ADVERSE MATERNAL-PERINATAL OUTCOMES AND ASSOCIATED RISK FACTORS IN HELLP SYNDROME AT KENYATTA NATIONAL HOSPITAL

-A cross-sectional study-

Principal Investigator: DR. MIJI ERNESTO

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A thesis submitted in partial fulfillment of the requirements for the award of the degree of Master of medicine in Obstetrics and Gynaecology of the University of Nairobi

2022

DECLARATION

DECLARATION

I certify that this thesis is my original work. It has not been presented for the award of a degree in any other institution.

Signature..... Date..06/06/2022.....

Dr. Miji Ernesto

Department of Obstetrics and Gynecology

University of Nairobi

CERTIFICATE OF SUPERVISION

CERTIFICATE OF SUPERVISION

This thesis has been submitted with our approval as the supervisors.

Dr. Alex Bosire

Lecturer

Department of Obstetrics and Gynaecology

University of Nairobi

Signature

Date: 06/06/2022

Dr. Diana Ondieki

Lecturer

Department of Obstetrics and Gynaecology

University of Nairobi

Signature

Date: 07/06/2022

Prof Moses Obimbo

Associate Professor

Department of Human Anatomy

Department of Obstetrics and Gynaecology

University of Nairobi

Signature

Date: 08/06/2022

II

CERTIFICATE OF AUTHENTICITY

CERTIFICATE OF AUTHENTICITY

This is to certify that **Dr. MIJI WA LUNGENA ERNESTO** registration number **H58/34091/2019,** intends to research upon this dissertation in the Department of Obstetrics and Gynecology, University of Nairobi under the guidance of **Dr. Alex Bosire, Dr. Diana Ondieki** and **Professor Moses Obimbo.**

Signature.....

Date.....10/06/22

Professor Eunice Cheserem

Chair, Department of Obstetrics and Gynecology,

University of Nairobi

III

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DEDICATION

To my family for the sacrifice endured, I dedicated this thesis.

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ABSTRACT

Background: HELLP syndrome complicates around 0.9% of all pregnant women and up to 20% of women with severe preeclampsia and eclampsia. HELLP Syndrome has been significantly associated with adverse maternal-perinatal outcomes. Adverse maternal outcomes associated with HELLP include maternal death as well as severe morbidity such as placental abruption, renal failure, and intensive care unit admissions. The associated perinatal adverse include jaundice, respiratory distress syndrome, neonatal intensive care admissions, small for gestational age, and perinatal death. However, factors associated with these adverse outcomes have not been exhaustively investigated particularly in the local context.

Objectives: To determine adverse maternal-perinatal outcomes associated factors in patients with HELLP syndrome at Kenyatta National Hospital (KNH) from 1st January 2016 to December 31st, 2020.

Methodology: This will be an analytical cross-sectional study conducted at KNH. A systematic sampling technique will be used to enroll 385 patients diagnosed with HELLP Syndrome from 1st January 2016 to 31st December 2020. A data abstraction tool will be used to collect data from patient files. Data extracted will include patient demographic characteristics, clinical presentation, biological factors as well as maternal and perinatal adverse outcomes. The collected data will be entered in Epi-data version 3.1 and exported to Statistical Package for Social Sciences (SPSS version 26).

Results: The mean patients´ age at diagnosis was 28.9 (SD±6.07) years and the average gestational age was 33 weeks at recognition. The common symptoms included epigastric/RUQ pain 67.8%, headache 59.7%, and blurry vision 29.1%. The average ALT was 209.5 IU/L, AST was 281.7 IU/L, and LDH was 951 IU/L while the mean platelet count was 78.1 per microliter. Globally, the maternal and perinatal complications were 76.4% and

81.3% respectively. In mothers, we observed 64.9% eclampsia, 44.7% blood/blood products transfusion, 34.5% renal failure, 18.2% bleeding disorders, and 18.1% ICU admission, 7% cerebrovascular accident, 6.5% placental abruption, 4.7% brain edema and 9.1% maternal mortality. In infants, 73% were premature, 35% were stillbirths, and 63.9% were perinatal death. Gestational age bellow 37 weeks (aOR = 4.5), blurry vision (aOR =2.1), elevated systolic BP (aOR =11.4), high diastolic BP (aOR =10.3), increased ALT (aOR =2.3), higher AST (aOR =1.6) and elevated total bilirubin (aOR = 1.4,) were associated with high adverse maternal outcomes. Gestational age below 37 weeks (aOR = 3.5) was associated with adverse perinatal outcomes.

Conclusion: HELLP syndrome is a pregnancy complication associated with a higher rate of maternal and perinatal morbidity and mortality. The diagnosis may be difficult as the symptoms are not specific, but lab investigations are helpful. Gestational age at diagnosis, ANC attendance, and clinical factors have been seen to be associated with adverse outcomes in both mother and infant. Biological parameters such as elevated ALT, AST, creatinine, and total bilirubin are more associated with maternal complications but not with adverse perinatal outcomes.

CHAPTER ONE: INTRODUCTION

HELLP syndrome is a critical disorder characterized by a biological triad: hemolysis, low level of platelet, and high enzymes (1). This condition may occur in patients without Preeclampsia with prevalence ranging between 0.1% and 0.9% in all pregnancies as well as between 4% and 12% in patients with eclampsia (2). Approximately 70% of HELLP syndrome cases occur before delivery, with a higher occurrence occurring between the 27th and 37th weeks of gestation. Further, only 10% of HELLP syndrome cases occur before the 27th week of gestation, while 20% occur beyond the 37th week of pregnancy (3).

The prevalence of HELLP syndrome in Africa has been increasing gradually in the recent past. In a systematic review conducted assessing obstetric complications in Africa, the prevalence of HELLP ranged between 1.2% to 3.4% among pregnant women (4). However, there are limited studies that have assessed the outcomes in this condition as well as their associated risk factors. In a study conducted in Kenya, it was found that the syndrome was associated with a clinical history of epigastric pain and elevated serum creatinine of 110 micromoles per liter or greater (5).

The diagnosis of HELLP syndrome varies, although the most common presentations are pain, nausea, vomiting, and epigastric pain. These symptoms do not occur isolated but in conjunction with abnormal liver tests, moderate to severe thrombocytopenia, and hemolytic anemia (6). Studies have shown that there are varied factors that are associated with adverse outcomes in patients with HELLP syndrome which include advanced maternal age, nulliparity, and chronic hypertension among women (7) (6). These factors can be effectively managed to reduce the occurrence of HELLP syndrome.

Studies have shown that HELLP syndrome increases the risk of adverse maternal and neonatal events (3) (7). Maternal death that is associated with HELLP syndrome ranges

between 0 and 24 percent while perinatal mortality range between 6.6-60 percent in women with this condition (8). Other complications that have been identified include renal failure, liver hematoma, hypovolemic shock, lung and brain oedemas, consumption coagulopathy, and placental abruption (9) (10).

Maternal complications of preeclampsia such as HELLP may lead to maternal and fetal death and increased morbidity, and efforts should be made to detect this condition before the life-threatening complications occur (11). Understanding the factors associated with these complications forms the basis of this study.

CHAPTER TWO: LITERATURE REVIEW

2.1. Pathogenesis of HELLP Syndrome

The origin of HELLP syndrome is still controversial as many authors thought that it is the complication of Preeclampsia (PE), while some patients with this condition do not meet the criteria of Preeclampsia (PE) as found in the majority of cases. The initial development of HELLP syndrome in pregnancy has been identified by the presence of insufficient levels of immune tolerance which occurs as a result of the damage to the invading fetal trophoblast. This tends to occur during early pregnancy and should be significantly controlled to create a more specific and diversified understanding of this condition. In patients with HELLP syndrome, the Messenger RNA levels are extremely high reaching abnormal levels in maternal blood. This shows that early trophoblastic lesion is more widespread among patients with HELLP (12).

Similarly, gene expression is abnormal in HELLP patients. The existing levels of antiangiogenic factors in maternal blood are similar though not identical (13). The thrombotic microangiopathy in HELLP may be driven by a complex of triggered coagulation and supplement, as well as high circulating levels of sEndoglin, sFlt1, TNFa, and active von Willebrand factor. The damage to the liver is most likely due to circulating FasL from the placenta, which is exacerbated by angiopathy. In HELLP, compensated DIC is likely to be common, whereas uncompensated DIC is uncommon (14).

2.2. Classification of HELLP Syndrome

Classification systems have been elaborated to facilitate the recognition of pregnant women at risk for increased morbidity, to direct the management, evaluate efficacy or result, and to come up with a standard basis for the assessment of investigation reports. The 2 most

consensual classification systems employed were elaborated by researchers at the Universities of Tennessee and Mississippi.

The Tennessee system distinguishes ‘‘true’’ or “complete’’ HELLP syndrome if all of the following criteria are met: (1) platelets count of 100,000/mL or less; (2) liver dysfunction with AST 70 IU/L or more; and (3) hemolysis proven with an abnormal peripheral smear associated to either total serum LDH ≥600 IU/L or bilirubin ≥1.2 mg/dL. However, if the women present one or more but not all of these elements, it is named ‘‘partial’’ or ‘‘incomplete’’ HELLP syndrome.

The Mississippi classification is commonly used in HELLP syndrome. This classification assesses the severity of the syndrome based on the lowest observed platelet count together with the other three main biological parameters (LDH, AST, and ALT) (15). The classifications are as shown in Table 1.

Table 2.2.1. 1: HELLP classification systems (Mississippi VS Tennessee).

Mississippi classification	Tennessee classification
Class 1 • Platelets <50,000 • AST or ALT > 70 IU/L • LDH >600 IU/L	True or Complete • Platelets < 100,000 • AST > 70 IU/L • LDH >600 IU/L
Class 2 • Platelets = 50,000-100,000 • AST or ALT > 70 IU/L • LDH >600 IU/L	Partial or incomplete • Severe preeclampsia with any one of the following: ELLP, HEL, EL, LP
Class 3 • Platelets = 100,000-150,000 • AST or ALT >40 IU/L • LDH >600 IU/L	

ELLP, Absence of hemolysis; HEL, Absence of low platelets; EL, Elevated liver function; LP, Low platelets.

