TREND IN BLOOD PRESSURE AND RENAL FUNCTION AMONG SURVIVORS OF
SEVERE PREECLAMPSIA AND ECLAMPSIA IN MULAGO HOSPITAL:

A prospective cohort-study

BY

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THE AWARD OF MASTER OF MEDICINE (OBSTETRICS AND GYNAECOLOGY) DEGREE
OF MAKERERE UNIVERSITY

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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 (Obstetrics and Gynecology) of Makerere University, Kampala, Uganda

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DEDICATION

I dedicate this book to my beloved wife, VYANDO NGO NGERA July and my beloved children MUTEKE Achim, MUTEKE Siloe and MUTEKE Laetitia for their extreme support, prayers, encouragement, patience and understanding during the entire period of my course.
ACKNOWLEDGEMENT

Great thanks to God who provided life and all resources required for this work to be successful.

I would like to express my sincere appreciation to my supervisors; Ass. Prof. Kiondo Paul and Dr Beyeza Jolly for their supervision and guidance throughout the period of this work.

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I would like to express my gratitude to my research assistants Agatha and Mbambu F who worked very hard to ensure the process of data collection. Special thanks go to Dr. Dickens who assisted with data management and analysis.
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ABSTRACT

Background
Hypertensive disorders in pregnancy include mostly preeclampsia and eclampsia which are associated with multi organs involvement. The kidney is one of organs involved. Our purpose is to assess the time course in blood pressure and renal function after delivery among survivors of severe preeclampsia and eclampsia and to investigate associated factors with the time course.

Methods
This was a prospective cohort study that involved 97 women with severe preeclampsia and eclampsia, followed up to 6 weeks after delivery. It was conducted at Mulago National referral hospital from August 2017 to April 2018. Data were recorded at admission, then on day- 1, 7, 21 and day 42 after delivery. Counts, means, median and percentage and cumulative percentage were used to express results. Survival analysis with Kaplan-Meier was used to estimate time to resolution of hypertension, renal dysfunction and proteinuria; and Cox-proportional Regression and Log-Rank test to determine association of participant variables with time-to normalization of blood pressure, renal function and urine protein. Association was considered significant with a P-value ≤0.05.

Results
In this study

- The mean time to resolution of hypertension is 2.49 weeks (CI 2.13-2.82)
- The mean time to resolution of renal dysfunction is 24.54 days (CI 20.14-28.95)
➢ The mean time to resolution of urine protein is 32.85 days (CI 30.31-35.39).

There is an association of time to resolution of hypertension and multiple/single pregnancy with a P-value of 0.013.

There was no statistically significant association of time to resolution of renal dysfunction and proteinuria with participant variables.

**Conclusion**

In this study, most of participants got their Blood pressure and renal function normalized by the end of postpartum period, only fiew had persistent hypertension, renal dysfunction and proteinuria.
OPERATIONAL DEFINITIONS

1. **Postpartum**: Postpartum is defined as a period of 6 weeks following delivery during which maternal anatomical and physiological changes induced by pregnancy return to the non pregnant state[1]

2. **Hypertension**: Hypertension in pregnancy is defined as a systolic blood pressure ≥ 140mmHg and/or a diastolic blood pressure ≥ 90mm Hg on two consecutive readings at least four hours apart and no more than 7 days[2]. Maternal blood pressure ≥160/110; hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy[3].

3. **Trend**: A general direction in which a situation is changing or developing

4. **Preeclampsia**
   - **Blood pressure**: A new onset of hypertension with a systolic ≥ 140mmHg and/or diastolic ≥ 90mmHg on 2 occasions at least 4 hours apart at a gestation age of 20 weeks or more. Hypertension can be confirmed in short interval or few minutes when is ≥160mmHg and/or ≥110mmHg [4].

   - **Proteinuria**: ≥300mg/24h or protein/creatinin ratio ≥ 0.3 or a dipstick reading ≥1+. In the absence of proteinuria, preeclampsia is defined as a new onset of hypertension with association of one or more of severe features of pre-Eclampsia [4]

5. **Severe preeclampsia**: It is one or more of the following: [1, 5]
   - Severe hypertension
     - Systolic ≥160 mmHg and/or
• Diastolic ≥110 mmHg

✓ Neurological involvement: Persistently severe cerebral symptoms such as headache, vision disturbance, etc

✓ Hematologic involvement: Thrombocytopenia: ≤100,000/mm3

✓ Liver involvement: aspartate transaminase or alanine transaminase >2 times the upper limit for the laboratory or severe persistent right upper quadrant/epigastric pain. Aspartate and Alanine transaminase values seldom exceed 500U/L but have been reported to be greater than 2000U/L in some women.

✓ Pulmonary edema

✓ Renal involvement: Serum creatinine: ≥1.1 mg/dl

6. **Eclampsia:** A convolution in a woman with preeclampsia that cannot be attributed to other cause[6]
CHAPTER ONE

INTRODUCTION

1.1 Background

Hypertension in pregnancy is defined as a systolic blood pressure $\geq 140\text{mm Hg}$ and/or a diastolic blood pressure $\geq 90\text{mm Hg}$ on two consecutive readings at least four hours apart and no more than 7 days[2, 7].

Hypertensive disorders complicate 10 percent of all pregnancies around the word[8], 5 to 10 percent in USA and together they are one member of the deadly triad—along with hemorrhage and infection —that contributes greatly to maternal morbidity and mortality[2, 8, 9]

A systematic review of maternal death worldwide was done by WHO and revealed a maternal mortality of 16 percent in developed countries due to hypertensive disorders. This proportion appears greater than three other leading causes that include hemorrhage—13%, abortion—8%, and sepsis—2%[6].

In Africa and Asia, about one tenth of maternal deaths are associated with hypertensive disorders in pregnancy and in Latin America one quarter of maternal deaths have been associated with hypertensive complication in pregnancy [10], [8].

Furthermore, hypertensive disorders in pregnancy lead to preterm delivery, fetal intrauterine growth restriction, low birth weight and perinatal death [11].

The majority of deaths due to hypertensive disorders can be avoided by providing an effective care to women presenting with such complications during pregnancy and an
efficient follow up after delivery[8]. This is why in this study, women with severe preeclampsia and eclampsia were followed up in puerperum period.

1.2 Problem statement

In 2010, about 287,000 maternal deaths occurred worldwide, most of which were in developing countries and were avoidable [12].

In 2013, every day an estimated number of 800 women died due to complications during pregnancy and childbirth, 62.5% of them occurred in sub-Saharan Africa, 23.75% in southern Asia compared to 0.75% in developed countries [13].

An estimated 289,000 maternal deaths occurred worldwide in 2013, the primary causes were hemorrhage, hypertension disorders and infections[13].

WHO did a systematic analysis of global causes of maternal death occurred between 2003 and 2009 and found about 73% of all of them were due to direct obstetric causes and 27% to indirect causes; Hemorrhage accounted for 27.1%, Hypertension disorders 14% and infections 10.7%[12, 14]. Risk factors for the development of preeclampsia are nulliparity, familial history of preeclampsia, multiple gestation, pre-existing diabetes, chronic hypertension, a rapidly growing hydatidiform mole, fetal hydrops, and extremes of maternal age. Women are less likely to develop preeclampsia if they smoke, but the reason is unclear [3].

