with eclampsia is unknown though proposed etiologies include cerebral vasospasm with local ischemia, hypertensive encephalopathy with hyper perfusion, vasogenic edema, and endothelial damage (Morriss, 1997)

2.1.2 HELLP Syndrome

HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets) is a serious complication of preeclampsia that was first described by Pritchard et al in 1954 (Pritchard, 1954). It is therefore a triad of signs. Diagnosis of the complete form of the HELLP syndrome requires the presence of all 3 major components, while partial or incomplete HELLP syndrome consists of only 1or 2 elements of the triad (H or EL or LP) (Martin Jr, 2006).
In his Study, Sibai demonstrated that among women with severe preeclampsia, 6% will manifest with one abnormality suggestive of HELLP syndrome (usually elevated liver enzymes or low platelets), 12% would develop two abnormalities, and about 10% would manifest with all three abnormalities (Sibai, 1990). Thrombocytopenia is a common feature of this syndrome. Based on the severity of the thrombocytopenia, Martin et al further categorized HELLP syndrome into three classes (Martin Jr, 1990). Class 1 is defined as a platelet count less than 50,000/mm3, class 2 as a platelet count 50,000 to 100,000/mm3 , and class 3 as a platelet count more than 100,000/mm3' This classification does appear to correlate to some degree with the prognosis and speed of resolution and is not widely accepted.

Sibai (2202) was able to show that unlike preeclampsia, HELLP syndrome occurs more often in the Caucasians, in multipara, and in women older than 35 years.

2.1.3 Liver Rupture

Smith et al showed that liver rupture was one of the most severe consequences of severe preeclampsia/HELLP syndrome, with a reported maternal death rate of more than 30%. (Smith Jr, 1991) The precise cause remains unknown though Smith et al speculated that endothelial dysfunction with intravascular fibrin deposits and hepatic sinusoidal obstruction leads to intrahepatic vascular congestion, increasing intrahepatic pressure, and distention of Glisson's capsule, and finally leads to the development of a sub-capsular hepatic hematoma and liver rupture.

Pain in the right upper quadrant and/or epigastric area and focal tenderness are the most important clinical features, especially if they occur in the setting of preeclampsia/HELLP syndrome.

2.1.4. Pulmonary Edema

Pulmonary edema refers to an excessive accumulation of fluid in the pulmonary interstitial and alveolar spaces and may develop in up to 2.9% of pregnancies as a complication of severe preeclampsia (Sibai, 1987). Causes of pulmonary edema are often multi-factorial. According to the Starling equation, any factor that results in a reduction in colloid osmotic pressure (or in the Colloid osmotic pressure/pulmonary capillary wedge pressure gradient), an increase in capillary permeability, or an increase in intravascular hydrostatic pressure will lead to extravasation of fluid from the vasculature and predispose to the development of pulmonary edema. 70 – 80% of cases of pulmonary edema in the setting of preeclampsia develop after delivery (Benedetti, 1985) with only 30% occurring antenatal.

In addition, Oina P and colleagues indicated that another feature that may predispose to the development of pulmonary edema in the setting of preeclampsia is an increase in capillary leak and capillary fluid extravasation secondary to vascular endothelial damage (Oian, 1986). According to Sibai and coworkers, the vast majority (90%) of patients with pulmonary oedema have underlying chronic hypertension, and are more likely to be multiparous and of advanced maternal age.(Sibai, 1987)

2.1.5. Renal Failure

Acute renal failure is a rare complication of preeclampsia, though the actual incidence remains undetermined. This acute condition in the setting of pregnancy is characterized by an abrupt reduction in the maternal glomerular filtration rate, leading to excessive retention of urea and water as well as numerous electrolyte and acid-base abnormalities (Naqvi, 1996). Glomerular endotheliosis is the characteristic histological lesion in which glomeruli are enlarged and swollen with vacuolated endothelial cells. This histological feature, coupled with the generalized

vasoconstriction that characterizes preeclampsia, leads to a 25 – 30% decrease in renal plasma flow and glomerular filtration compared with normal pregnancy (Lindheimer, 1998).

2.1.6. Disseminated Intravascular Coagulopathy

Disseminated Intravascular Coagulopathy (DIC) is a hematologic disorder characterized by a generalized increase in both fibrin formation and fibrinolysis, leading to excessive Consumption of clotting factors and presents clinically as a bleeding diathesis.

Though the most common causes of DIC in pregnancy are excessive blood loss with inadequate blood component replacement, placental abruption and amniotic fluid embolism, severe preeclampsia/HELLP syndrome is also a possible cause.

2.1.7 Other rare complications of SPE

Cortical blindness, though rare, is another known complication of severe preeclampsia. Other ophthalmologic manifestations of sever preeclampsia include retinal detachment, retinal arteriolar vasospasm, and thrombosis of the central retinal arteries (Kesler, 1998). The incidence of cortical blindness as a manifestation of hypertensive encephalopathy in severe preeclampsia is 1–15% (Jaffe, 1987).

Hypertensive encephalopathy is a sub-acute neurologic syndrome characterized by headache, seizures, visual aberrations, and other neurologic disturbances (altered mental status, focal neurologic signs) in the setting of elevated blood pressure (Chester, 1977). Although the syndrome is usually reversible if the hypertension is treated early, it may be fatal if it is unrecognized or if treatment is delayed (Gifford, 1991).