2.3. Socio-demographic, clinical, and biological characteristics of patients with HELLP syndrome

Patients with HELLP syndrome present with varied socio-demographic and clinical characteristics. In a population-based study conducted by *Lisonkova et al*, investigating the adverse effects of HELLP, the findings showed that 35% of the women were aged between 30 and 34 years with few, 3.2% aged between 15 and 19 years, 7% had pre-pregnancy hypertension, 16% presented with chronic renal disease, 22.2% had chronic hepatic condition while 9.2% had placental disorders (7). However, the present study investigated the socio-demographic characteristics of patients with HELLP syndrome in a hospital-based setting.

Turgut et al. (2010) revealed that the average maternal age was 27 years and the mean gestational age at diagnosis was 33 weeks. The presenting symptoms reported in the majority of the women were 52.3% headache, 36% had visual change, 32.4% epigastric pain, and 6.3% complained having nausea and vomiting and 0.9% dizziness. The study also assessed biological factors among patients with HELLP syndrome and showed the average hemoglobin level was 12.2g/dl, the mean platelet count was 93972.5mm^3, creatinine level 0.8mg/dl while uric acid was 72mg/dl (8). This study was conducted in Turkey hence the findings cannot be generalized to represent the local Kenyan context.

Haddad et al also found that the most common symptoms in the diagnosis of HELLP syndrome included abdominal pain, nausea, vomiting, and epigastric pain (16). Other symptoms such as headache and visual symptoms have been reported although their occurrence is rare (17). Similarly, in another cross-sectional study conducted in Thailand by *Kongwattanakul et al*, it was found that 15% of women who were enrolled in the study were aged 35 years or older with half of the respondents being nulliparous. The findings further showed that 11% of the mothers were obese, 5% had been diagnosed with preeclampsia in the previous pregnancy and 22% of the patients had a family history of hypertension in first-degree relatives (18).

A prospective study conducted by *Anitha et al* in 2020 among patients with HELLP syndrome revealed that 54% had nausea and vomiting, 48% had a headache, 25% blurred vision, and 11% of the respondents presented with all of these symptoms (19).

A study conducted in Mali by *Abdoulaye et al* in 2004 revealed that out of 1559 patients who were hospitalized, 0.5% of patients were admitted to ICU of which 9 cases had HELLP syndrome. There were 6.2% obstetric emergencies and 18% of gravid toxemias. The identified clinical signs among the patients included high blood pressure, nausea, icterus, and epigastric pain (20).

2.4. Adverse outcomes in patients with HELLP syndrome

HELLP syndrome has been associated with increased maternal and perinatal death varying between 0 to 24% and 6 to 60% respectively. In a community-based study done in Canada by Lisonkova et al. in 2020, it was revealed that patients with HELLP syndrome had a 10-fold increased maternal mortality as well as severe maternal morbidity of 121.7 per 1000. The study further found that HELLP syndrome was associated with increased perinatal mortality at 21 per 1000 and severe perinatal morbidity of around 202.4 per 1000 (7).

Haddad et al, in a cross-sectional study conducted in the United States, found that 6% of women had eclampsia, 10% had a placental abruption and 22% necessitated transfusion of blood products. Other adverse maternal complications observed in the study were pulmonary edema, pleural effusion, ascites, acute kidney injury, liver hematoma, cesarean delivery, and death (16).

Liu et al, 2020, conducted a systematic review investigating the effects of HELLP syndrome on acute kidneys in pregnancy, in which data from PubMed, Embassy, and Cochrane databases were analyzed. The findings revealed that in 11 cohort studies that were reviewed, patients with HELLP syndrome were 4.87 times more likely to develop acute renal failure,

3.7 times more likely to lead to maternal death, and 1.56 times likely to experience fetal demise (21). The results have provided an understanding that HELLP syndrome contributes significantly to the development of acute kidney injury and increased risk of maternal and perinatal death.

Similarly, AKI in HELLP syndrome has been found to have an incidence between 7% and 15% (22), whereas the patients with HELLP syndrome and disseminated intravascular coagulation were more predisposed to acute renal failure in comparison to those without DIC (9). Hemodialysis may be necessitated where acute renal failure develops as an adverse event due to HELLP, however, in most of these women, kidney function is reversibly deteriorated (23). Another major cause of morbidity in HELLP syndrome patients that has been reported is placental abruption, which has an incidence of between 9 to 20% (24).

Erdemoğlu et al, in a cross-sectional study conducted in Turkey, assessing outcomes associated with HELLP syndrome, the findings revealed that 35% had a vaginal delivery, 65% had cesarean delivery while 14.2% were with in utero stillbirth. Further, there were 11.9% perinatal deaths, 20.6% of the women developed placental abruption, 11.1% went to acute renal insufficiency while 10.3% had postoperative subcutaneous hematomas, and 7.9% of women deceased (25).

In a retrospective study conducted by *Erkilinc et al*, it was identified that younger age, the presence of headache and LDH ≥1290 increase the risk of eclampsia, while acute renal failure appears to multiply fifteen times with bilirubin of more than 2 mg/dl and low platelets in mothers with HELLP syndrome (26). Thus, this study seeks to provide more information regarding the occurrence of these symptoms with adverse outcomes.

In another study conducted in Turkey by *Cavkaytar et al*, the findings revealed that 34% of the patients had had hemorrhagic manifestations, 46.7% oliguria, 20% ARF, 33.3% required

blood transfusions, 6.7% pulmonary edema and 3.8% died. The findings further revealed that 41% of mothers had anemia and deduced that the clinical symptoms are more efficient as compared to laboratory tests to predict the adverse results in HELLP syndrome patients (24).

A systematic review conducted by *Liu et al.* in 2020 revealed that patients with HELLP syndrome were five times more prone to develop AKI compared to those without HELLP while additionally, they were two times more likely to lead to fetal death than those without HELLP syndrome (21).

A cross-sectional study conducted in Thailand by *Kongwattanakul et al.* identified that the majority of the women in this study had a primary cesarean section, and 16% had a non-reassuring fetal status during the intrapartum interval, 15.6% presented severe preeclampsia had no proteinuria, 9% developed acute kidney failure, 3.3% had liver dysfunction and 2.2 % new-onset cerebral or blurring of vision (18). Another study conducted, by *Anitha et al.* in 2020, it was demonstrated that 60% of patients developed undesirable events including preterm deliveries, AKI, transfusion of blood products, and DIC, while the perinatal complications included 42.5% perinatal death, 40% NICU admission, 37% fetal growth retardation and 20% stillbirth (19).

Katz et al., observed in their study that HELLP is a threatening disease, with the occurrence of increased maternal morbidity and mortality in patients. Common complications were impaired renal function and consumption coagulopathy with the frequent requirement of transfusions of blood products. Mortality was seen to attain 3.8% (27). *Abdoulaye et al.* in a study done in Mali in 2004 revealed that the most threatening event was the ARF, but hemodialysis was useful for 4 of women (44.4%) after the failure of diuretic use. The evolution was successful in 6 cases and unsuccessful in 3 (33.3 % with maternal deaths) (20).

In another study conducted in Nigeria, it was revealed that none of the 6 HELLP patients was in class I, out of 34 cases admitted in ICU, 4 were in class II while 2 were in class III. The findings also reported that of the 4 eclamptic patients who died with associated 15% were perinatal deaths (28). The findings have shown that HELLP syndrome is highly likely in eclamptic patients and if so, it appears to be more hazardous.

2.5. Risk Factors associated with adverse maternal and perinatal outcomes

Different factors have been associated with various adverse outcomes that occur in HELLP syndrome. Thus, clearly understanding these factors may play a fundamental role in minimizing the adverse events when managing patients with this condition. The occurrence of HELLP syndrome has been ascribed to the worsening of the maternal and fetal prognosis from previous studies (29) and often the only effective management is prompt delivery of the infant. Before 34 weeks of gestation, there exist fetal concerns, but after 37 weeks of gestation, induction of labor in these patients may be considered a high priority. It has been documented that the gestational age is more crucial than the severity of the syndrome in deciding the baby's outcome and that after diagnosis, cesarean section rates of up to 100% with an 8-hour wait have been observed (10).

The risk associated with delay in labor may not be as serious as the risk of continuing the pregnancy since HELLP is a serious condition (30), and although vaginal birth is the preferred mode of delivery (31), a cesarean section may be preferable as an unfavorable cervix particularly distant from term may hamper vaginal delivery. Controversially, there were more rates of cesarean sections observed by *Saibai et al.* amongst patients with incomplete HELLP in comparison with those with true HELLP syndrome (32).

Abroug et al., in their study, found that HELLP syndrome in pregnant women was not linked to a decline in fetal prognosis. However, they concluded that fetal prognosis was markedly

affected by the small number of HELLP patients in their study (33). *Miranda M et al.* in Spain, concluded in their study on clinical features and maternal-fetal outcome in 172 women with HELLP syndrome, that the severity of the condition, as per Mississippi classification, was correlated with the rate of poor maternal outcomes but did not influence the fetal results. The findings significantly related to the absence of fetal viability were a history of preeclampsia in previous pregnancies, the GA at the onset of the syndrome, BP levels, needs for transfusion, development of abruptio placentae, and fetal birth weight. Only D-dimers were seen to be associated with an absence of fetal viability among the biological findings. The features strongly associated with the occurrence of adverse maternal outcomes were the postpartum onset of HELLP, complaints of headache or blurred vision, a requirement for blood products transfusion, levels of hemoglobin, and all other laboratory parameters analyzed in the study except the D-dimers (17).

Cavaignac-Vitalis M et al.(2017), in their study conducted in France, demonstrated that conservative actively with corticosteroids may be helpful for both women and their infants in case of stable HELLP syndrome, with markedly lower rates of complications such as PPH, ascites, pleural effusions, and hospital stay as well as reduced complications related to preterm delivery. However active management caused a high risk of PPH and neonatal morbidity including RDS, sepsis, NEC, ICH, and blood transfusion (34). These results are similar to those found by *Katz et al.* that the use of these drugs is efficient and cost-effective in improving the symptoms, decreasing significantly the adverse outcomes, and shortening the recuperation time after delivery (35). Similarly, *Makinde et al.* found in Nigeria that all the cases of HELLP syndrome that succumbed and all the perinatal losses recorded were among unbooked patients and concluded that early diagnosis and appropriate management with corticosteroids as well as timely delivery were seen to help decrease complications and mortality (31).

Controversy has existed on the importance of these subjective symptoms since the majority of them be not significant in determining adverse maternal-perinatal outcomes that are likely to occur (36). However, *Cavkaytar et al*. asserted that the clinical manifestations are more reliable in anticipating poor maternal outcomes among HELLP patients than laboratory findings (24).