In Uganda, 5,900 of maternal death were recorded in 2013[15]. Furthermore, hypertensive disorders in pregnancy were a leading cause of maternal and perinatal morbidity and mortality, accounting for up to 16% of maternal deaths after obstetric hemorrhage which accounts for 25%[18]. In Mulago Hospital in Uganda in 2000, it
contributed 17.6% to maternal morbidity and 21.4% to maternal mortality[16].

Approximately one-third of Eclampsia occurs in postpartum period, nearly half beyond 48 hours after childbirth. Half of the women who sustain an intracerebral haemorrhage in association with pre-eclampsia do so following birth [17] and the period following delivery up to one week is more critical due to extravascular fluid re-absorption resulting in rising of blood pressure, risk of pulmonary edema, cerebral vascular accident and congestive cardiac failure [4, 18]

The kidney is one of organs involved in preeclampsia/eclampsia[19]. Unfortunately the nephrological evaluation has received only little attention in follow up studies[20]. According to Pauuw et.al, women with a history of preeclampsia experience a 5 to 12-fold increased risk of end-stage renal disease and a 2-fold increased risk of long term cardiovascular disease [21].

After delivery, hypertension and renal dysfunction are supposed to resolve progressively [22].

The concern is how long they take to resolve. A follow up should be planned after delivery whether or not the patients develop a hypertensive disease before discharge because the critical period appears one week after delivery[4, 18].

Unfortunately no study has been done in Mulago hospital about the time-course of the blood pressure and renal function to return to normal after affected women deliveries. It is not known how long the blood pressure and the renal dysfunctional take to resolve after delivery of women with severe preeclampsia and eclampsia.
1.3 Justification of study

Preeclampsia syndrome resolves with delivery of the placenta with normalization of blood pressure and renal function[3, 22]. However, the period following delivery up to one week is more critical due to extravascular fluid re-absorption resulting in rising of blood pressure, risk of pulmonary edema, cerebral vascular accident and congestive cardiac failure [4, 18]

Approximately one-third of Eclampsia occurs in postpartum period, nearly half beyond 48 hours after childbirth. Half of the women who sustain an intracerebral haemorrhage in association with pre-eclampsia do so following birth [17]

And epidemiological studies reveal long-term risks associated with a history of gestational hypertensive disorders: it is not surprising that the long-term complications include a predisposition to chronic hypertension, cardiovascular complications, and renal complications[3].

Persisting hypertension has been reported (34%) among the mothers delivering at Mulago hospital with Preeclampsia/Eclampsia beyond twelve weeks [10]. A similar study was done at the same setting and found a persisting hypertension of 27.7% at 6 weeks postpartum and renal dysfunction was associated with a persisting hypertension [23].

However, these studies can’t tell how hypertension regresses along the postpartum period and about trends in renal function and proteinuria. This study attempts to provide an answer to the question of the the time to normalization of blood pressure and renal function over the postpartum period of women with severe preeclampsia and
eclampsia.

It is important to conduct this study so that we find out the length-time of hypertension and renal dysfunction after delivery, that we can plan for a special follow-up care of affected mothers, and reduce morbidity and mortality preeclampsia-related that can occur either in postnatal wards or long time later in medical wards.

1.4 Importance of the study

In view of results of this study, recommendations about a special follow up care are suggested:

- A follow up protocol of patients of severe preeclampsia and eclampsia in Mulago should be worked on in view of results of this study.

- Involvement of a multidisciplinary team including a physician, an obstetrician and a specialized midwife in preeclampsia is needed in follow up of these mothers with preeclampsia/Eclampsia.

1.5 Research questions

- What is the time to resolution of hypertension of women with severe preeclampsia and Eclampsia over the postpartum period?

- What factors are associated with time to normalization of blood pressure after delivery of these women?

- What is the the time to resolution of renal dysfunction after delivery of mothers with severe preeclampsia and Eclampsia?
• What factors are associated with time to normalization of renal function of these women?
• What is the time to resolution of urine protein among survivors of severe eclampsia and eclampsia after delivery?
• What factors are associated with time to resolution of urine protein after delivery of these women.

1.6 Objectives of the study
1.6.1 General objective
To determine among survivors of severe preeclampsia and eclampsia how long blood pressure and renal function take to return to normal and the factors associated with their normalization.

1.6.2 Specific objectives
• To determine the time to resolution of hypertension of survivors of severe preeclampsia and eclampsia over the postpartum period.
• To determine factors associated with time to resolution of hypertension of women delivering with severe preeclampsia and eclampsia.
• To determine the time to resolution of renal dysfunction of women with severe preeclampsia and eclampsia over the postpartum period.
• To determine the factors associated with time to resolution of renal dysfunction of women with severe preeclampsia and eclampsia over the postpartum period.
• To determine the time to resolution of urine protein over the postpartum period of women delivering with severe preeclampsia and eclampsia.

• To determine factors associated with resolution of urine protein among women delivering with severe preeclampsia and Eclampsia

1.7 Conceptual Framework
CHAPTER TWO

LITERATURE REVIEW

2.1 Definition and classification of hypertension disorders

Hypertension in pregnancy is defined as a systolic blood pressure \( \geq 140 \text{mmHg} \) and/or a diastolic blood pressure \( \geq 90 \text{mm Hg} \) on two consecutive readings at least four hours apart and no more than 7 days[2].

The classification promulgated by the Working group of National High blood pressure Education program (2000) was maintained by the American College of Obstetricians and Gynecologists (2013) and described 4 types of hypertension disorders in pregnancy[6].

The Four categories are:

a. **Gestational hypertension**

The blood pressure elevation occurs after 20 weeks of gestation in absence of proteinuria or any of severe features of preeclampsia listed below and the blood pressure returns to normal by 12 weeks postpartum. Most of these women develop preeclampsia syndrome including findings like headaches, epigastric pain, proteinuria, and thrombocytopenia [6].

b. **Preeclampsia and eclampsia syndrome**

  ➢  **Preeclampsia**

  - **Blood pressure**: A new onset of hypertension with a systolic \( \geq 140\text{mmHg} \)
and/or diastolic ≥ 90mmHg on 2 occasions at least 4 hours apart at a gestation age of 20 weeks or more. Hypertension can be confirmed in short interval or few minutes when is ≥160mmHg and/or ≥110mmHg[19].

- **Proteinuria**: ≥300mg/24h or protein/creatinin ratio ≥ 0.3 or a dipstick reading ≥1+

  In the absence of proteinuria, preeclampsia is defined as a new onset of hypertension with association of one or more of severe features of preeclampsia[19]

  ➢ **Severe features of preeclampsia** [1], [19],

  One or more of the following permits to make a diagnosis of severe preeclampsia [1]

  ✓ Severe hypertension

  • Systolic ≥160 mmHg and/or

  • Diastolic ≥110 mmHg

  ✓ Neurological involvement: Persistently severe cerebral symptoms such as headache, vision disturbance, etc

  ✓ Hematologic involvement: Thrombocytopenia: ≤100,000/microlitre.