2.2 Maternal Age, Social-Economic Situations and Severe Pre-Eclampsia

Many studies have shown that maternal age, somewhat, has an important influence on the incidence of hypertensive disorders of pregnancy. Zibaeenazhad et al. reported that young prim gravidae less than 20 years and all patients over 30 years have an increased chance of hypertension (Zibaeenazhad MJ, 2010). Similarly, Sheraz et al. reported that PE was more frequent in patients younger than 21 years of age and in older than 35 year (Sheraz S, 2006).

Eclampsia is most common in non-Caucasians, nulliparous women from lower socioeconomic backgrounds. Peak incidence is in the teenage years and early 20s, but there is also an increased prevalence in women older than 35. (Sibai, 2002).

Social Economic Status (SES) may be referred to as the relative position attained by an individual in a cultural and financial hierarchy. Differences in socio-economic status may account for important disparities in the nutrition, housing, safety, and health of large groups of people. In general, the lower one's SES, the greater one's risk of malnutrition, infectious diseases, maternal risk factors and early mortality from all causes. Income, education, occupation, vocation, and wealth all contribute to SES. (Mosby's Medical Dictionary,. (2009)., 2018). From an epidemiological perspective, poverty means low socioeconomic status (measured by social or income class), unemployment and low levels of education (Saraceno B, 1997). Several lines of evidence indicate that socioeconomic disadvantages are related to maternal complications during or after childbirth (Lindquist, 2013).

Starfield and coworkers, (1991) observed that the risk of perinatal adverse outcomes, such as preeclampsia, lower birth weight, and preterm or early term birth were higher in lower income groups than in higher income groups ((Starfield B, 1991); (Borders AE, 2007)). Lee, 2005 observed that even in developed countries, lower socioeconomic status may pose additional risks for poorer maternal health (Lee SI, 2005).

2.3 Access To Health Care And Complications Of Severe Preeclampsia

In the early years of the 21st century, the millennium development goals explicitly placed maternal health at the core of the struggle against poverty and inequality. (Hogberg, 2005). The WHO fact sheet, 2015, shows that approximately 800 women die each year across the globe, from preventable causes of pregnancy and childbirth; 99% of these deaths occur in low and middle-income countries (LMICs). Most of the maternal deaths in LMICs occur at the community-level where the majority of women do not have access to the health care facility. In these sites, healthcare access is often poor and routine antenatal coverage not universal or of poor quality resulting in most patients visiting a clinician at the stage of severe preeclampsia or eclampsia. Such cases are an obstetric emergency considering the impending danger to the mother and the baby. Failure to identify preeclampsia along with a delay in responding to the clinical signs and symptoms is responsible for nearly half of maternal deaths. (Weindling, 2003).

Access to health care, distance, and cost remain major obstacles for women in Sub-Saharan Africa, to seek care for preeclampsia. Antenatal care utilization is around 68% in this part of the world compared with 98% in high resource settings. (Firoz, 2011).

CHAPTER THREE: METHODOLOGY

3.1 Study Site

This study was conducted at the Mother and New Born Hospital (MNBH) of the University Teaching Hospital (UTH) in Lusaka. This site is a tertiary level referral hospital with a catchment population of over 3 million people. The MNBH is a consultant led maternity centre with 205 beds allocated to ante and postnatal care. The labour suite has 25 delivery beds and is complemented by a five-bed high dependence care unit suitable for management and care of various pregnancy emergencies and complications. More severe complications necessitating life support are transferred to the central Intensive Care Unit (ICU).

Midwifery and obstetrics staff provide combined efforts in patient team management on a 24 hours basis.

Parturient women with complications are referred from surrounding primary level hospitals and urban clinic within the province of Lusaka and occasionally from beyond.

3.2 Study Design and Duration

This was a prospective descriptive study conducted from June to December 2017 by analysing case notes, patient registers and face-face interviews with postpartum patients admitted with severe pre-eclampsia and its complications, through the labour ward admission.

3.3 Sample Size

Using the single proportion formula (shown below) at 95 % confidence interval the calculated sample size was 175.

Formula

$$N = \frac{Z^2 \times P(1-P)}{d^2}$$

N = Sample Required

Z = Statistic at 95% confidence interval = 1.96

P =Expected prevalence = 0.12

d = Acceptable accuracy range = 0.05

The sample size from calculation was 175

3.4 Methods Of Study

Each patient with SPE admitted to labour or antenatal ward and providing consent was enrolled in the study. A serial number was allocated to serve as a unique identifier. Demographic data was, including age, sex, gravidity and parity, residence, education attainment and occupation was obtained from the clinical records, and where necessary clarified with the participant. The participant was allowed to follow the usual care and management for SPE as per hospital protocol and guidelines with no undue interference on management plan from the investigator. The Investigator worked as a Senior Resident in the maternity unit at the time of this study and declared interest by involving a colleague in the active therapy of any research participant enrolled. This was done to avoid biases and the need to avoid modifying patient outcome which forms the core output of this study. The role of the Investigator in such circumstances was limited to liaising with the patient (participant) care teams to monitor outcome variables. Final data collection was taken from the participant medical records and additional face-face interview prior discharge after all the treatment informed had been written by the attending medical officer. Outcome data of interest was recorded and included all complications of SPE suffered by the participant.