Emphasis on clinical and laboratory values in HELLP syndrome should be viewed with some level of suspicion as there is a great risk of overlap with many of the medical and/or surgical conditions in pregnancy, and other obstetric complications which have also been associated with adverse obstetric outcomes. Maternal unfavorable outcomes may also arise from error in diagnosis, delayed or retrospective diagnosis, mismanagement, and other patient-related factors (18). Most of these studies comparing both clinical and biological factors have utilized a smaller sample size making it difficult to effectively determine which among these factors are associated with adverse outcomes.

Some researchers have speculated on long course use of high dose corticosteroids to improve the maternal clinical and biological parameters and consequently the perinatal outcome by postponing the timing of delivery (37) (38), but many of these studies were limited by the sample size where dexamethasone was a drug experimented in the studies. On the other hand, another study has not proven any improvement in mortality, length of ICU stay, and the platelet counts in patients with HELLP syndrome with dexamethasone treatment (39).

2.6. Conceptual Framework

2.6.1. Conceptual Framework Narration

The study aims at determining the incidence as well as associated risk factors of adverse outcomes among women with HELLP syndrome. The independent variables that are assessed

include demographic characteristics and clinical and biological factors. The intervening variable which might influence the dependent/outcome variable is the management approach that is used on women with HELLP syndrome. The key management approaches for HELLP syndrome include corticosteroids and blood transfusion. The dependent variable includes the assessment of adverse outcomes in both maternal and perinatal.

2.6.2. Conceptual framework Figure

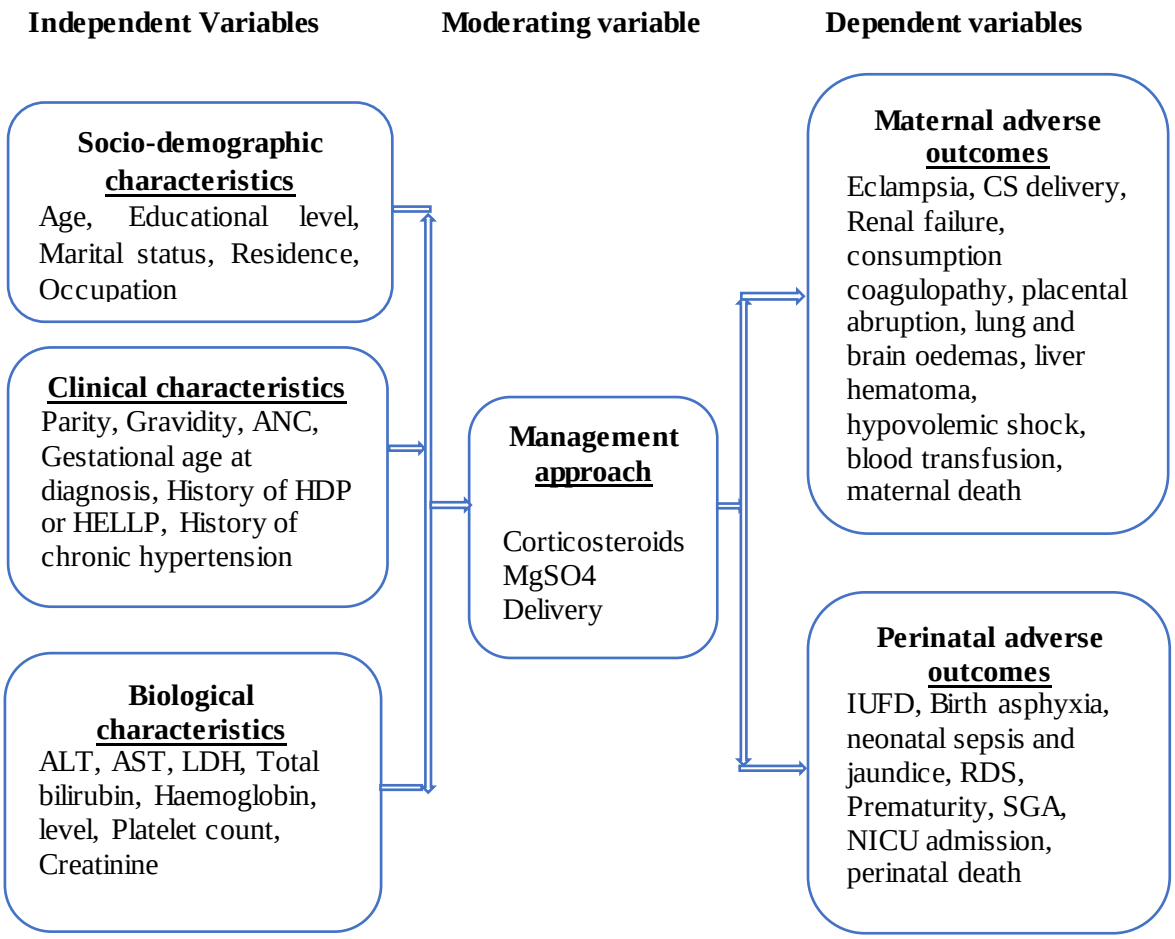

Figure 1 0 : Conceptual framework

2.7. Justification of the Study

HELLP syndrome however has been seen to be associated with high maternal mortality and complications such as DIC, AKI, stroke as well as perinatal mortality, and mobility. However, factors associated with these adverse outcomes have not been extensively addressed. In Sub-Saharan Africa, particularly in Kenya, limited studies are focusing on this

issue. Therefore, this study seeks to bridge this gap and create improved knowledge on the maternal and perinatal adverse outcomes of HELLP syndrome. Further, there have been controversies regarding the ability of clinical and biological factors to predict adverse outcomes. This study seeks to identify adverse maternal and perinatal adverse outcomes as well as associated factors related to specific adverse outcomes.

2.8. Research Question

What are the adverse maternal and perinatal outcomes and associated risk factors in women with HELLP syndrome at KNH from 1st January 2016 to 31st December 2020?

2.9. Broad Objectives

To determine adverse maternal-perinatal outcomes and associated risk factors in patients with HELLP syndrome at KNH from 1st January 2016 to 31st December 2020.

2.9.1. Specific Objectives

Among patients with HELLP syndrome attended at KNH:

(i) To establish the socio-demographic, clinical, and biological characteristics;

(ii) To determine adverse maternal outcomes;

(iii) To determine the adverse perinatal outcomes.

2.9.2. Secondary objectives

(i) To ascertain the risk factors associated with adverse maternal and perinatal outcomes in patients with HELLP syndrome at KNH from 1st January 2016 to 31st December 2020.

CHAPTER THREE: METHODOLOGY

3.1. Study Design

This was a cross-sectional study with a subgroup analysis of patients with HELLP Syndrome admitted and delivered at Kenyatta National Hospital from 1st January 2016 to 31st December 2020. The study aims at identifying the adverse outcomes, both maternal and perinatal as well as the associated risk factors which can be effectively captured in patients' files in the Hospital making it easier to obtain accurate outcomes retrospectively.

3.2. Study Area

The study was conducted at Kenyatta National Hospital. The Hospital is the major referral hospital in the country with a bed capacity of 1800 and is located approximately 3km from the Central Business District in Nairobi, Kenya. The Hospital has well-structured outpatient and inpatient systems where different patients are engaged based on their healthcare needs. The labor ward is divided into two sections, which include a general wing and a private wing. In 2020, there were approximately 12944 deliveries in General wards and 862 in the private wing. The number of admissions was 13722 in both General and private wards. The average number of deliveries daily was 35 in the general wing and three deliveries in the Private wings. The hospital has well-structured record keeping which makes it possible to obtain data from 1st January 2016 to 31st December 2020 of patients who were diagnosed with HELLP syndrome. The labor ward has 20 beds. The pregnant mothers report to the labor ward where they are managed by a team of healthcare providers including residents in obstetrics and gynecology, midwives, and qualified nurses. A consultant on call is always ready to provide guidance and assistance in emergencies. There is an acute room with a labor ward where there are three beds for managing very sick mothers with complications including HELLP syndrome.

Different treatment approaches are used in the management of HELLP syndrome patients which depend on the severity and patient condition. In the prevention of seizures among patients, magnesium sulphate is largely used in this study setting. Further, anti-hypertensive medications aimed at controlling blood pressure are also given. Corticosteroid drugs have also been used with a key focus on improving a baby's lung maturity in situations where their early delivery. Blood transfusion has also been identified as key management of anaemia and low platelet levels.

3.3. Study Population

The study population included women diagnosed with HELLP syndrome who were admitted and delivered at KNH from 1st January 2016 to 31st December 2020.

3.4. Inclusion Criteria

- All pregnant women with HELLP Syndrome were admitted and delivered at KNH from 1st January 2016 to 31st December 2020.
- All complete files that include an outcome (maternal and perinatal outcome).

3.5. Exclusion Criteria

- Women with other disorders that may cause alteration in liver enzymes, platelet count, or cause hemolysis in pregnancy, such as viral hepatitis, gastroenteritis, cholecystitis, pancreatitis, sepsis, gestational thrombocytopenia, acute fatty liver, immune thrombocytopenic purpura, etc.
- Patients with partial HELLP syndrome.
- Incomplete patients' files (files without an outcome will be considered incomplete)

3.6. Sample Size Determination

The sample size was calculated using Fisher's formula (44): $n = \frac{Z^2 x\, P(1-P)}{d^2}$

Where,

n = Desired sample size

Z = value from standard normal distribution at 95%

P = expected true proportion (estimated at 14.7%,

d = desired precision (0.05)

3.6.1. Sample size based on objective 1: Prevalence of HELLP Syndrome

According to Lakshmi et al. (2020), the prevalence of HELLP syndrome was 14.7%

Thus, $n_0 = \frac{1.96^2 x\ 0.147(1-0.147)}{0.05^2} = 193$

A sample size of 193 patients will be required for the study.

3.6.2. Sample size based on Objective 2: Adverse Outcomes

In another study conducted in Turkey by *Cavkaytar et al.*, the findings revealed that 34% of the patients had had hemorrhagic manifestations,

Thus, $n_0 = \frac{1.96^2 x\ 0.34(1-0.34)}{0.05^2} = 345$

Sample size of 345 patients will be required for the study.