  ✓ Liver involvement: aspartate transaminase or alanine transaminase >2 times the upper limit for the laboratory with severe persistent right upper quadrant or epigastric pain unresponsive to medication in the absence of
other diseases. Serum hepatic transaminase values exceed 500 U/L, and have been reported to be greater than 2000U/L in some women.

✓ Pulmonary edema

✓ Renal involvement: Progressive renal insufficiency with serum creatinine \( \geq 1.1 \text{ mg/dL} \) or with a doubling of the serum creatinine in the absence of other renal disease.

✓ Heavy proteinuria and fetal growth restriction are no longer criteria of severe preeclampsia [5, 24]

➢ Eclampsia

A convulsion in a woman with preeclampsia that cannot be attributed to other causes is termed eclampsia [4]. A wide range of signs and symptoms ranging from severe to minimal hypertension, massive to no proteinuria, and to prominent to no edema precede Eclampsia [5]. The seizures are generalized and may appear before, during, or after labour [4]. Clinical symptoms such as persistent occipital or frontal headaches, blurred vision, photophobia, epigastic pain or upper quadrant pain, altered mental status, etc predict impending eclampsia [5]

c. Chronic hypertension

During pregnancy, chronic hypertension is defined as a systolic blood pressure \( \geq 140\text{mmHg} \) and/or a diastolic blood pressure \( \geq 90\text{mmHg} \) preceding conception or
diagnosed before 20 weeks of gestation. This category includes essential hypertension as well as hypertension secondary to a range of conditions. [5]

d. **Preeclampsia superimposed on chronic hypertension**

Superimposed preeclampsia is diagnosed when a woman with chronic hypertension develops one or more of the systemic features of preeclampsia after 20 weeks gestation[5]

1. **Renal changes in preeclampsia**

The placenta is the central organ in the pathogenesis of preeclampsia. Soluble factors are released from an ischemic placenta into maternal circulation resulting in endothelial dysfunctional. The cause of preeclampsia is not known but thought to be due to excess levels of soluble factors like tyrosine kinase 1 (sFlt 1) than normal seen in pregnancy [19]. The ischemic placenta makes sFlt 1 in large amounts, but circulating mononuclear cells are an extra source of sFlt 1. sFlt 1 decreases or inhibits the binding of vascular endothelial growth factor (VEGF) involved in glomerular function and glomerular capillary repair[22]. Its inhibition leads to glomerular capillaries lesions: prominent endothelial swelling, as well as the characteristic features of thrombotic microangiopathy in the glomerular capillary[22]. The proteinuria seen in women with preeclampsia is due to podocyte injury, and the reduced renal perfusion and glomerular filtration is secondary to endothelial dysfunction[19]

2. **Postpartum considerations**

After delivery, hypertension and renal dysfunction are supposed to resolve
progressively[22]. Hypertension related to pregnancy should resolve within 12 weeks postpartum, its persistence beyond this period is considered to be chronic hypertension[6].

Gestational hypertension usually resolves by 6 weeks after delivery while the hypertension of severe preeclampsia may take 12 to 24 weeks postpartum[19].

After delivery, appreciable amount of interstitial fluids are mobilized for excretion as endothelial damage is repaired. This fluid mobilization can result in cerebral or pulmonary edema, heart failure, renal dysfunction, or cerebral hemorrhage, especially within the first 48 hours [6]

Today, renal failure is most often associated with severe preeclampsia. In most women, renal failure develops postpartum, thus management is not complicated by fetal consideration. An acute serum creatinine is usually due to renal ischemia and oliguria is an important sign of an acute renal dysfunction. With time, renal function usually returns to normal or near normal [6].

CHAPTER THREE

METHODOLOGY

3.0 Study materials and methods

3.1 Study design
This was a prospective cohort study that was conducted in Mulago hospital.

3.2 Setting
This study was conducted in Mulago National referral hospital of Uganda which also doubles as the teaching hospital for Makerere University. It is located in Kampala city,
serving patients from Kampala District and the surrounding districts of Wakiso, Mukono and Mpigi and occasionally from other Uganda’s districts and outside of the country. There is a lack of obstetricians and neonatal special care unit in other public hospitals and these surrounding districts are within a radius of 10 to 20 km from Mulago Hospital, thus many mothers are referred including those with pre-eclampsia and eclampsia.

In addition to the referred women, local women routinely deliver in Mulago Hospital and there are 80-90 deliveries per day and more than 30,000 deliveries per year.

Among services delivered in Mulago, there is a postnatal clinic, labor suit and laboratory which were key as this study is conducted.

For serum cretinine, MBN clinical laboratory was chosed as an extension of this study. It is a private laboratory located in Kampala capital city, at Nakasero road. It has 5 branches over the country. It has been used as a study setting for other many researches.

3.3 Study population

The study targeted women with hypertensive disorders in pregnancy delivering at Mulago National referral hospital during the period of this study.

3.3.1 Eligibility criteria

3.3.1.1 Inclusion criteria

All women delivering within Mulago with:

- Severe preeclampsia based on blood pressure
- Eclampsia
3.3.1.2 Exclusion criteria

- Women with a known history of hypertension, diabetes mellitus and kidney disease were excluded to minimize confounding.
- Women who resided more than 20 km from Mulago hospital to minimize loss to follow up.
- Women who died or lost the follow up.

3.4 Sample size

To determine the sample size, Fleiss formula for cohort unmatched cases was used.

Kaze et.al did a similar study titled postpartum recovery in blood pressure levels, renal function and proteinuria in women with severe preeclampsia and eclampsia in subsaharan Africa, with a sample size of 54 participants, and found 42.6% did not resolve at 6 weeks after delivery. An other study done in Mulago found a high parity to be the biggest risk factor of preeclampsia with an odd ratio of 3.71[16, 20]. An online calculator of a cohort study sample size was used

used http://www.openepi.com/SampleSize/SSCohort.htm

Sample Size: X-Sectional, Cohort, & Randomized Clinical Trials

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<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-sided significance level(1-alpha)</td>
<td>95</td>
</tr>
<tr>
<td>Power(1-beta, % chance of detecting)</td>
<td>80</td>
</tr>
<tr>
<td>Ratio of sample size, Unexposed/Exposed:</td>
<td>1</td>
</tr>
<tr>
<td>Percent of Exposed with Outcome:</td>
<td>42.6</td>
</tr>
<tr>
<td>Odds Ratio:</td>
<td>3.71</td>
</tr>
<tr>
<td>Risk/Prevalence Ratio:</td>
<td>2.9</td>
</tr>
<tr>
<td>Risk/Prevalence difference:</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Kelsey</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Sample Size – Exposed</td>
<td>41</td>
</tr>
<tr>
<td>Sample Size-Nonexposed</td>
<td>41</td>
</tr>
<tr>
<td><strong>Total sample size:</strong></td>
<td><strong>82</strong></td>
</tr>
</tbody>
</table>

We took the sample size of \( n = 92 \) but we recruited 97 participants.