3.5 Data Collection And Analysis

Essential statistical data were obtained from hospital registry and participant's information from patient medical file. Where necessary, participant details were clarified with a brief face – face interview. The data was entered directly onto an Excel-based, predesigned data entry form on a pass word-protected computer lap top. Personal identifiers such as participant's name was omitted from the data set and replaced with a study number to conceal personal identity.
The data was verified, cleaned, validated and exported to SPSS for analysis.

3.6 Ethical Considerations

Permission to conduct this research was obtained from the Administration of the WNBH for use of the hospital infrastructure and patients. Permission was also obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) on approval letter No. 010-1016, which is attached in the Appendix.

At admission in labour ward, the researcher approached all patients presenting with SPE. Detailed information about the study was explained to enable them make an informed choice to participate. Participation was absolutely voluntary and patients were free to decline participation with no consequences to the medical care they would receive in the hospital if they did not wish to enrol. This information was provided using the language most familiar and best understood by the participant. Written consent was obtained from each participant and for those unable to sign, a finger print was obtained.

Information and consent procedures were deferred in cases of severe illness, emergency admission and unconscious patients, till they were well enough to give informed consent. Where possible such consent was obtained from caregivers and the next of keen.
Confidentiality of patient data was assured.

CHAPTER FOUR: RESULTS

Altogether 6,738 deliveries occurred in the labour ward at the Women and New Born Hospital in the period from January to December 2017. Altogether, 175 post-partum women with complications of SPE were recorded in this study, in the six months between June and December 2017. Though many complications are likely to arise from severe pre-eclampsia, this study documented the following specific primary outcomes, on the basis of their frequency and clinical significance; HELP syndrome, renal dysfunction, CVA, placenta abruption, DIC, maternal death and IUFD. Some patients with SPE, recruited in the study did not illustrate any clinical complications while a few others showed rare symptoms that were of non-clinical significance.

The exposure variables of interest were maternal age, occupation of the parturient, her educational attainment, area of residence, the gestational age at delivery, gravidity, marital status and her delivery intervention.

4.1 Baseline Characteristics

The age range of women was 15- 41 years.

Table 1 shows that maternal complications from severe PET increased with age, with more women older than 35 years (24%). Teenage women made up 11%.

Table 1. Frequency of maternal social and demographic characteristics of women with SPE.

Maternal Characteristics	n	%
Age		
15 - 19	19	10.9
20 - 24	33	18.9
25 - 29	40	22.9
30 - 34	41	23.4
≥ 35	42	24.0
Gravidity		
Once	55	31.4
Twice	29	16.6
More than twice	91	52.0

Marital Status		
Single	29	16.6
Married	142	81.1
Divorced	3	1.7
Widowed	1	0.6
Residence		
Low cost	143	81.7
Medium cost	30	17.1
High cost	2	1.1
Education		
None	5	2.9
Primary	54	30.9
Secondary	84	48.0
Tertiary	32	18.3
Occupation		
Unemployed	107	61.1
Employed	42	24.0
Self employed	26	14.9

The table also shows that women with higher parity (more than two) had a higher frequency (52%) of SPE in the period under review. It is likely that parity increased with age. Married women were associated with a higher frequency of complications arising from SPE (81.1%), a finding which could be attributed to the higher frequency of pregnancies in this category of women.

Table 1 further shows that women from the low cost residential areas, were associated with a higher frequency of complications due to SPE (81.7%). Low cost residential areas of Lusaka, are characteristically high density population communities. The Women and new Born Hospital which is the site for this study, is situated in the heart of a medium and high cost residential areas and so provides fare access to members of the surrounding community.

More women with secondary level education (48%) were associated with complication while the illiterate women had the least.

Unemployed women admitted to the hospital with SPE had the most complication of the disease.

4.2 Maternal Complications

From the 175 participants enrolled in the study, 73 (41.7%) of the women with SPE developed at least one of the complications of interest.

Figure1. Shows the various specific complications observed. HELLP syndrome and abruption of the placentae each affected 10.3% of the women. Though not necessary a maternal complication, Intra Uterine Fetal Death occurred in 28% of the women. The larger proportion of women (58.3%) however, did not suffer additional complication above SPE.