3.6.3. Sample size based on objective 3: Risk factors associated with HELLP Syndrome

In a population-based study conducted by Lisonkova et al, investigating the adverse effects of HELLP, the findings showed that 35% of the women were aged between 30 and 34 years

Thus, $n_0 = \frac{1.96^2 x\ 0.35(1-0.35)}{0.05^2} = 350$

Sample size of 350 patients will be required for the study.

Thus, the largest sample size to meet all the study objectives is 350.

Including a 10% attrition = (350+35)= 385.

The sample size considered in this study will be 385.

3.7. Sampling Procedure

The study adopted a systematic sampling technique in selecting files that meet the inclusion criteria. All files of women who developed HELLP syndrome will be obtained from files of women who delivered from 1st January 2016 to 31st December 2020. Once the files have been retrieved, files that met the inclusion criteria were extracted to provide a sampling frame which formed the basis of the selection of files for the study. An interval was calculated based on total files extracted based on sample size proportion to ensure that every file has an equal chance of being selected.

Table 3.1 1: Data variables

Objectives	Exposure Variables	Outcome Variables	Source of Data
Demographic, clinical, and biological characteristics in women with HELLP Syndrome	Age, Marital status, parity, gravidity, Symptoms, GA, history of HTN, DM, PE or HELLP, Gestational HTN or DM, ALT, AST, LDH, PLT count, Hemoglobin, albumin levels, Total bilirubin, Creatinine.	- Hemolysis - Elevated Liver enzymes - Low Platelet count	Patients' files/ record.
To determine adverse maternal and perinatal outcomes in women with HELLP Syndrome at KNH	- Hemolysis - Elevated Liver enzymes - Low Platelet count	- **Maternal**: Eclampsia, CS delivery, ARF, DIC, placental abruption, lung and brain edema, liver failure, liver hematoma, hypovolemic shock, ICU admission, sepsis, Blood transfusion, death - **Perinatal**: IUFD, birth asphyxia, neonatal sepsis and jaundice, RDS, prematurity, neonatal death, fetal injuries, LBW, IUGR, NICU admission	Patients' files/ Record
Risk factors associated with maternal adverse outcomes in women with HELLP syndrome	- Sociodemographic - Clinical factors - Biological parameters	- **Maternal**: Eclampsia, CS delivery, ARF, dialysis, DIC, placental abruption, lung and brain edema, liver failure, liver or wound hematoma, hypovolemic shock, ICU admission, sepsis, Blood transfusion, death	Patients' files/ Record
Risk factors associated with perinatal adverse outcomes in women with HELLP syndrome	- Sociodemographic - Clinical factors - Biological parameters	- **Perinatal**: IUFD, birth asphyxia, neonatal sepsis and jaundice, RDS, prematurity, neonatal death, fetal injuries, LBW, IUGR, NICU admission	Patients' files/ Record

Table 3.8.1: Variables in the study

3.8. Research tool

A data abstraction tool was used to collect data from extracted patient files (Appendix 1). The data abstraction tool has been developed based on the research objectives to ensure that it is developed with an emphasis on the underlying research problem being investigated.

3.9.Research assistant's recruitment

The Principal investigator employed the help of research assistants to collect information from patient files. The research assistants sought clinical officers with experience in the extraction of data from patient files. This was essential in ensuring that valid, reliable, and accurate data is extracted from the patient files. The research assistants underwent a two-day training to ensure that they understand the purpose of the study and the best approach to extract patient data from the files. The first day involved familiarization with the data abstraction tool while the second day involved how to extract files from the health information department.

3.10. Data collection procedure

The data collection process began after approval from the KNH-UoN Ethics review committee and KNH administration. The principal investigator together with the help of recruited research assistants accessed the labor ward admission register to identify the Inpatient numbers of all patients who were diagnosed with HELLP syndrome from 1st January 2016 to 31st December 2020. This was essential for easy file retrieval in the health information department. After documenting the Inpatient numbers of all patients who were diagnosed with HELLP, the Principal investigator visited the Health information department where the files are stored. The files are stored per department and admission numbers of patients. Maternity files were targeted. Thus, the files were retrieved based on the list obtained from the admission register. Once the files were retrieved, the principal investigator then systematically select 193 files from the extracted files. The interval used in selecting the files was based on the total number of files retrieved including patients who were diagnosed with HELLP syndrome within the study period. Once all files were selected, the demographic, clinical history, and detailed laboratory investigations which included complete hemogram, peripheral blood smear, coagulation profile, liver profile, and renal profile values

were recorded and patients were classified according to Mississippi classification of HELLP Syndrome. Once this information was extracted, the files were returned for filing.

3.11. Study data collection flow chart

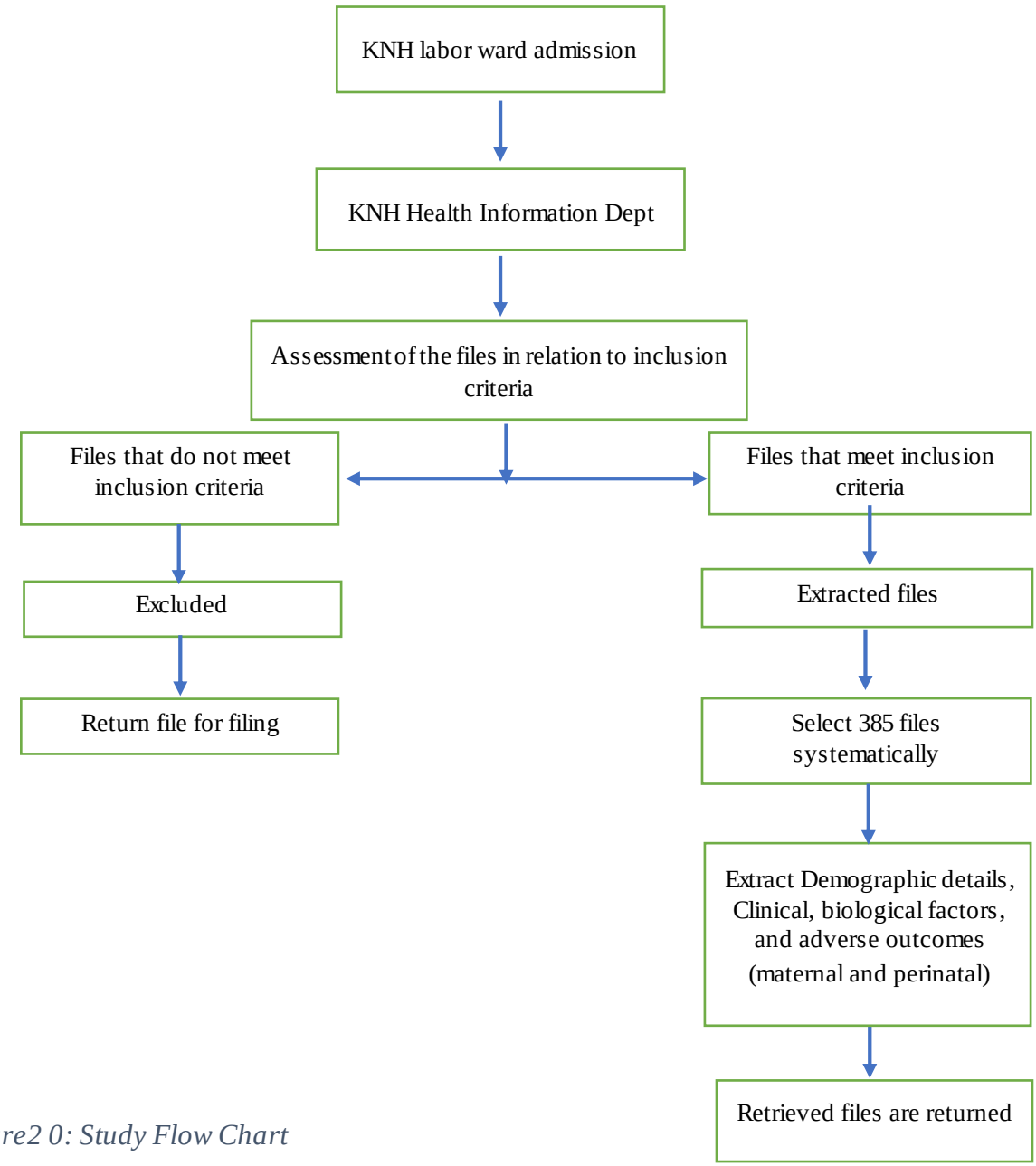

Figure2 0: Study Flow Chart

3.12. Pretest, validity, and Reliability

A pilot test was done at KNH before the start of the actual data collection. This helped in the familiarization of the study setting, the data collection process as well as testing of the data

abstraction tool. This helped in maintaining a high level of reliability of the data abstraction tool in attaining the needed outcomes.

Internal validity of the study was achieved by severally reviewing the information collected and recorded during the data abstraction. External validity was achieved through the use of randomly selected participants. In addition, the research achieved reliability through the review by experts in the field as well as ensuring that there is no missing data obtained. Further reliability was achieved by ensuring that the same methodology is applied when abstracting all relevant data.

3.13. Quality assurance

The data abstraction tool was assessed by experts in fetal-maternal medicine. Research assistants were trained to ensure that they fully understand the objectives of the study and better data retrieval methods. Data collected was checked for completeness daily. A qualified statistician was recruited.

3.14. Data management

Data were abstracted from patient files using the developed data abstraction tool. The collected data was entered into epi-data 3.1. Once the data collection process is completed, the data was exported to SPSS version 26 for analysis. A biostatistician was recruited to perform data analysis.

3.15. Data analysis

Data were analyzed using both descriptive and inferential approaches with the level of significance considered at 0.05.

The socio-demographic, clinical, and biological factors in women with HELLP Syndrome at KNH from 1st January 2016 to 31st December 2020 were analyzed descriptively utilizing both

continuous and categorical data. Grouped data were analyzed using frequencies and percentages while continuous data were analyzed using mean and standard deviation.

The prevalence of maternal adverse outcomes associated with HELLP Syndrome at Kenyatta National Hospital from 1st January 2016 to 31st December 2020 will be calculated as a proportion of mothers who develop an adverse outcome (morbidity and mortality) and the total sample population.

The prevalence of perinatal adverse outcomes associated with HELLP Syndrome at Kenyatta National Hospital from 1st January 2016 to 31st December 2020 was calculated as a proportion of neonates who develop an adverse outcome (morbidity/mortality) and the total sample population.