### 3.6 Sampling method and sampling procedure

A consecutive sampling technique was used in order to reach the sample size. Every subject meeting the criteria of inclusion and consenting to participate was selected till the required sample size was achieved.

### 3.7 Data collection methods

Researcher assistants: two midwives and one lab technician were involved in this study. Midwives and the principal investigator were identifying, counseling, and recruiting participants in the labour ward before.

Mothers who met the inclusion criteria underwent the routine management and their files were marked with a sign known to the principal investigator and the research assistants for identification. Mothers were counseled, allowed to consent for the study and were recruited soon after delivery was completed. For those mothers under 18 year-old consented as emancipated minors.

Data were collected through interviews using an interviewer-administered questionnaire. Other data were collected by participants' examination, biochemical investigations and review of participants' medical records. These data included social-demographic
factors (age, parity, new sexual partner, etc); obstetric factors (such as gestational age at delivery, history of diabetes mellitus, of hypertension or pre-eclampsia and severity of pre-eclampsia etc). Biochemical data included serum creatinine levels and urine protein. Estimated glomerular filtration rate was calculated using a software package. Blood pressure was measured using a digital blood pressure machine in a sitting position and urine protein was determined by dipstick examination. The guidelines below was followed.

1. **Recording blood pressure**

   - The woman should be seated comfortably with her legs resting on a flat surface and her arm resting at the level of her heart. Supine posture was avoided because of supine hypotension syndrome. Blood pressure was taken at admission, the day of delivery, day one, 7, 21, and on day 42 after delivery. The blood pressure at admission was considered as a baseline for this study.

2. **Recording of urine protein**

   A 24 hours urine collection is the gold standard tool for assessing total urinary excretion of protein. However a spot urine of participants followed up at postnatal clinic after delivery was used. A dipstick was used and Interpreted as following [25]:

   + = 30mg/dl
+++ = 100mg/dl

+++ = 300mg/dl

++++ > 2g/dl

3. Recording of serum creatinine:

A blood sample was taken off by midwives and sent as soon as possible to the laboratory. A software package was useful to calculate estimated glomerular filtration rate using current serum creatinine, patient race, gender and age. An online calculator was used for determining the estimated glomerular filtration rate https://patient.info/doctor/estimated-gglomerular-filtration-rate-gfr-calculator.

This calculator uses the abbreviated MDRD equation (MDRD = Modification of Diet in Renal Disease Study), which is the one recommended by NICE and The Renal Association of the United Kingdom.
Table 1: Stages of Chronic Kidney Disease [https://patient.info/doctor/estimated-glomerular-filtration-rate-gfr-calculator]

<table>
<thead>
<tr>
<th>Stage</th>
<th>Glomerular Filtration Rate</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>90+</td>
<td>Normal renal function</td>
</tr>
<tr>
<td>II</td>
<td>60-89</td>
<td>Mildly reduced renal function</td>
</tr>
<tr>
<td>IIIa</td>
<td>45-59</td>
<td>Moderate decrease in renal function, with or without other evidence of kidney damage.</td>
</tr>
<tr>
<td>IIIb</td>
<td>30-44</td>
<td>Moderate decrease in renal function, with or without other evidence of kidney damage.</td>
</tr>
<tr>
<td>IV</td>
<td>15-29</td>
<td>Severely reduced renal function.</td>
</tr>
<tr>
<td>V</td>
<td>&lt;15</td>
<td>Very severe (end-stage) kidney disease.</td>
</tr>
</tbody>
</table>

4. New partner or short duration sperm exposure

Couples with short period less than 6 months of sexual cohabitation shall be considered as new partner [26].

5. Interpregnancy interval

Interpregnancy interval is calculated as the time between the last childbirth and the last normal menstrual period of the current pregnancy[27] or if prior pregnancy ended by abortion, the date of abortion is considered.

Follow up

- Laboratory parameters: urine protein and serum creatinine were recorded on day- 1, day 7, day 21 and day 42 following delivery

- Some patients were observed in the hospital up to day 7 or more because of
their critical conditions and/or their premature babies admitted in special care unit.

- Phone number of participants and their next of kin were taken and their residence addresses.
- We considered visiting those who failed to follow up.
- Mothers who were found with high blood pressure were treated according to Mulago’s protocol of hypertension in pregnancy.
- A urine dipstick test was performed on a random urine sample to evaluate the presence of proteinuria at each visit.
- The blood pressure was measured at every visit and considered normal when it was less than 140/90 mmHg without any antihypertensive medications for at least one week.
- A serum creatinine levels and estimated glomerular filtration were measured at every visit and were considered normal when the estimated glomerular filtration was $\geq 90 \text{ mL/min/1.73 m}^2$.

3.8 Quality control

Researcher assistants were trained by the principal investigator about severe preeclampsia and eclampsia, the purpose of the research, ethical considerations, objectives and procedures of the study.

The principal investigator reviewed questionnaires from time to time to ensure consistency and completeness. Data were double entered to minimize errors.
3.9 Data analysis

The questionnaires were coded and the data entered using the epi-data Version 3.1. Each record was assigned a unique identifier to maintain patient confidentiality. Verification of data was done using the double entry procedure.

Counts, means, median, percentage and cumulative percentage were used to express results. Data were analyzed with SPSS. Survival analysis with Kaplan-Meier was used to estimate time to normalization of blood pressure, renal function and urine protein. Cox-proportional regression and Log rank test were used to determine association of participant variables with time-to resolution of hypertension, renal dysfunction and urine protein. Factors were considered statistically significant if they had a P-value of less or equal to 0.05

3.10 Ethical consideration

Approval to carry out this research was sought from:

- The Directorate of Obstetrics and Gynaecology, Mulagohospital,
- Makerere University, School of Medicine Research and Ethics committee (SOMREC)
- National Council for Science and Technology.

Patients were informed that their participation is voluntary and that they reserve the right to withdraw from the study anytime they feel like.

For confidentiality purposes, the questionnaires were coded.

Participants were informed that there was no monetary benefits and that
they were free to refuse to participate in the study. However they were counseled about their disease and the advantages of follow up.

Those with abnormal blood pressure and renal function were getting treatment.

3.11 Dissemination of study findings

Findings of the study will be disseminated to the following places;

School of Graduates studies Makerere University.

School of Medicine Research and Ethics Committee.

Department of obstetrics/Gynaecology Mulago hospital

Albert Cook Library Makerere University.

Results will be published in peer-review journals.

CHAPTER FOUR
RESULTS

The study enrolled 97 women with severe preeclampsia or Eclampsia who delivered at Mulago National Referral Hospital from August 2017 to March 2018 and were followed up and were involved in determination of time to resolution of hypertension and its associated factors.

Among 97 participants 20 were censored: 2 of them died, 12 lost their follow-up from the third visit, and 6 did not achieve the event (= resolution) at the end of this study.