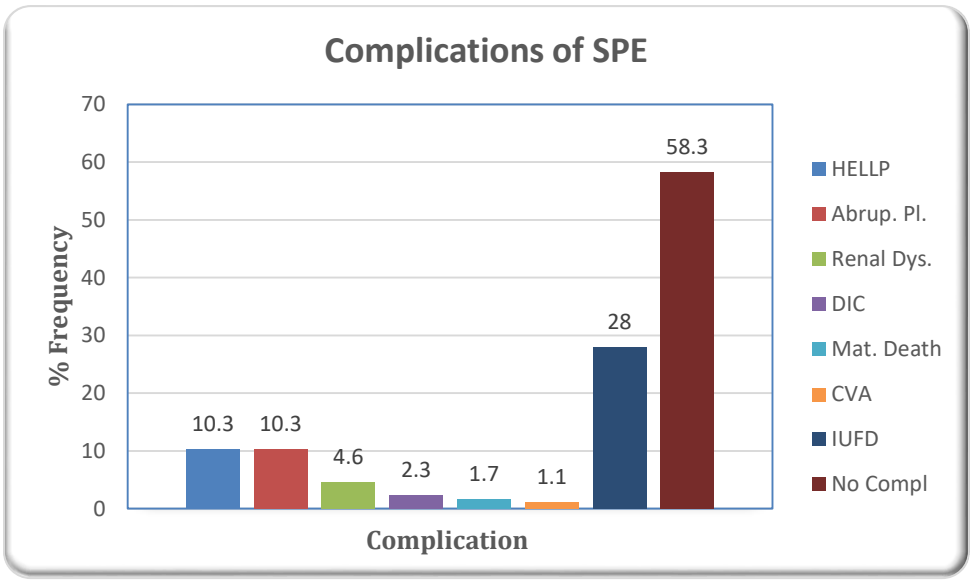

Figure 1: Percentage frequency of complications of SPE in women from June to December 2017 at the WNBH.

Three women died from complications of SPE, representing 1.7% of the women affected by the disease condition.

4.3 Delivery Interventions

Women with SPE were admitted to labour ward at different stages of pregnancy with some of them in the initial stages of labour while other remote from term and not in labour.
Figure 2 shows intervention performed in women admitted to labour ward to expedite delivery as a measure to treat SPE and its complications.

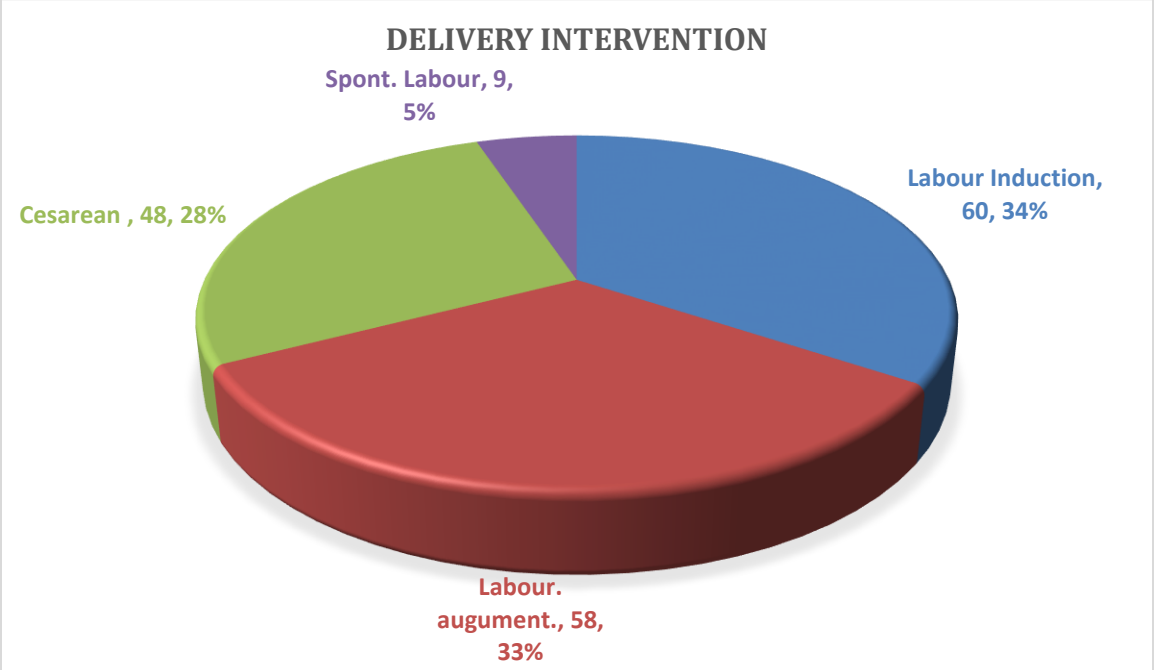

Figure 2: Delivery interventions in women admitted to labour ward with SPE.

Induction of labour was performed in 34% of the women while 5% had spontaneous labour. Cesarean section was indicated in 28% of the women and the rest of them (33%) were admitted in the initial stages of labour requiring artificial rupture of the membranes (ARM) and augmentation with oxytocin.

4.4 Gestation Age At Delivery

Women were included in the study from the gestation age of 20 weeks through to postpartum. The gestation age was stratified across four weeks in each age category.

Figure 3 shows the frequency of complications of SPE in women at different gestation age categories.