In investigating risk factors associated with maternal and perinatal adverse outcomes, Chi-square or Fischer's test for exactness were used to compare grouped factors and adverse maternal and perinatal outcomes, performing the univariate, bivariate, and multivariate analysis. A student t-test was conducted to help understand the underlying relationship between the continuous variables associated factors with maternal adverse outcomes.

3.16. Ethical Consideration

The study sought approval from the KNH-UoN Ethics committee. Approval was sought from the KNH administration to ensure that there is compliance with laid down research procedures and access to patient information within the hospital.

The researcher also maintained anonymity and confidentiality by using none identifiers such as codes that cannot link a participant with the information provided during the study. The information obtained was solely for this study and to improve the implementation of service integration policy and not to divulge personal information to the public. Recorded data was

under the custody of the principal researcher until validation within one year after which the data will be destroyed.

3.17. Study limitations and delimitation

- The study captured information that was only included in patient files to make decisions, but due to its retrospective nature, there were missing data from the files extracted which meant that some crucial files with unique data were left out because they were missing some information relevant in our study.

CHAPTER FOUR: RESULTS

4.1. Introduction

This was a five-year cross-sectional study conducted to investigate adverse maternal-perinatal outcomes and associated risk factors in patients with HELLP Syndrome in Kenyatta National Hospital. A total of 385 patient files which met the inclusion criteria were retrieved. The study flow chart showing the data collection process is shown in Figure 3.

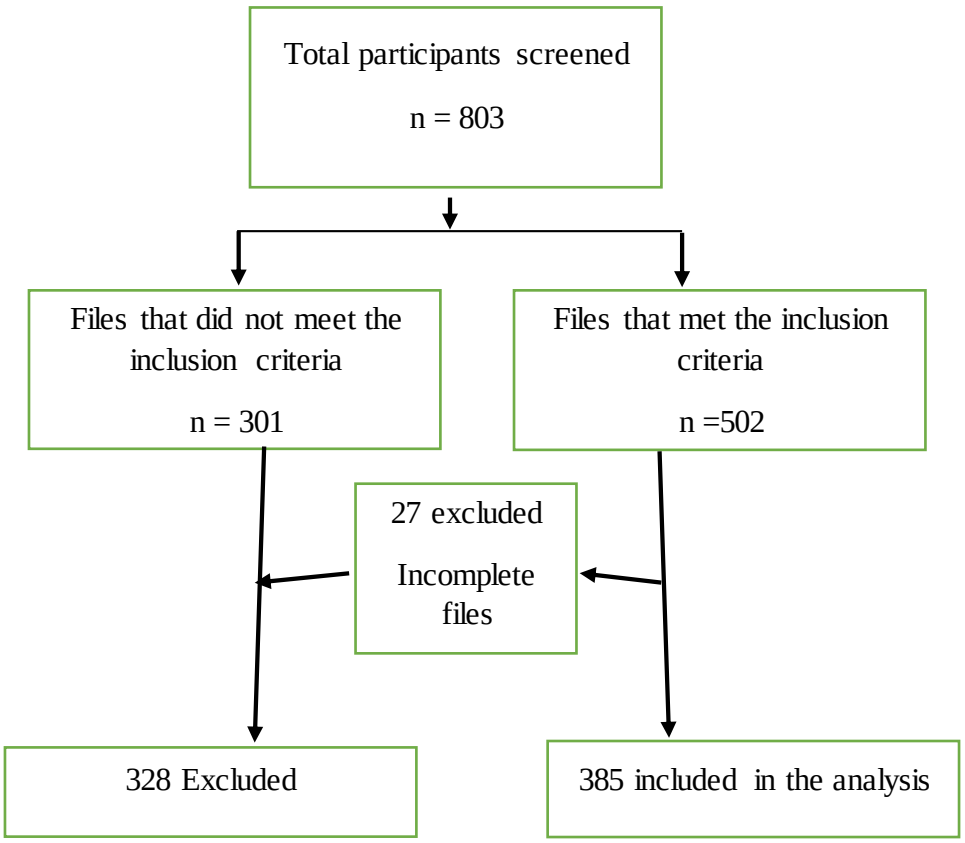

Figure 3 0: Patients selection Flowchart

4.2. Sociodemographic characteristics of HELLP syndrome patients seen at the Kenyatta National Hospital

The average age of patients with HELLP syndrome was 28.92(SD±6.07) years, 43.9% (n =169) had secondary level education, 63.6% (n =245) were unemployed while 84.4% (n =325) were married and shown in Table 1.

Table 4.1 1: Descriptive statistics of the sociodemographic characteristics of HELLP syndrome patients seen at the Kenyatta National Hospital

Socio-demographic factors	N=385	Frequency n (%)
Age (years)(Mean ±SD)		28.92±6.07
≤20		35(9.1)
21 – 25		93(24.2)
26 – 30		101(26.2)
Above 30		156(40.5)
Education level		
None		16(4.2)
Primary level		101(26.2)
Secondary level		169(43.9)
Tertiary level		99(25.7)
Employment status		
Unemployment		245(63.6)
Employed		34(8.8)
Self-employment		106(27.5)
Marital status		
Single		60(15.6)
Married		325(84.4)

4.3. Clinical characteristics of HELLP syndrome patients seen at the Kenyatta National Hospital

The findings revealed that 24.7% (95) were nulliparous, and 65.2% (251) of the patients were between para 1 and para 3. In investigating gestational age at diagnosis, 74.3% (286) were diagnosed before 37 weeks gestation, 27.8% (107) were 34 to less than 37 weeks of gestation, 11.2% (43) were diagnosed with HELLP when they were less than 28 weeks of pregnancy while 10.6% (41) were diagnosed after delivery. A history of chronic hypertension was present in 5.5% (21) of the patients, previous history of pre-eclampsia in 10.6% (41), and only 0.3% (1) had a previous history of HELLP syndrome. Further assessment revealed that 87.8% (338) had attended at least one antenatal care visit. The common symptoms experienced among patients included epigastric pain 67.8% (261), headache 59.7% (230), and blurry vision 29.1% (112) as shown in Table 2.

Table 4.2 1: Clinical characteristics of HELLP syndrome patients seen at the Kenyatta National Hospital

Clinical characteristics	**N=385**	**n (%)**
Parity		
Nulliparous		95(24.7)
Para 1 -3		251(65.2)
Para ≥4		39(10.1)
Gravidity		
G1		110(28.6)
G2 – 3		102(26.5)
G≥4		173(44.9)
Gestational age		
Preterm		286(74.3)
< 28 weeks		43(11.2)
28 to < 32 weeks		69(17.9)
32 to <34 weeks		67(17.4)
34 to <37 weeks		107(27.8)
Term		99(25.7)
≥37 weeks		58(15.1)
Post-delivery		41(10.6)
History of previous pre-eclampsia		
Yes		41(10.6)
No		344(89.4)
History of previous HELLP syndrome		
Yes		1(0.3)
No		384(99.7)
History of chronic hypertension		
Yes		21(5.5)
No		364(94.5)
History of diabetes		
Yes		4(1.0)
No		381(99.0)
ANC Visit attendance		
Yes		338(87.8)
No		47(12.2)
Number of ANC visits (n =338)		
Less than 4 visits		165(48.8)
4 or more visits		173(51.2)
Epigastric pain		
Yes		261(67.8)
No		124(32.2)
Blurry vision		
Yes		112(29.1)
No		273(70.9)
Headache		
Yes		230(59.7)
No		155(40.3)
Systolic		
Normal (<140mmHg)		138(35.8)

Abnormal (>=140mmHg)	247(64.2)
Diastolic	
Normal (<90mmHg)	106(27.5)
Abnormal (>=90mmHg)	279(72.5)

4.4. Biological characteristics of HELLP syndrome patients seen at the Kenyatta National Hospital

Biological factors investigated have shown that the average ALT was 209.5(SD±118.4) IU/L. The AST average was 281.7 (SD±151.4) units/L. The mean LDH was 951 (SD±342.9) units/L while the platelet count was 78.100 (SD±41) per microliter.

Table 4.3 1: Biological factors of HELLP syndrome patients seen at the Kenyatta National hospital

Biological factors N=385	Mean ±SD
Alanine Transferase (ALT)	209.5±118.4
Aspartate Aminotransferase (AST)	281.7±151.4
Lactate Dehydrogenase (LDH)	951±342.9
Platelet count	78.1±41
Creatinine	144.3±118
Albumin levels	28.8±6
Uric acid	536±232
G-GT level	70.8±20
Hemoglobin levels	12.2±10
Total bilirubin	43±18.1

4.5. HELLP Syndrome classification among patients seen at the Kenyatta National Hospital

HELLP was classified based on the Mississippi classification and we found that 38.4% (120) of patients were in class II, 31.2% (120) were in class I category while 30.4% (117) were in class III as presented in Figure 4.

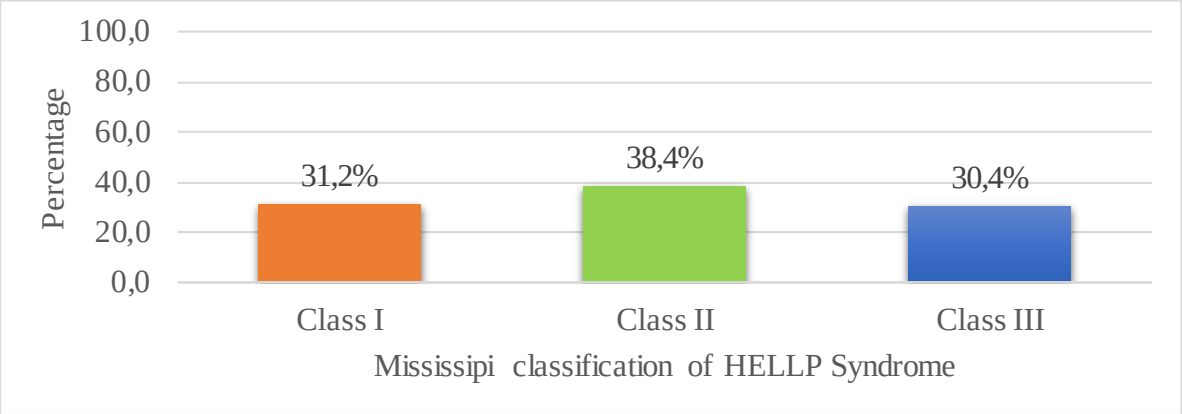

Figure 4 0: HELLP Syndrome classification

4.6. Maternal adverse outcomes in HELLP syndrome patients seen at Kenyatta National Hospital

The results of the study revealed that 76.4% (294) of the mothers with HELLP syndrome developed at least an adverse outcome, with 64.9% (250) of eclampsia, 44.7% (172) blood/blood products transfusion, 34.5% (133) renal failure, 18.2% (70) bleeding disorders, 18.1% (71) ICU admission, 7% (27) cerebrovascular accident (CVA), placental abruption 6.5% (25) and 4.7% (18) brain edema. Further, 61.3% (236) of women were delivered by a caesarean section whereas the majority of 83.9% (198) underwent a primary caesarean section. Maternal death occurred in 9.1% (35) as shown in Table 4.