Then, initially 47 participants had abnormal renal functions using estimated gorderular filtration rate and were involved in determination of time to resolution of renal
dysfunction and its associated factors: 10 were censored because of 9 did not achieve the event (= resolution) at the end of the study and 1 participant lost her follow up.

Finally, among 97 participants, 92 had initially proteinuria and were involved in determination of time to resolution of proteinuria and associated factors: 29 were censored because 15 did not achieve the event (= resolution) at the end of this study and 14 lost their follow up before.

The mean age of the participants was 26.6±5.4 year-old, mean gestation age of 35.9±4.0 weeks and a modal parity of 2 with a range of 1-6.
Diagram 1: Flow chat of participants

Total number recruited
N = 97 with PET/Eclampsia

- 77 achieved the event
- 20 were censored
  - Died = 02
  - Persistent: 6
  - Lost follow up: 12

47 had renal dysfunction

- 37 achieved the event
- 10 were censored
  - Lost follow up: 1
  - Persistent: 9

92 had urine protein

- 29 were censored
- 63 achieved the event
  - Lost follow up: 14
  - Persistent: 15

Table 2: Time to resolution of Hypertension
The mean time to resolution of hypertension is 2.49 weeks (CI: 2.13-2.84)
Graph 1: Kaplan-Meier curve of time to resolution of hypertension

Cumulative Survival

Time to normalisation of blood pressure (Weeks)

- Survival Function
- Censored
Table 3: Log rank test: Time to resolution of hypertension and single versus multiple pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Means and Medians for Survival Time</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>Std. Error</td>
</tr>
<tr>
<td>single</td>
<td>2.355</td>
<td>.180</td>
</tr>
<tr>
<td>multiple</td>
<td>4.000</td>
<td>.707</td>
</tr>
<tr>
<td>Overall</td>
<td>2.487</td>
<td>.181</td>
</tr>
</tbody>
</table>

**Overall Comparisons**

<table>
<thead>
<tr>
<th></th>
<th>Chi-Square</th>
<th>df</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>6.151</td>
<td>1</td>
<td>.012</td>
</tr>
</tbody>
</table>

There is a statistically significant association of time to resolution of Hypertension with multiple pregnancy versus singleton pregnancy ($p=0.013$).
Graph 2: Kaplan-Meier curve, time to resolution of hypertension and single versus multiple pregnancy

There is a statistically significant association of time to resolution of Hypertension with multiple pregnancy versus singleton pregnancy (p=0.013)
Table 4: Log rank test of time to resolution of hypertension and vaginal delivery versus cesarean delivery

Means and Medians for Survival Time

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>Means</th>
<th>95% Confidence Interval</th>
<th>Median</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std. Error</td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>svd</td>
<td>2.463</td>
<td>0.260</td>
<td>1.954</td>
<td>2.972</td>
</tr>
<tr>
<td>emcs</td>
<td>2.524</td>
<td>0.244</td>
<td>2.046</td>
<td>3.003</td>
</tr>
<tr>
<td>Overall</td>
<td>2.487</td>
<td>0.181</td>
<td>2.132</td>
<td>2.842</td>
</tr>
</tbody>
</table>

Overall Comparisons

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>0.10</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of hypertension and mode of delivery  
P=0.891
Graph 3: Kaplan-Meier curve of mode of delivery and time to resolution of hypertension and mode of delivery

There is no statistically significant association of time to resolution of hypertension and mode of delivery P=0.891
Table 5: Log rank test of time to resolution of hypertension and onset of preeclampsia

<table>
<thead>
<tr>
<th>RECODE of gestation (gestational age at delivery)</th>
<th>Mean(^\text{a})</th>
<th>95% Confidence Interval</th>
<th>Median</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early onset</td>
<td>2.400</td>
<td>.476</td>
<td>1.467</td>
<td>3.333</td>
</tr>
<tr>
<td>Late onset</td>
<td>2.513</td>
<td>.196</td>
<td>2.128</td>
<td>2.898</td>
</tr>
<tr>
<td>Overall</td>
<td>2.483</td>
<td>.183</td>
<td>2.123</td>
<td>2.842</td>
</tr>
</tbody>
</table>

Overall Comparisons

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>634</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of hypertension with the onset of preeclampsia (P value=0.426)
Graph 4: Kaplan-Meier curve of time to resolution of hypertension and the onset of preeclampsia

There is no statistically significant association of time to resolution of hypertension with the onset of preeclampsia (P value=0.426)
Table 6: Log Rank test of Time to resolution of Hypertension and parity

<table>
<thead>
<tr>
<th>RECODE of parity (parity)</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>primiparity</td>
<td>2.201</td>
<td>.229</td>
<td>1.751</td>
<td>2.650</td>
<td>2.000</td>
<td>.197</td>
<td>1.614</td>
<td>2.366</td>
</tr>
<tr>
<td>multiparity</td>
<td>2.700</td>
<td>.272</td>
<td>2.167</td>
<td>3.233</td>
<td>2.000</td>
<td>.219</td>
<td>1.571</td>
<td>2.429</td>
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<tr>
<td>Overall</td>
<td>2.456</td>
<td>.181</td>
<td>2.102</td>
<td>2.810</td>
<td>2.000</td>
<td>.148</td>
<td>1.710</td>
<td>2.290</td>
</tr>
</tbody>
</table>

Overall Comparisons

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>LogRank (Mantel-Cox)</td>
<td>2.139</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of Hypertension with parity (P=0.139)
There is no statistically significant association of time to resolution of Hypertension with parity (P=0.139)
Table 7: Time to resolution of renal dysfunction

Means and Medians for time to resolution of renal dysfunction

<table>
<thead>
<tr>
<th>Estimate</th>
<th>Mean</th>
<th>95% Confidence Interval</th>
<th>Estimate</th>
<th>Median</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
<td></td>
<td>Lower Bound</td>
</tr>
</tbody>
</table>

The mean time to resolution of renal dysfunction is 24.54 days (CI 20.14-28.95)
Graph 6: Kaplan-Meier curve of time to resolution of renal dysfunction

Table 8: Log Rank test: Time to resolution of renal dysfunction and single pregnancy versus multiple pregnancy
### Means and Medians for Survival Time

<table>
<thead>
<tr>
<th>pregnancy</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval</th>
<th>Median</th>
<th>Std. Error</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
</table>

### Overall Comparisons

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>2.102</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no significant association of time to resolution of renal dysfunction with order of pregnancy (single or multiple)  \( P = 0.147 \)
Graph 7: Kaplan-Meier curve of time to resolution of renal dysfunction and single pregnancy versus multiple pregnancy

There is no significant association of time to resolution of renal dysfunction and order of pregnancy (single or multiple) \( P=0.147 \)
Table 9: Log Rank test of time to resolution of renal dysfunction and mode of delivery

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Mean 95% Confidence Interval</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Median 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>svd</td>
<td>22.302</td>
<td>2.809</td>
<td>16.797</td>
<td>27.807</td>
<td>3.078</td>
<td>11.046</td>
</tr>
<tr>
<td>Overall</td>
<td>24.545</td>
<td>2.248</td>
<td>20.139</td>
<td>28.950</td>
<td>3.827</td>
<td>13.500</td>
</tr>
</tbody>
</table>