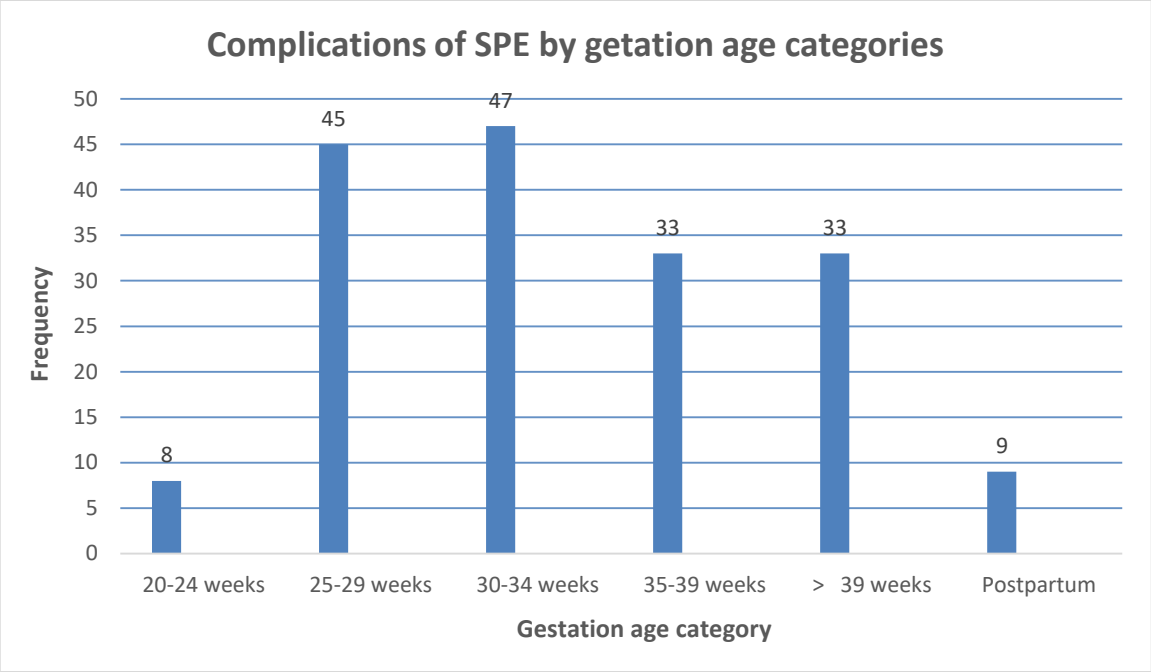

Figure 3: Complications of SPE at different gestation age categories in 175 women studies

The figure shows a higher frequencies of complications arising from SPE in women admitted to the hospital at 30 – 34 weeks gestation. As pre-eclampsia manifests at mid trimester, fewer complications were observed at 20 – 24 weeks gestation. Post-partum complications accounted for 9 (5.14%) of the women with the disease.

CHAPTER FIVE: DISCUSSION

Hypertensive disorders are the most common medical complication of pregnancy, affecting 8% to 10% of all pregnancies ((National High Blood Pressure Education Program, 2000). While 30% of hypertensive disorders in pregnancy are caused by chronic hypertension, 70% are pregnancy induced. This study is unable to categorize SPE due chronic or that due to gestational hypertension as participants were recruited post-partum.

The spectrum of disease ranges from mildly elevated blood pressure with minimal clinical significance to severe hypertension and multi-organ dysfunction.
This study has shown a series of complications that may arise from the effect of the disease process on the various body organs including the liver, kidney, uterus, the heart, the blood and other physiological systems.

Furthermore, the study has shown an increase in the frequency of complications in relation to advancing age, in women with SPE. Age seems to have an important influence on the incidence of hypertensive disorders of pregnancy. This opinion was reported by Zibaeenazhad et al. who demonstrated that young prim-gravidae less than 20 years and all patients over 30 years have had increased chance of hypertension (Zibaeenazhad, 2010). In this study we see that women over 35 years were associated with more complications. This finding compares well with the finds in a Japanese study (Ogawa, (2017)) that found women older than 45 years to have elevated risk of adverse pregnancy outcome, including hypertensive disorders of pregnancy. Advancing age often entails uncontrolled chronic hypertension which is first uncovered in pregnancy with tendency to organ dysfunction and other complications.

Prim-gravidity has often been associated with pregnancy complications including pregnancy induced hypertension and sever preeclampsia. In this study, while 31.4% of women with complications of SPE were prim-gravidae, 52% were parous women (3 and more). It is likely that multi-parous women were older and so reinforcing the effect of advancing age as an important factor.

Most women in Zambia desire to bear children while in a wedlock. The higher proportion (81.1%) of married women with Complication of SPE in this study is a reflection of the many married women over the single women (16.6%) who get pregnant.

Several studies have concluded that low socioeconomic status can increase the risk of adverse pregnancy outcomes, though it remains unclear whether this negative association is attributed to inadequate prenatal care due to lack of access or is a factor of the lack of material wealth and conducive living environment that affect quality of life and subsequently health outcomes. In this study most women (81.7%) with complications came from low cost residential communities of Lusaka. Such communities are densely populated and vulnerable to periodic outbreaks of epidemic diseases. Though access to maternity health care in Zambia is at no substantial cost to the pregnant women, because government takes up the cost, immediate access to emergency care at the tertiary hospital among women from the less affluent communities can be impeded by lack of readily available transport at night and other problems. This finding is similar to the findings in the Korean (Kim, 2018) study that determined that Social Economic Status (SES) can affect pregnancy outcomes even under a universal healthcare system.

Education attainment did not seem to affect pregnancy outcome significantly though more women (48%) with complications had secondary education. Higher education attainment empowers women to make choices about their health, including maternal health care. According to the Demographic and Health Survey of 2013-14 (ZDHS, 2013-14), only 8% of women have no education. Nearly half of women have attended primary school. Forty-five percent of women have attended secondary or higher education. Two-thirds of Zambian women are literate. The low proportion of women with complications in this study is therefore down to the higher literacy levels among women in Lusaka.