Table 4.4 1: Adverse maternal outcomes in HELLP syndrome patients seen at Kenyatta National Hospital

Maternal adverse outcomes	**N=385**	**n (%)**
Mode of delivery		
Spontaneous vaginal delivery		149(38.7)
Caesarean section		236(61.3)
Primary CS (n =236)		198(83.9)
Maternal Adverse outcomes		294(76.4)
Eclampsia		250(64.9)
Renal failure		133(34.5)
Bleeding disorder (DIC, PPH)		70(18.2)
Blood/blood products transfusion		172(44.7)
Hypovolemic choc		3(0.8)
Placental abruption		25(6.5)
Pulmonary edema		10(2.6)
Brain edema		18(4.7)
Stroke/ CVA		27(7)
Liver hematoma		10(2.6)
Intensive Care Unit (ICU) admission		71(18.1)
Maternal death		35(9.1)
Length of hospital stay (Mean ±SD) days		11.1±9.3 (Min=1day, max =61 days)

4.7. Adverse perinatal outcomes in patients with HELLP syndrome seen at Kenyatta National Hospital

This investigation demonstrated that 81.3% (313) of the infants presented at least an adverse outcome. The majority 73% (281) were premature, with 29.1% (112) born between 34 weeks and 37 weeks, 27.8% (107) between 28 - 32 weeks, and 9.6% (37) before 28 weeks of gestation. The study found that 35% (135) of pregnancies ended in stillbirths with 24.9% (96) macerated and 10.1% (39) fresh stillbirths. There were 63.9% (246) as shown in Table 5.

Table 4.5 1: Adverse perinatal outcomes in patients with HELLP syndrome seen at the KNH

Adverse perinatal outcomes	**N=350**	**n (%)**
Adverse perinatal outcome		313 (81.3)
Preterm birth (<37 weeks)		281(73)
SGA		81(21)
Low birth weight (<2500g)		278(72.2)
Apgar score at 5th min (<7)		167(43.4)
Stillbirths (MSB+FSB)		135(35.0)
Macerated Still Birth (MSB)		96(24.9)
Fresh stillbirth (FSB)		39(10.1)
Neonatal sepsis		3(0.8)
Jaundice		4(1)
Respiratory Distress Syndrome (RDS)		101(26.2)
Neonatal Intensive Care Unit (NICU) admission		190(49.4)
Neonatal death		111(28.8)
Perinatal death		246(63.9)

4.8. Factors associated with maternal and perinatal adverse outcomes in women with HELLP syndrome at the Kenyatta National Hospital

4.8.1. Demographic factors associated with adverse maternal and perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

There was no significant association between demographic characteristics and both maternal and perinatal adverse outcomes as shown in Table 6.

Table 4.6 1: Demographic factors associated with adverse maternal and perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

	Maternal adverse outcome				**Perinatal adverse outcome**			P-value
	No	**Yes**	**Odds Ratio**	**P-value**	No	Yes	Odds Ratio	
Age (Years)								
≤20	7(7.7)	28(9.5)	Ref		7(7.7)	28(9.5)	Ref	
21 – 25	20(22)	73(24.8)	0.8(0.33 - 1.99)	0.637	20(22)	73(24.8)	0.9(0.24 - 2.38)	0.842
26 – 30	27(29.7)	74(25.2)	0.9(0.48 - 1.63)	0.688	27(29.7)	74(25.2)	0.8(0.43 - 1.67)	0.623
Above 30	37(40.7)	119(40.5)	1.2(0.66 - 2.09)	0.585	37(40.7)	119(40.5)	1.2(1.22 - 2.22)	0.531
Marital status								
Single	12(13.2)	48(16.3)	Ref		11(15.3)	49 (15.7)	Ref	
Married	79(86.8)	246(83.7)	1.3(0.65 - 2.54)	0.471	61(84.7)	264 (84.3)	1.0(0.51 - 2.11)	0.937
Level of education								
None/Primary	25(27.5)	92(31.3)	Ref		27(36.5)	90(28.7)	Ref	
Secondary	39(42.9)	130(44.2)	0.7(0.39 - 1.35)	0.313	32(44.4)	137(43.8)	1.9(0.96 - 4.1)	0.064
Tertiary	27(29.7)	72(24.5)	0.8(0.45 - 1.41)	0.442	13(18.1)	86(27.5)	1.6(0.77 - 3.11)	0.222
Employment status								
Unemployment	57(62.6)	188(63.9)	0.9(0.74 - 1.26)		51(70.8)	194(62)	Ref	
Employed	34(37.4)	22(7.5)			21(29.1)	29(9.3)	0.8(0.6 - 1.1)	0.185

4.8.2. Clinical characteristics associated with adverse maternal and perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

In investigating factors associated with maternal adverse outcome, gestational age at diagnosis (<37 weeks) (COR =2.2, 95% CI:1.2-4.2, p = 0.011), ANC attendance (COR =7.8, 95% CI:1.9-33.0, p = 0.005), number of ANC visits (<4) (COR =1.8, 95% CI:1.1-2.9, p = 0.005), blurry vision (COR =2.7, 95% CI:1.3-3.1, p<0.001), systolic (COR =6.4, 95% CI:2.7-15.3, p<0.001) and diastolic pressure (COR =7.3, 95% CI:4.3-12.2, p<0.001) were associated with increased likelihood of adverse maternal outcome.

The findings also revealed that, gestational age at diagnosis (COR =5.4, 95% CI: 2.1-3.1, p<0.001), number of ANC visits (COR =1.7, 95% CI: 1.7-3.02, p=0.049) and epigastric pain (COR =2.1, 95% CI: 1.2-3.5, p=0.007) were associated with increased risk of adverse perinatal outcomes as shown in Table 7.

Table 4.7 1: Clinical characteristics associated with adverse maternal and perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

	Maternal adverse outcome				Perinatal adverse outcome			
	No	**Yes**	**COR**	**P-value**	**No**	**Yes**	**COR**	**P-value**
Parity	No	Yes						
Nulliparous	19(20.9)	76(25.9)	Ref		13(18.1)	82(26.2)	Ref	
Para 1 -3	64(70.3)	187(63.6)	0.9(0.4-2.5)	0.946	55(76.4)	196(62.6)	1.3(0.4-4.6)	0.589
Para ≥4	8(8.8)	31(10.5)	1.3(0.6-3.1)	0.504	4(5.6)	35(11.2)	2.3(0.8-7.2)	0.102
Gestational age at diagnosis								
<37	77(84.6)	209(71.1)	2.2(1.2-4.2)	**0.011**	32(44.3)	254(81.1)	5.4(2.1-3.1)	**p<0.001**
≥37	14(15.4	85(28.9)	Ref		40(35.5)	59(18.9)	Ref	
Previous pre-eclampsia								
Yes	13(14.3)	28(9.5)	0.6(0.3-1.3)	0.201	7(9.7)	34(10.9)	0.9(0.2 - 2.6)	0.671
No	78(85.7)	266(90.5)	Ref		65(90.3)	279(89.1)	Ref	
Chronic hypertension								
Yes	7(7.7)	14(4.8)	0.6(0.2-1.5)	0.287	2(2.8)	19(6.1)	0.3(0.2-1.6)	0.134
No	84(92.3)	280(95.2)	Ref		70(97.2)	294(93.9)	Ref	
Attended Antenatal Clinic (ANC)								
Yes	89(97.8)	45(15.3)	7.8(1.9-33)	**0.005**	66(91.7)	273(87.2)	0.6(0.3-1.5)	0.298
No	2(2.2)	249(84.7)			6(8.3)	40(12.8)		
Number of ANC visits								
< 4	52(59.1)	137(54.8))	1.8(1.1-2.9)	**0.026**	25(37.9)	140(51.5)	1.7(1.0-3.02)	**0.049**
≥4	36(40.9)	113(45.2	Ref		41(62.1)	132(48.5)	Ref	
Epigastric pain								
Yes	63(69.2)	198(67.3)	0.9(0.6-1.5)	0.737	39(54.2)	222(70.9)	2.1(1.2-3.5)	**0.007**
No	28(30.8)	96(32.7)			33(45.8)	91(29.1)	Ref	
Blurry vision								
Yes	20(22)	92(31.3)	2.7(1.3-3.1)	**p<0.001**	16(22.2)	96(30.7)	1.7(0.9-3.2)	0.113
No	71(78)	202(68.7)			56(77.8)	217(69.3)	Ref	
Headache								
Yes	52(57.1)	178(60.5)	1.2(0.7-1.9)	0.563	190(60.7)	40(55.6)	1.2(0.7-2.1)	0.161
No	39(42.9)	116(39			123(39.3)	32(44.4)	Ref	
Systolic								
Normal	85(93.4)	53(18)	Ref		112(35.8)	26(36.1)		
Abnormal	6(6.6)	241(82)	6.4(2.7-15.3)	**p<0.001**	201(64.2)	46(63.9)	0.9(0.6-1.7)	0.958
Diastolic								
Normal	55(60.4)	51(17.3)	Ref		91(29.1)	15(20.8)		
Abnormal	36(39.6)	243(82.7)	7.3(4.3-12.2)	**p<0.001**	222(70.9)	57(79.2)	1.6(0.8-2.9)	0.161
Classification of HELLP								
Class I	33(36.3)	87(29.6)	Ref		20(27.8)	100(31.9)	Ref	
Class II	29(31.9)	119(40.5)	1.2(0.6-2.1)	0.635	29(40.3)	119(38)	0.6(0.8-1.6)	0.512
Class III	29(31.9)	88(29.9)	0.7(0.41-1.33)	0.311	23(31.9)	94(30)	0.9(0.5-1.8)	0.651

4.8.3. Biological factors associated with adverse maternal and perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

An increase in one IU/L of ALT was associated with 2.5 times more likely to have an adverse maternal outcome (COR =2.5, 95% CI: 1.2-4.2, p =0.029). An increase in one units/L of AST was associated with a 2.1 times higher chance of having a maternal adverse outcome (COR =2.1, 95% CI: 1.2, 5.3, p = 0.001. An increase in one-unit mg/dL of creatinine was associated with an 80% increased chance of having maternal adverse outcomes (COR = 1.8, 95%CI: 1.2-3.6, p= 0.002). An increase in total bilirubin by one µmol/L was associated with a 20% increased chance of having adverse maternal outcomes (COR = 1.2, 95%CI: 1.0-5.1, p= 0.049). There was no significant association between biological factors and adverse perinatal outcomes as shown in Table 8.