**Overall Comparisons**

<table>
<thead>
<tr>
<th>Test</th>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>1.291</td>
<td>1</td>
<td>0.256</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of renal dysfunction with the mode of delivery ($P=0.256$)
Graph 8: Kaplan-Meier curve of time to resolution of renal dysfunction and mode of delivery

There is no statistically significant association of time to resolution with the mode of delivery (P=0.256)
Table 10: Log Rank test of time to resolution of renal dysfunction and onset of preeclampsia

<table>
<thead>
<tr>
<th>RECODE of gestage (gestational age at delivery)</th>
<th>Mean Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval Lower Bound</th>
<th>95% Confidence Interval Upper Bound</th>
<th>Median Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval Lower Bound</th>
<th>95% Confidence Interval Upper Bound</th>
</tr>
</thead>
</table>

**Overall Comparisons**

<table>
<thead>
<tr>
<th>Test</th>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>1.799</td>
<td>1</td>
<td>.180</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of renal dysfunction with the onset of preeclampsia (P=0.180)
Graph 9: Kaplan-Meier curve of time to resolution of renal dysfunction and onset of preeclampsia

There is no statistically significant association of time to resolution of renal dysfunction with the onset of preeclampsia (P=0.180)
Table 11: Log Rank test of time to resolution of renal dysfunction and parity

<table>
<thead>
<tr>
<th>RECODE of parity (parity)</th>
<th>Mean</th>
<th>95% Confidence Interval</th>
<th>Median</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>Std. Error</td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>primiparity</td>
<td>23.100</td>
<td>3.725</td>
<td>15.799</td>
<td>30.401</td>
</tr>
<tr>
<td>Overall</td>
<td>24.631</td>
<td>2.296</td>
<td>20.130</td>
<td>29.132</td>
</tr>
</tbody>
</table>

**Overall Comparisons**

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>LogRank (Mantel-Cox)</td>
<td>.139</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of renal dysfunction with parity (P=0.709)
Graph 10: Kaplan-Meier curve of time to resolution of renal dysfunction and parity

There is no statistically significant association of time to resolution of renal dysfunction with parity (P=0.709)
Table 12: Time to resolution of urine protein

<table>
<thead>
<tr>
<th>Mean</th>
<th>95% Confidence Interval</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimate</td>
<td>Std. Error</td>
<td>Lower Bound</td>
</tr>
<tr>
<td>32.852</td>
<td>1.296</td>
<td>30.312</td>
</tr>
</tbody>
</table>

Mean time to resolution of urine protein is 32.85 days (CI 30.31-35.39)
Graph 11: Kaplan-Meier curve of time to resolution of urine protein

Cumulative Survival

Time to resolution of proteinuria (Days)
Table 13: Log Rank test of Time to resolution of urine protein and single pregnancy versus multiple pregnancy

<table>
<thead>
<tr>
<th>single or multiple pregnancy</th>
<th>Mean Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval Lower Bound</th>
<th>Upper Bound</th>
<th>Median Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>32.346</td>
<td>1.371</td>
<td>29.658</td>
<td>35.033</td>
<td>42.000</td>
<td>2.363</td>
<td>37.369</td>
<td>46.631</td>
</tr>
<tr>
<td>Multiple</td>
<td>38.500</td>
<td>3.913</td>
<td>30.830</td>
<td>46.170</td>
<td>42.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Overall</td>
<td>32.836</td>
<td>1.299</td>
<td>30.290</td>
<td>35.381</td>
<td>42.000</td>
<td>2.415</td>
<td>37.268</td>
<td>46.732</td>
</tr>
</tbody>
</table>

**Overall Comparisons**

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>3.168</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of urine protein with order of pregnancy (single versus multiple) P=0.075
There is no statistically significant association of time to resolution of urine protein with order of pregnancy (single versus multiple) \( P=0.075 \)
Table 14: Log Rank test of time to resolution of urine protein and mode of delivery

Means and Medians for Survival Time

<table>
<thead>
<tr>
<th>mode of delivery</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Mean 95% Confidence Interval</th>
<th>Median 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>svd</td>
<td>31.040</td>
<td>1.710</td>
<td>27.689</td>
<td>34.391</td>
</tr>
<tr>
<td>emcs</td>
<td>35.473</td>
<td>1.938</td>
<td>31.675</td>
<td>39.271</td>
</tr>
<tr>
<td>Overall</td>
<td>32.836</td>
<td>1.299</td>
<td>30.290</td>
<td>35.381</td>
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</tbody>
</table>

Overall Comparisons

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>1.234</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of proteinuria with mode of delivery

P=0.267
Graph 13: Kaplan-Meier curve of time to resolution of urine protein and mode of delivery

There is no statistically significant association of time to resolution of proteinuria with mode of delivery $P=0.267$
Table 15: Log Rank test of time to resolution of urine protein and onset of preeclampsia

<table>
<thead>
<tr>
<th>RECODE of gestage (gestational age at delivery)</th>
<th>Estimate</th>
<th>SD. Error</th>
<th>Mean 95% Confidence Interval</th>
<th>Median 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>early onset</td>
<td>32.882</td>
<td>3.123</td>
<td>26.760, 39.004</td>
<td>27.943, 56.057</td>
</tr>
<tr>
<td>late onset</td>
<td>32.561</td>
<td>1.458</td>
<td>29.822, 35.359</td>
<td>36.879, 47.121</td>
</tr>
<tr>
<td>Overall</td>
<td>32.720</td>
<td>1.310</td>
<td>30.152, 35.287</td>
<td>37.118, 46.882</td>
</tr>
</tbody>
</table>

**Overall Comparisons**

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>.194</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of urine protein with onset of preeclampsia (P=0.660)
Graph 14: Kaplan-Meier curve of time to resolution of urine protein and onset of preeclampsia

There is no statistically significant association of time to resolution of urine protein with onset of preeclampsia (P=0.660)
Table 16: Log-Rank test of time to resolution of urine protein and parity

<table>
<thead>
<tr>
<th>RECODE of parity (parity)</th>
<th>Mean Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval Lower Bound</th>
<th>95% Confidence Interval Upper Bound</th>
<th>Median Estimate</th>
<th>Std. Error</th>
<th>95% Confidence Interval Lower Bound</th>
<th>95% Confidence Interval Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>primiparity</td>
<td>31.762</td>
<td>1.806</td>
<td>28.222</td>
<td>35.302</td>
<td>42.000</td>
<td>2.278</td>
<td>37.535</td>
<td>46.465</td>
</tr>
<tr>
<td>Multiparity</td>
<td>34.218</td>
<td>1.873</td>
<td>30.546</td>
<td>37.890</td>
<td>42.000</td>
<td>3.684</td>
<td>34.779</td>
<td>49.221</td>
</tr>
<tr>
<td>Overall</td>
<td>32.992</td>
<td>1.306</td>
<td>30.433</td>
<td>35.551</td>
<td>42.000</td>
<td>2.410</td>
<td>37.276</td>
<td>46.724</td>
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**Overall Comparisons**