Despite the reported high literacy levels among women, unfortunately unemployment remains unpleasantly high. This study has shown that 61.1% of women with complication are not in any formal employment compared to 24% who are employment. Lack of employment leads to depleted family income and threatens food security which is an important indicator of the quality of life and health status.

The study highlight complications related to vital organs' dysfunction as a result of SPE. HELLP syndrome is a serious complication in pregnancy characterized by hemolysis, elevated liver enzymes and low platelet count that occurs in 0.5 to 0.9% of all pregnancies and in 10–20% of cases with severe preeclampsia (L, 2003). In this study 10.3% of the women had HELP syndrome. This syndrome is currently regarded as a variant of severe preeclampsia or a complication (BM, 1990) .

Similarly, complications of the placenta accounted for 10.3% of the complication of SPE in this study. Placenta abruption is associated with severe maternal morbidity and almost exclusively with fetal death in the absence of urgent interventions. It has been proposed that decidual (placental bed) occlusive vasculopathy, caused by shallow invasion of fetal trophoblasts in the decidual spiral arteries observed in preeclampsia, is the cause of abruption of the placenta (Khong, 1986;).

In this study, 5% of the women presented with renal dysfunction. Derangements in renal function tests (urea and creatinine) and diminished urine output was a prominent feature in the 15-19 year old category (see attachment in the appendix). Renal failure was defined as elevation of urea and creatinine with failure of urine output requiring dialysis. A study in Brazil (Silva, 2008) analyzing a series of 55 cases of renal failure concluded that AKI was a rare but potential fatal complication in obstetric patients with pregnancy-induced hypertension as the main (41.8%) cause of the condition.

Intrauterine fetal death is a known complication of SPE. In this study fetal death affected 28% of the women. Preeclampsia developing preterm, has particularly been shown to be at her risk for fetal death. Preeclampsia is characterized by generalized vasoconstriction and hypovolemia, which affects fetal-placental perfusion and oxygen delivery to the fetus.

Several studies have evaluated modes of delivery and neonatal outcomes in patients with SPE (Jacques, Jan 2011) . In this study, women with SPE were admitted to labour ward at different stages of their pregnancy. Some remote from term while others at 37 completed weeks and more.

Although the etiology and progression of SPE has not been fully understood, it has been demonstrated that delivery of the fetus and the placenta is definitive to successful treatment (Amorim MMR, 2011.) In this study 34% of women had labour induction either because they did not meet the obstetrics criteria for cesarean delivery or the pregnancies were too premature to guarantee neonatal survival even after cesarean section. Induction of labour in grossly premature pregnancies was performed as a pregnancy interruption in maternal interest.

Augmentation of labour was done in 33% of women who were admitted with clinical evidence of early labour and who did not fit into the criteria for cesarean section. Women at term in latent or active phase of labour presenting with complications of SPE that would be detrimental to surgical delivery had labour augmented with ARM and parenteral oxytocin.

Twenty eight percent of the women required emergent cesarean section. Cesarean section is the preferred mode of delivery for pregnancies between 32-34 weeks gestation at the mother and New Born hospital, the site for this study. This gestation period takes into account the expected fetal weight of 1500-2000 grams which carries a good prognostic value for neonatal survival in the neonatal unit at the hospital. Cesarean section in pregnancies at term was performed in women with SPE to reduce the period of fetal exposure to the harmful effects of the disease. In contrast to this opinion, some studies have documented benefits of vaginal delivery to neonatal outcome. For example, in their study, Jacques and colleagues (sited above) concluded that in patients who develop severe preeclampsia, vaginal delivery decreased the risk of 5 min Apgar score of <7 and admission to the NICU. They further recommended strongly to consider vaginal delivery in women with SPE.

This study shows that most complication of SPE (47: 26.9%) manifested in women at the gestation period between 30-34 weeks. It has been known for a long time that the pathology of preeclampsia initiate at the time of placental implantation but start to manifest its clinical presentation at mid pregnancy. Disease progression thereafter varies in different women on the basis of their biological variability, living environment, access to maternity care and other factors. Results of this study would suggest a peak incidence at 30-34 weeks. Thereafter there is

a decline in the frequency towards term to reach a mid-term (20-24 weeks) pregnancy value post-partum.

30-34 weeks gestation is a period of fetal prematurity which cannot assure absolute neonatal survival in the NICU at this hospital. This therefore presents substantial challenges in clinical decision making regarding timing and mode of eminent delivery in the face of SPE.

CHAPTER SIX: CONCLUSION AND RECCOMENDATIONS

6.1 Conclusion

This study has shown that complications from severe preeclampsia in women at the WNBH-UTH are wide ranging. The common complications being HELLP syndrome, abruption placentae, renal dysfunction and intrauterine fetal death.

The study has also revealed that maternal age is an important factor in the origin of these complications. Social economic factors, including marital status, living standards and educational attainment could be other possible determinants.

6.2 Recommendations

1) Further research is necessary to study the neonatal complications from severe pre-eclampsia.
2) Secondary and Tertiary level Hospitals must allocate enough resources towards laboratory investigations to enable timely access of results in patients with SPE to help model management plan before complications set in.
3) Similarly, there's need to enhance basic laboratory tests at Primary Health care level, to streamline timely referrals of patients with hypertensive disorders.
4) Caution should be taken when making clinical decisions to whether manage a preterm pregnancy aggressively or expectantly. This means efforts must be made to ensure necessary 'prerequisites' are available before embarking on either route.