Table 4.8 1: Biological factors associated with adverse maternal and perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

Biological factors	Maternal adverse outcome				Perinatal adverse outcome			
	No	Yes	Odds Ratio	P-value	No	Yes	Odds Ratio	P-value
ALT (IU/L)	153.62	226.78	2.5(1.2-4.2)	**0.029**	168.97	218.79	1.2(0.4-2.3)	0.156
AST (IU/L)	169.56	316.47	2.1(1.2-5.3)	**0.001**	231.28	293.35	0.6(0.4-1.4)	0.2
LDH (U/L)	865.76	982.32	1.5(0.5-4.1)	0.332	911.91	986.14	0.6(0.3-1.3)	0.229
Platelet (×1000/mcL)	75.94	78.8	0.6(0.2-2.12)	0.563	82.9	77.03	0.5(0.3-0.9)	0.276
Creatinine (mg/dL)	110.29	154.88	1.8(1.2-3.6)	**0.002**	137.04	146.02	0.1(0.01 - 1.8)	0.562
Albumin (g/dL)	29.4	28.67	0.8(0.2-1.21)	0.323	29.88	28.61	0.3(0.02 - 2.7)	0.11
Uric acid (mg/dL)	451.28	565.31	1.2(0.7-2.3)	0.209	567.39	529.49	1.4(0.2 - 4.3)	0.722
G-GT level (IU/L)	76.14	69.12	1.0(0.6-3.2)	0.592	56.19	74.16	0.7(0.1 - 3.2)	0.211
HB levels (g/dl)	12.69	12.05	2.5(0.9-5.3)	0.623	13.87	11.81	0.15(0.07 - 1.5)	0.146
Bilirubin (µmol/L)	30.36	46.85	1.2(1.0-5.1)	**0.049**	36.13	44.57	0.4(0.1 - 3.5)	0.353

4.8.4. Multivariable logistic regression of factors associated with maternal adverse outcomes among HELLP patients at the Kenyatta national hospital

Multivariable analysis revealed that gestational age at diagnosis, blurry vision, systolic, diastolic, AST, ALT, and total bilirubin were independently associated with adverse maternal outcomes in patients with HELLP syndrome. Patients diagnosed less than 37 weeks were five times more likely to have maternal adverse outcomes compared to those diagnosed at term, (aOR = 4.5, 95% CI: 1.6-12.4, p =0.004).

Patients who had blurry vision were two times more likely to have the adverse maternal outcome (aOR =2.1, 95% CI: 1.1-5.2, p <0.001). Women who had abnormal systolic BP levels were 11 times more likely to have an adverse maternal outcome (aOR =11.4, 95% CI: 3.5-15.6, p<0.001) and 10 times more likely for abnormal diastolic BP (aOR =10.3, 95% CI: 3.8-27.8, p<0.001). An increase in one units/L of ALT was associated with 2.3 times increased likelihood of having an adverse maternal outcome, aOR =2.3, 95% CI: 1.1-4.5, p = 0.023, and an elevation in one IU/L of AST was associated with 1.6 times increase in the likelihood of having maternal adverse outcome, aOR =1.6, 95% CI:1.2-4.3, p =0.003. An increase in one unit of total bilirubin was associated with a 1.4 times increase in the likelihood of having maternal adverse outcomes (aOR = 1.4, 95% CI: 1.0-2.3, p= 0.007), as shown in Table 9.

Table 4.9 1: Multivariable logistic regression of factors associated with adverse maternal outcomes among HELLP patients at the Kenyatta National Hospital

Factors	aOR (95%CI)	P-value
Gestational age at diagnosis (<37 weeks)	4.5(1.6-12.4)	**0.004**
ANC Visits (<4)	1.4(0.6-3.2)	0.496
Blurry vision	2.1(1.1-5.2)	**<0.001**
Systolic (Abnormal)	11.4(3.5-15.6)	**<0.001**
Diastolic (Abnormal)	10.3(3.8-27.8)	**<0.001**
Alanine Transferase (ALT)	2.3(1.1-4.5)	**0.023**
Aspartate Aminotransferase (AST)	1.6(1.2-4.3)	**0.003**
Creatinine	1.0(0.7-1.8)	0.188
Total bilirubin	1.4(1.0-2.3)	**0.007**

4.8.5. Multivariable logistic regression of factors associated with adverse perinatal outcomes among HELLP syndrome patients at the Kenyatta National Hospital

Multivariable analysis revealed that gestational age at diagnosis (<37) was significantly associated with an increased risk of adverse perinatal outcomes. Those who were diagnosed with HELLP syndrome at gestational age <37 weeks were 3.5 times more likely to have adverse perinatal outcomes compared to those diagnosed at term (aOR = 3.5, 95% CI: 1.6-8.7, p<0.001) as shown in Table 10.

Table 4.10 1: Multivariable logistic regression of Factors associated with perinatal adverse outcomes among HELLP patients at the Kenyatta National hospital

Factors	aOR (95%CI)	P-variable
Gestational age at diagnosis (<37 weeks)	3.5(1.6,8.7)	<0.001
ANC visits (<4)	1.5(0.8,2.6)	0.193
Epigastric pain	1.3(0.7,2.4)	0.337

4.9. Factors associated with selected adverse maternal outcomes among women with HELLP syndrome at the Kenyatta National Hospital

The study examined selected maternal adverse outcomes among women with HELLP Syndrome as shown in Table 16. The findings from the analysis showed that age (p = 0.036),

parity (p = 0.03), history of preeclampsia (p =0.001), ANC attendance (p =0.019), and uric acid were significantly associated with eclampsia among women with HELLP syndrome.

The findings revealed that gestational age at diagnosis (p =0.003), ANC attendance (p <0.001), blurry vision (p<0.001), ALT (p<0.001), ALT (p<0.001), creatinine level (p<0.001), albumin (p = 0.001) and total bilirubin (p<0.001) were significantly associated with renal failure among HELLP syndrome.

The level of education (p =0.049), gestational age at diagnosis (p =0.029), ANC attendance (p =0.006), blurry vision (p<0.001), class I HELLP (p<0.001), AST (p<0.001), ALT (p<0.001), platelets (p<0.001), creatinine levels (p<0.001), HB levels (p =0.001) and bilirubin (p =0.002) were significantly associated with bleeding disorders.

The history of preeclampsia (p =0.016), ANC attendance (p =0.042), blurry vision (p =0.049), HELLP classification (p =0.028), AST (p<0.001), ALT (p<0.001), platelets (p = 0.037), creatinine level (p<0.001), albumin levels (p =0.001) and bilirubin levels (p<0.001) were significantly associated with maternal death.

Table 4.11 1: Factors associated with selected adverse maternal outcomes among women with HELLP syndrome at the Kenyatta National hospital

Variable	Eclampsia P-value	Renal failure P-value	Bleeding disorders P-value	Maternal death P-value
Socio-demographic				
Age	**0.036**	0.819	0.919	0.779
Marital status	0.229	0.257	0.315	0.472
Education level	0.836	0.495	**0.049**	0.486
Employment status	0.275	0.653	0.075	0.347
Clinical characteristics				
Parity	**0.03**	0.222	0.369	0.718
Gestational age at diagnosis	0.195	**0.003**	**0.029**	0.735
History of preeclampsia	**0.04**	0.178	0.053	**0.016**
History of hypertension	0.157	0.445	0.348	0.412
ANC attendance	**0.001**	**<0.001**	**0.006**	**0.042**
Epigastric pain	0.406	0.297	0.098	0.458
Blurry vision	**0.019**	**<0.001**	**<0.001**	**0.049**

Headache	0.09	**0.008**	0.052	0.562
HELLP Classification	0.845	0.077	<**0.001**	**0.028**
Biological characteristics				
ALT	0.066	<**0.001**	**0.025**	<**0.001**
AST	0.008	<**0.001**	**0.002**	<**0.001**
LDH	0.964	0.073	0.585	0.508
Platelets	0.555	0.068	<**0.001**	**0.037**
Creatinine	0.204	<**0.001**	<**0.001**	<**0.001**
Albumin	0.656	**0.001**	0.77	**0.001**
Uric acid	**0.03**	0.947	0.232	0.592
G-GT levels	0.38	0.068	0.476	0.343
HB levels	0.724	0.709	**0.001**	0.475
Bilirubin	0.447	<**0.001**	**0.002**	<**0.001**

4.9.1. Multivariable analysis of factors associated with selected maternal adverse outcomes among women with HELLP syndrome at the Kenyatta National Hospital

The findings showed that multiparity and previous history of preeclampsia were independent factors associated with eclampsia among women with HELLP Syndrome. ANC attendance, headache, AST, and total bilirubin levels were independent factors associated with renal failure among women with HELLP syndrome. Having blurry vision, AST, and hemoglobin levels were independent factors associated with bleeding disorders. ANC attendance, AST, and albumin levels were independent factors associated with maternal death among women with HELLP syndrome.