<table>
<thead>
<tr>
<th>Chi-Square</th>
<th>df</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank (Mantel-Cox)</td>
<td>2.229</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no statistically significant association of time to resolution of urine protein and parity (P=0.135)
Graph 15: Kaplan-Meier curve of time to resolution of urine protein and parity

There is no statistically significant association of time to resolution of urine protein with parity ($P=0.135$)
CHAPTER FIVE

DISCUSSION

Time to resolution of hypertension after delivery of mothers with severe preeclampsia and Eclampsia

In this study, 97 participants were involved in the analysis of the time to resolution of hypertension among mothers with severe preeclampsia and Eclampsia. Survival analysis model was used: Kaplan-Meier test to determine the course-time of Blood pressure normalization over the postpartum period. Among 97 participants, 20 were censored: 14 after their second visit because of 2 that died and 12 that lost their follow up and 6 had persistent hypertension at 6 weeks postpartum. This study did not ignore the 20 censored participants in data analysis because they provided some information before to get lost and others did not achieve the event at 6 weeks of follow up: all had to be involved in survival analysis [28].

After delivery, hypertension and renal dysfunction are supposed to resolve progressively [22].

In this study, the mean Time to resolution of hypertension was 2.49 weeks (CI 2.13-2.82) after delivery. This result agrees with other published study findings. For Wei et al in their research entitled “Clinical study on the factors affecting the postpartum recovery of patients with hypertensive pregnancy disorders at a Chinese hospital”, the mean interval for Blood pressure normalization was $24.1 \pm 22.8$ days with a median of 7 days [29].
Yattinamani et al in their study “Post partum Recovery trends in women with hypertension disorders of pregnancy” quoted that women with hypertension in pregnancy show varying trends of Blood pressure normalization, nearly three fourth of women had normalized Blood pressure by 6 weeks [30].

In their study entitled “Postpartum recovery course in patients with gestational hypertension and preeclampsia”, Mikami et al found a mean interval for normalization of Blood pressure of 41.8 ± 29.4 days [31].

Ferrazzani et al, in their study entitled “The duration of hypertension in the puerperium of preeclamptic mothers”, explained the time to normalization of blood pressure as the recovery time of the endothelial damage in preeclampsia [30].

In this study, the mean gestational age was 35.9±4.0 weeks which is a near term pregnancy. This could explain the early mean time to resolution of Hypertension within the second to the third week after delivery. Many studies have shown an association of a late onset of preeclampsia with early recovery of hypertension [30, 31].

Another aspect is that all participants in this study found with severe preeclampsia or Eclampsia were put on antihypertensive treatment. They continued their treatment after delivery though the moment to stop it was not communicated to them: Cairns et al in their Random Controlled trial review titled “postpartum management of hypertensive disorders of pregnancy” did not found any literature suggesting what Blood pressure thresholds should be used for antihypertensive treatment adjustment and cessation in postpartum [17]. Yattinamani et al found in their study that the normalization of blood pressure was also influenced by antihypertensive medicines [30].
**Association of time to reversion of hypertension with patient variables.**

To determine association of time to reversion of hypertension with patient variable, the Log-Rank test was used.

In this study, there was a statistically significant association of time to resolution of hypertension with Single pregnancy versus multiple pregnancy, the mean time being 2.36 weeks versus 4 weeks respectively with a P value of 0.013. For this study, reversion of hypertension in singleton pregnancy was faster than in multiple pregnancy. This finding disagrees with Mikami et al study: normalization of Blood pressure being significantly longer in singleton pregnancy (43.5±31.4 days) than in multiple pregnancy (35.3±18.6 days) [31].

Gestation hypertensions disorders are more likely to develop in case of exposure to a superabundance of chorionic villi as with twins [6].

The superabundant chorionic villi in multiple pregnancies secrete an enlarged amount of factors like Tyrosine-kinase 1 and Endoglogin that inhibit the vascular endothelial growth factor involved in endothelial function and repair. This may be the explanation of occurrence of preeclampsia in multiple pregnancy and longer time to reversion of Blood pressure [6, 19]

In this study, there was no statistically significant association of other factors with time to resolution of Hypertension after delivery of mothers with severe preeclampsia and
Eclampsia.

**Time to reversion of renal dysfunction**

Estimated glomerular filtration rate was used to evaluate the renal function. It was estimated using an online calculator, and it was considered abnormal if an estimated glomerular filtration rate was less than 90 mL/min/1.72m². Among participants, 47 had initially abnormal gomerular filtration rate and were involved in data analysis of time to recovery of renal dysfunction after delivery of preeclamptic/eclamptic women. Their blood sample for serum ceatinine was taken off on day 1, 7, 21, and 42 after delivery. The renal function was determined by an estimated glomerular filtration rate calculated using serum ceatinine, age, sex and race of the participant. Initially, among 47 participant, 24(52.4%) were in sage 2, 18(39.1%) in stage 3 and 4(8.7%) in stage 4 of chronic kidney disease. At 6 weeks postpartum, the end of this study, among 47 participants, 38(80.4%) resolved and 9(19.6%) had persistent renal dysfunction at 6 weeks: 6 in stage 2 and 3 in stage 3.

**The mean time**

In this study, the mean time to resolution of renal dysfunction was 24.54days [CI 20.14-28.95] and No factors was statistically significant associated with time to resolution of renal dysfunction.

In a study conducted by Hladunewich et al. cited by Hertig et al., the glomerular ultrafiltration coefficient remained reduced 4 weeks after delivery in preeclamptic women, suggesting that endothelial injury had not completely healed at this time [22].
For other studies, findings are conflicting. For Francois Kaze et al., about a quarter of their participants (24.1%) had acute kidney injury at delivery which all resolved within 6 weeks and for Prakash et al. in their study in India found a persistent renal failure of 35.3%. [20].

Glomerular endotheliosis occurring in preeclampsia/Eclampsia decreases glomerular filtration rate and renal flow resulting in an elevated serum creatinine and predisposing the patients to renal failure [6].

**Time to reversion of urine protein**

The mean time to resolution of proteinuria was 32.85 days [CI 30.31-35.39] and there was no statistically significant association of time to resolution of proteinuria with participant variables.

This result agrees with other published study results.

For Mikami et al., resolution of proteinuria was 30.0±39.6 days [31] and Kaze et al. found a resolution of 51.9% at 6 weeks[20].

Proteinuria is one of the essential symptoms for the clinical diagnosis of eclampsia. Any process that induces a disturbance of the glomerular endothelium, and the glomerular basement membrane or changes in podocyte function can lead to proteinuria [32].

After delivery, serum sFlt-1 and Eng levels decline rapidly, falling to normal values within 48 hours [22]. The kinetic profile of sFlt-1 and Eng suggests that proteinuria should decrease steadily from the second week after delivery and complete resolution is expected within the 6 weeks following childbirth [22].
CHAPTER SIX

CONCLUSION

In this study, most of participants got their Blood pressure and renal function normalized by the end of postpartum period, only few had persistent hypertension, renal dysfunction and proteinuria.