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APPENDIX 1. Participant Information Sheet.

STUDY TITLE: MATERNAL COMPLICATIONS OF SEVERE PRE ECLAMPSIA AT UNIVERSITY TEACHING HOSPITAL. LUSAKA.

I am **James Nyirenda** a post-graduate student pursuing a master's degree in Obstetrics and Gynaecology at the University of Zambia, School of Medicine. I am conducting the above named study at UTH as part of the requirements for the award of a Master of Medicine in Obstetrics and Gynaecology. I hereby ask your participation in the study to help me achieve my goal. The information given here is to explain to you what the study is about and what your role will be should you agree to participate.

Study Purpose

The study aims to study the prevalence of maternal complications of severe preeclampsia in pregnant women admitted at UTH. This will help provide information of the disease trends and patterns as seen at UTH. It is also hoped that the study will highlight areas of patient care that should be addressed to improve both maternal and fetal outcomes.

Study Procedure: What you will be asked to do

Should you agree to participate in this study, you will be asked to provide some personal details about yourself and your condition. The information you provide will be entered into a database together with that of others for comparison and drawing of conclusions. Some information will be collected from your patient records and where possible a questionnaire will be administered to clarify any information. Once processed, the information will be shared with the relevant interested groups.

The information collected will be very useful for the study as it will help identify areas of medical practice that need improvement for a woman with severe pre-eclampsia. It will also help us develop treatment plans that will benefit all pregnant women with severe pre-eclampsia.

We may ask you for some contact information like your name, place of residence and your phone number, so that healthcare providers may be able to contact you if they need further information from you, or need to follow you up. You do not need to provide your contact information if you do not want to.

Risks and Procedures

You will not be subjected to any procedure that may pose risk to you and your baby. The study will simply be observational where what the attending doctors find and or do will be noted. We may approach you at varying times during your hospital stay, either immediately after admission, prior to or after delivery, or prior to your discharge from UTH

Benefits

There will be no direct benefit to you for participating in the study. Please note that no enumeration will be done and no cost will be charged to you for participating in this study. The study will however help

generate information on certain disease patterns and outcomes thereby helping manage women with severe pre-eclampsia better.

Confidentiality

No identifiers will be used to ensure that confidentiality is maintained and that no information provided will be traceable back to you. A numbering system shall be used instead of names.

Consent

Before you enrol into the study it will be required that you give permission to have your information included in the study. After fully understanding what participating involves and being agreeable, you or your guardian will then sign or thumb print a pre-designed consent form. Your participation is voluntary and you are free to withdraw from the study at any point you feel uncomfortable to continue.

For any further clarification or concerns please feel free to contact me, Dr James Nyirenda or the Chairperson of the University of Zambia Biomedical Research Ethics Committee (UNZABREC) on the contacts given below.

Thank you.

Dr James Nyirenda

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The Chairperson
University of Zambia Biomedical Research Ethics Committee
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APPENDIX 2: Participant's Consent Form

Study of prevalence of maternal complications of severe pre-eclampsia at university teaching hospital, Lusaka.

I _____ (Participant's name), have been clearly explained to and understand that my personal information and details of my condition shall be used in the above mentioned study. I also understand that this information shall be treated with the strictest confidentiality and that no identifying features shall be used that can be traced back to me. I am fully aware that I shall not benefit in monetary form or otherwise and that I may withdrawal from the study at any point without suffering any consequences. I hereby willingly agree to participate and give consent that with due regard to confidentiality my personal information be used in this study.

_____	_____	_____
Participant's Name	Signature/Thumbprint	Date
_____	_____	_____
Witness' Name	Signature	Date

For any clarification please feel free to contact the following:

1. Principal Investigator:
   Dr James Nyirenda
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   Private Bag RW 1X
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2. The Chairperson
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   Ridgeway Campus
   Po Box 50110
   Lusaka
   Tel: +260-1-256067
   Email: unzarec@unza.zm

APPENDIX 3: Participants' assent Form (Women aged 16 years and below)

Study of prevalence of maternal complications of severe pre-eclampsia at university teaching hospital, Lusaka.

I _____ (Participant's name), have been clearly explained to and understand that my personal information and details of my condition shall be used in the above mentioned study. I also understand that this information shall be treated with the strictest confidentiality and that no identifying features shall be used that can be traced back to me. I am fully aware that I shall not benefit in monetary form or otherwise and that I may withdrawal from the study at any point without suffering any consequences. I hereby willingly agree to participate and give assent that with due regard to confidentiality my personal information be used in this study.

_____ _____ _____

Participant's Name Signature/Thumbprint Date

_____ _____ _____

Witness' Name Signature Date

For any clarification please feel free to contact the following:

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2. The Chairperson
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   Ridgeway Campus

   Po Box 50110 Lusaka. Tel: +260-1-250667. Email: unzarec@unza.zm

APPENDIX 4: Guardian Consent Form

This consent form is meant for guardians/parents of all prospective participants who have not reached the legal age of consent and therefore may not fully understand the purpose, the procedures, the potential risks and benefits of their involvement, and their alternatives to participation. In addition this consent is subject to the participant agreeing and signing the assent form to participate in the study.

Study of prevalence of maternal complications of severe pre-eclampsia at university teaching hospital, Lusaka.

I _____ (Guardian's name), have been clearly explained to and understand that _____ (Participant's name) my_____ (state relationship) shall participate in the above mentioned study. I also understand that her personal information used for this purpose shall be treated with the strictest confidentiality and that no identifying features shall be used that can be traced back to her. I am fully aware that there shall be no monetary gain or otherwise and that she may withdrawal from the study at any point without suffering any consequences. I hereby willingly agree on her behalf and in her best interest she (the participant) participates in this study with due regard to strict confidentiality.

_____	_____	_____
Guardian's Name	Signature/Thumbprint	Date
_____	_____	_____
Witness' Name	Signature	Date

For any clarification please feel free to contact the following:

1. Principal Investigator:
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Table 2: Data Summary of Maternal Characteristics and pregnancy outcomes.

	Total	HELLP		Renal dysf.		CVA		Abruptio Pl.		DIC		Death		IUFD		Other Complications	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Age																	
15-19	19	2	*10.5*	2	*10.5*	0	*0.0*	0	*0.0*	0	*0.0*	1	*5.3*	1	*5.3*	13	*68.4*
20-24	33	1	*3.0*	0	*0.0*	1	*3.0*	3	*9.1*	0	*0.0*	1	*3.0*	6	*18.2*	21	*63.6*
25-29	40	6	*15.0*	2	*5.0*	1	*2.5*	6	*15.0*	2	*5.0*	1	*2.5*	18	*45.0*	4	*10.0*
30-34	41	5	*12.2*	2	*4.9*	0	*0.0*	7	*17.1*	1	*2.4*	0	*0.0*	9	*22.0*	17	*41.5*
> 35	42	4	*9.5*	2	*4.8*	0	*0.0*	2	*4.8*	1	*2.4*	0	*0.0*	15	*35.7*	18	*42.9*
Residence																	
Low cost	143	15	*10.5*	7	*4.9*	1	*0.7*	13	*9.1*	4	*2.8*	3	*2.1*	36	*25.2*	64	*44.8*
Medium cost	30	2	*6.7*	1	*3.3*	1	*3.3*	4	*13.3*	0	*0.0*	0	*0.0*	13	*43.3*	9	*30.0*
High cost	2	1	*50.0*	0	*0.0*	0	*0.0*	1	*50.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*
Education																	
None	5	1	*20.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	1	*20.0*	3	*60.0*
Primary	54	8	*14.8*	4	*7.4*	1	*1.9*	5	*9.3*	3	*5.6*	2	*3.7*	18	*33.3*	13	*24.1*
Secondary	84	6	*7.1*	3	*3.6*	0	*0.0*	8	*9.5*	1	*1.2*	1	*1.2*	20	*23.8*	45	*53.6*
Tertiary	32	3	*9.4*	1	*3.1*	1	*3.1*	5	*15.6*	0	*0.0*	0	*0.0*	10	*31.3*	12	*37.5*
Occupation																	
Unemployed	107	13	*12.1*	5	*4.7*	0	*0.0*	10	*9.3*	2	*1.9*	3	*2.8*	30	*28.0*	44	*41.1*

Employed	42	4	*9.5*	2	*4.8*	2	*4.8*	6	*14.3*	1	*2.4*	0	*0.0*	11	*26.2*	16	*38.1*
Self employed	26	1	*3.8*	1	*3.8*	0	*0.0*	2	*7.7*	1	*3.8*	0	*0.0*	8	*30.8*	13	*50.0*
Gestation Age																	
20 to 24 weeks	8	0	*0.0*	1	*12.5*	0	*0.0*	1	*12.5*	0	*0.0*	0	*0.0*	4	*50.0*	2	*25.0*
24 to 30 weeks	45	8	*17.8*	1	*2.2*	1	*2.2*	5	*11.1*	2	*4.4*	1	*2.2*	24	*53.3*	3	*6.7*
31 to 34weeks	47	6	*12.8*	2	*4.3*	0	*0.0*	5	*10.6*	0	*0.0*	1	*2.1*	12	*25.5*	21	*44.7*
31 to 37 weeks	33	1	*3.0*	1	*3.0*	0	*0.0*	4	*12.1*	1	*3.0*	1	*3.0*	6	*18.2*	19	*57.6*
> 37 Weeks	33	1	*3.0*	0	*0.0*	0	*0.0*	2	*6.1*	1	*3.0*	0	*0.0*	2	*6.1*	27	*81.8*
Postpartum	9	2	*22.2*	3	*33.3*	1	*11.1*	1	*11.1*	0	*0.0*	0	*0.0*	1	*11.1*	1	*11.1*
Delivery intervention																	
Induction of labor	60	6	*10.0*	0	*0.0*	1	*1.7*	4	*6.7*	2	*3.3*	2	*3.3*	29	*48.3*	16	*26.7*
Monitoring/ Augumentation	58	5	*8.6*	1	*1.7*	0	*0.0*	7	*12.1*	1	*1.7*	1	*1.7*	12	*20.7*	31	*53.4*
Cesarean Section	48	5	*10.4*	4	*8.3*	0	*0.0*	6	*12.5*	1	*2.1*	0	*0.0*	7	*14.6*	5	*52.1*