In this study

➢ The mean time to resolution of hypertension was 2.49 weeks (CI 2.13-2.82)

➢ The mean time to resolution of renal dysfunction was 24.54 days (CI 20.14-28.95)

and

➢ The mean time to resolution of urine protein was 32.85 days (CI 30.31-35.39).

There was an association of time to resolution of hypertension with multiple/single pregnancy with a P-value of 0.013.

There was no statistically significant association of time to resolution of renal dysfunction and proteinuria with participant variables.

6.1 Recommendations

➢ Special interdisciplinary follow up for this category of patients by an obstetrician and a physician is a requirement.

➢ A specialized postpartum clinic with a specialist nurse or doctor follow up including home visits, and telephone contacts is a requirement.

➢ Hertig et.all suggested the following recommendations [22]

✓ Renal follow up: At weeks 4 and 8 after delivery, measure of urine protein
to creatinin ratio. If proteinuria is not decreasing by week 8, then the patient is referred to the nephrologist for further management.

- Cardiovascular follow up: at week 8 after delivery and every 5 years:
  measure of blood pressure, fasting blood glucose, lipid profile, and serum creatine.

- Lifestyle: no tobacco, aim for a target BMI <25kg/m².

  ➢ This follow up can be adjusted according to this study result and Mulogo hospital coming protocol of preeclamptic patient follow up.

### 6.2 Limit of the study

Missed to determine the duration from diagnosis to delivery.

Not able to tell patients at which particular point of blood pressure they should reduce and/or stop taking their antihypertensive medicines.

### 6.3 Strength of the study

Study design: Prospective cohort study.

All censored participant were involved in data analysis.
REFERENCES

25. Sabatine, M.S., Pocket medicine: The Massachusetts General Hospital handbook of internal medicine. 2013: Lippincott Williams & Wilkins.
APPENDICES

Appendix I: PARTICIPANTS CONSENT

Title: Trend in blood pressure and renal function among survivors of severe preeclampsia and eclampsia in Mulago hospital: A prospective cohort study.

Principal investigator: Dr KASEREKA MUTEKE, Senior House Officer, department of obstetrics and Gynecology, Mulago hospital.

The purpose of this study is to determine the time course of hypertension and renal dysfunction and to describe associated factors with normalization in blood pressure and renal function among survivors of severe preeclampsia and eclampsia after delivery. The findings will help to plan for a follow up care of women delivering with severe preeclampsia and eclampsia.

Blood pressure, morning urine sample and 2mls of blood will be taken on day 1 and 6 after delivery then 2 weekly up to 6 weeks.

If you choose to participate in the study, you will voluntarily sign an informed consent form.

Risks: No risks will be posed to you as a result of participation in this study.

Costs and compensation: No payments are required for you to participate in this study.

Rights of the participant: Your participation in this study is completely voluntary. If you join the study, you will be free to withdraw from it any time, and if you decline to participate in the study you will still receive the same care and attention from the medical personnel.

Participants will be given a transport refund of 10,000Sh/=
**Confidentiality:** Your names will not appear anywhere on the study forms. A study identification number will instead be used. Your records will only be accessed by the research team. The information will only be used for the purpose of this study and no publication of this study will use your name or identify you personally.

**In case of questions:** If you have any questions you can contact the investigator, Dr KASEREKA MUTEKE, department of Obstetrics and Gynecology, Mulago hospital P.O. Box 7051 Kampala, Uganda. Mobile: 0758311269.

And/or the SOMREC chairperson, Associated Professor OCAMA on 0772421190

**VOLUNTARY CONSENT**

I ............................................................. confirm that the researcher has explained to me all the above information. I have understood what will be done and that my participation in this study is voluntary. I also understand that my identity will be kept confidential. By signing this form, I voluntarily and willingly agree to participate in this study.

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Appendix II: QUESTIONNAIRE

1. Visit 1

   a. Patient identification

      1. Participant’s study number
      2. Telephone number
      3. Home address
      4. Hospital registration number
      5. Age in year
      6. Date of visit

   b. Medical history:

      1. Diabetes mellitus: yes or no
      2. Renal disease: yes or no
      3. Chronic hypertension: yes or no

   c. Obstetric history

      1. Past obstetric history
         - Preeclampsia/eclampsia: yes or no
• If so, at Gravida........, ............, ..........., .............., .............

• When did BP come normal after delivery: ........weeks

2. Most last pregnancy history:

• LNMP...........................................................................................

• EDD..............................................................................................

• Date of delivery................................................................................

• Mode of delivery: SVD or EMCS .................................................

• Gestational age at delivery..............................................................

• Single or multiple pregnancy........................................................

• Parity ..............................................................................................

• Interpregnancy interval if multigravida: date of previous birth or abortion .....................................................................................

• Weight before pregnancy..............................................................

d. Family and social history

1. First degree relative

• Preeclampsia/eclampsia: yes or no ..................................................

• Chronic hypertension: yes or no ...................................................
• Renal diseases: yes or no .................................................................

2. Social history

   Marital status

   • Married: yes or no...........................................................................

   • New sexual partner (≤ 6 months before conceiving) yes or no...........

e. Physical exam

   1. Blood pressure

      • At admission.............................................................................

      • At delivery...................................................................................

      • On day 1 postpartum....................................................................

   2. Weight ..........................................................................................

   3. Height .........................................................................................

f. Lab exams

   1. Creatinine

      • At admission.............................................................................
• At delivery.................................................................

• On day 1 postpartum..................................................

2. Urine protein

• At admission............................................................

• At delivery............................................................

• On day 1 postpartum..................................................

3. Estimated glomerular filtration rate

• At admission............................................................

• At delivery............................................................

• On day 1 postpartum..................................................

g. Antihypertensive drugs use

1. Nifedipine: yes or no..............................................

2. Methyl dopa yes or no...........................................

3. Hydralazine yes or no...........................................

4. If no using drugs, since:

• One week yes or no..............................................

• Two weeks yes or no.............................................
• More than two weeks yes or no..................................................
Appendix III: FOLLOW UP

Visit 2.

1. Weight...........................................................................................................

2. Blood pressure................................................................................................

3. Serum creatinine............................................................................................

4. Urine protein....................................................................................................

5. Estimated glomerular filtration rate.................................................................

6. On antihypertensive medication yes or no......................................................

7. If no, since:
   - One week yes or no ......................................................................................
   - Two weeks....................................................................................................
   - More than two weeks..................................................................................

Visit 3

1. Weight..............................................................................................................

2. Blood pressure................................................................................................

3. Serum creatinine............................................................................................

4. Urine protein....................................................................................................

5. Estimated glomerular filtration rate.................................................................
6. On antihypertensive medication yes or no

7. If no, since:

   - One week yes or no
   - Two weeks
   - More than two weeks

**Visit 4**

1. Weight

2. Blood pressure

3. Serum creatinine

4. Urine protein

5. Estimated glomerular filtration rate

6. On antihypertensive medication yes or no

7. If no, since:

   - One week yes or no
   - Two weeks
   - More than two weeks