Table 4.12 1: Independent factors associated with selected adverse maternal outcomes among women with HELLP syndrome at the Kenyatta National hospital

	aOR (95%CI)	P-value
Eclampsia		
Age	0.93(0.74,1.16)	0.112
Parity		
Nulliparous	Ref	
Para 1 -3	(2.1(1.2, 4.32)	**0.008**
Para ≥4	0.39(0.22, 4.12)	0.546
History of previous pre-eclampsia	3.2(1.8, 6.51)	**0.041**
ANC	2.3(0.51, 5.11)	0.561
AST	1.0(0.998, 1.002)	0.912
Uric acid	0.996(0.990,1.002)	0.161
Renal failure		
Gestational age at diagnosis	0.96(0.59,1.58)	0.884
ANC attendance	5.04(2.15,11.82)	**<0.001**
Blurry vision	1.9(1.0, 3.56)	0.050
Headache	2.5(1.29,4.99)	**0.007**
ALT	1.0(0.999,1.003)	0.404
AST	2.3(1.4,5.44)	**0.020**
Creatinine	1.9(0.98,0.99)	**0.981**
Albumin levels	1.01(0.96,1.07)	0.610
Total bilirubin	2.21(1.3, 4.41)	**0.039**
Bleeding disorders		
Gestational age at diagnosis	1.07(0.72, 1.6)	0.731
Attended Antenatal Clinic (ANC)	1.89(0.87,4.09)	0.109
Blurry vision	2.39(1.38,4.12)	**0.002**
ALT	1.0(1.0, 1.004)	0.062
AST	2.5(1.3,6.41)	**0.032**
Platelet count	1.0(0.992,1.03)	0.335
Creatinine	1.1(0.993,0.999)	0.314
Haemoglobin levels	1.38(1.25,1.53)	**<0.001**
Total bilirubin	1.0(0.996,1.005)	0.849
Classification of HELLP Syndrome	1.25(0.53,2.97)	0.610
Maternal death		
History of previous pre-eclampsia		
Attended Antenatal Clinic (ANC)	3.04(1.08,8.54)	**0.035**
Alanine Transferase (ALT)	1.0(0.998,1.002)	0.870
Aspartate Aminotransferase (AST)	2.7(1.2, 8.11)	**0.023**
Platelet count	0.995(0.964,1.03)	0.754
Albumin levels	1.08(1.0,2.51)	**0.037**
Total bilirubin	0.991(0.986,0.996)	0.051
Classification of HELLP Syndrome	1.42(0.28,7.17)	0.673

3.17.1. Factors associated with selected adverse perinatal outcomes among women with HELLP syndrome at the Kenyatta National Hospital

The findings revealed that maternal age (p =0.005), gestational age at diagnosis (p<0.001), epigastric pain (p<0.001), headache, and G-GT levels were significantly associated with prematurity.

Parity (p =0.001), ANC attendance (p =0.019), HELLP classification (p =0.008), AST (p<0.001), ALT (p<0.001), LDH (p =0.028), platelets (p = 0.002), creatinine level (p<0.001), bilirubin levels (p =0.003) were significantly associated with stillbirth among women with HELLP syndrome.

Gestational age at diagnosis (p =0.005), epigastric pain (p =0.039), AST (p=0.011), ALT (p<0.001), LDH (p =0.028), creatinine level (p=0.008) and bilirubin levels (p =0.005) were significantly associated with respiratory distress syndrome among women with HELLP syndrome.

Parity (p =0.028), gestational age diagnosis (p<0.001), ANC attendance (p=0.007), epigastric pain (p <0.001), headache (p=0.017) and G-GT levels (p =0.02) were significantly associated with neonatal death among women with HELLP syndrome.

Table 4.13 1: Factors associated with selected adverse perinatal outcomes among women with HELLP syndrome at the Kenyatta National hospital

	G.A at birth P-value	Stillbirths P-value	RDS P-value	Neonatal death P-value
Age	**0.005**	0.946	0.858	0.412
Marital status	0.336	0.233	0.15	0.292
Education level	0.238	0.519	0.634	0.667
Employment status	0.639	0.685	0.726	0.295
Parity	0.233	**0.001**	0.06	**0.028**
G A at diagnosis	**<0.001**	0.066	**0.005**	**<0.001**
History of preeclampsia	0.571	0.522	0.326	0.266
History of hypertension	0.289	0.292	0.487	0.232
ANC attendance	0.481	**0.019**	0.57	**0.007**
Epigastric pain	**<0.001**	0.249	**0.039**	**<0.001**
Blurry vision	0.114	0.43	0.147	0.099
Headache	**0.003**	0.486	0.163	**0.017**
HELLP Classification	0.638	**0.008**	0.498	0.552
ALT	0.407	**<0.001**	**0.011**	0.481
AST	0.108	**<0.001**	**<0.001**	0.437
LDH	0.175	**0.028**	**0.028**	0.847
Platelets	0.678	**0.002**	0.119	0.498
Creatinine	0.936	**<0.001**	**0.008**	0.537
Albumin	0.776	0.278	0.877	0.542
Uric acid	0.983	0.15	0.633	0.108
G-GT levels	**0.001**	0.982	0.475	**0.02**
HB levels	0.528	0.188	0.904	0.79
Bilirubin	0.837	**0.003**	**0.005**	0.456

3.17.2. Multivariable logistic regression for factors associated with selected adverse perinatal outcomes among women with HELLP syndrome

The study demonstrated that maternal age and gestational age at diagnosis were independent factors associated with preterm births among women with HELLP syndrome. LDH and Creatinine levels were independent factors associated with stillbirths among women with HELLP syndrome. Having epigastric pain was an independent factor associated with RDS among women with HELLP syndrome. Parity and gestational age at diagnosis were independent factors associated with neonatal death among women with HELLP syndrome as shown in Table 14.

Table 4.14 1: Factors associated with selected adverse perinatal outcomes among women with HELLP syndrome at the Kenyatta National Hospital

	aOR(95%CI)	P-value
Gestational age		
Age	2.62(1.3-5.22)	**0.048**
Gestational age at diagnosis	5.13(3.39-7.76)	**<0.001**
Epigastric pain	1.4(0.8-2.55)	0.232
Headache	1.05(0.59-1.86)	0.863
G-GT level	061(0.21-3.22)	0.061
Stillbirths		
Parity		
Nulliparous	Ref	
Para 1 -3	1.81(0.25-13.24)	0.558
Para ≥4	0.93(0.19-4.63)	0.931
Attended Antenatal Clinic (ANC)	2.88(1.24-11.35)	0.406
Classification of HELLP Syndrome	2.0(0.2-4.11)	0.553
Alanine Transferase (ALT)	0.998(0.992-1.004)	0.484
Aspartate Aminotransferase (AST)	1.0(0.996-1.004)	0.862
Lactate Dehydrogenase (LDH)	0.996(0.997-1.00)	**0.049**
Platelet count	0.98(0.94-1.03)	0.426
Creatinine	0.99(0.98-0.999)	**0.033**
Total bilirubin	1.01(0.997-1.61)	0.206
RDS		
Gestational age at diagnosis	1.21(0.17-8.49)	0.850
Epigastric pain	2.3(1.5-9.55)	**0.024**
Alanine Transferase (ALT)	0.997(0.989-1.006)	0.554
Aspartate Aminotransferase (AST)	1.01(0.14-6.44)	0.175
Lactate Dehydrogenase (LDH)	1.0(0.56-4.11)	0.191
Creatinine	1.2(0.76-3.11)	0.206
Total bilirubin	0.997(0.989-1.006)	0.243
Neonatal death		
Parity		
Nulliparous	Ref	
Para 1 -3	3.11(1.32-7.47)	**0.010**
Para ≥4	2.34(1.09-5.0)	**0.029**
Gestational age at diagnosis	2.8(1.67-4.77)	**<0.001**
Attended Antenatal Clinic (ANC)	0.45(0.22-0.93)	0.030
Epigastric pain	1.86(1.04-3.3)	0.036
Headache	1.18(0.71-1.98)	0.529
G-GT level	0.999(0.997-1.001)	0.246

CHAPTER FIVE: DISCUSSION

The present study examined adverse maternal and perinatal outcomes and associated risk factors in patients with HELLP Syndrome in a referral hospital in Kenya. The results showed that 40.5% of patients were aged above 30 years with a mean age of 28.92 years; this is similar to the study by *Déruelle et al*. (2005/France) where the average maternal age was 28.9 years and comparable to that found by *Katz et al*. in a study done in Brazil which found that the average age was 26.7 years (35). *Malmstrom and Morken* in their population-based study in Norway also revealed that the risk of HELLP is higher in women aged between 25 years and 29 years (45). In contrast, *Chidanandaiah et al.* (2018/India) found in their study that the mean age in mothers was as lower as 22.5 years (46).

In this present study, 43.9% of participants had a secondary level of education. This may be because the majority of Kenyans have secondary level education as the highest level of education(47). In addition, our findings also revealed that 84.4% of patients were married and 64% were unemployed.

Our investigation revealed that 24.7% of the patients were nulliparous compared to 75.3% who were parous at diagnosis. These findings, however, contrast those from studies conducted in the Netherlands by *Roelofsen et al.(36)* and *Lisonkova et al.* in Canada where nulliparous accounted for 70.7% and 34%, respectively (7). The difference could be due to the late and planned onset of childbearing in high-income countries as well as the limited family as women are more empowered. Most of the patients with HELLP recruited in our study were diagnosed before 37 weeks of gestation. This is comparable to a review by *Haram et al.* in which they found that approximately 70% of the condition develops before delivery, with the majority occurring between the 27th and 37th gestational weeks (3).

Our study established that 88% had at least one ANC visit and 51.2% attended at least four visits. The common presenting symptoms in the present study included epigastric pain 67.8%, headache 59.7%, and blurry vision 29.1%. These findings align with a study conducted in Kenya by *Okello et al.* who found that HELLP was associated with a clinical history of epigastric pain(5). Similarly, *Wallace et al.* also found that the common symptoms in patients with HELLP syndrome were epigastric pain, nausea, blurry vision, and vomiting (6).

Our current study found that the average ALT was 209.5(SD±118.4) IU/L IU/L, AST was 281.7(SD±151.4) IU/L, LDH was 951 (SD±342.9) IU/L while the mean platelet count was 78.1 (SD±41) per microliter. These findings are comparable to *Roelofsen et al.* in a study conducted in the Netherlands which revealed that there were higher levels of AST (263 (IQR:53–2576), ALT 207 (IQR:11–2147), and LDH 840 (IQR:602–6064) (36). However, *Katz et al.* found values lesser than those in our investigation. Delayed diagnosis with disease progression may be thought to be the cause of these disparities (27).

According to the Mississippi classification, class II was leading with 38.4%, class I with 31.2%, and 30.4% were class III. These results are comparable with the study done in Lithuania by *Rimaitis et al.* which found that 47.1% of patients with HELLP syndrome were classified in Class II. The difference in proportion between the two studies could be explained by the difference in sample size which was 53 compared to 385 in our present study (48). Moreover, the study conducted by *Martin et al.* in the USA showed that 44% were class I, 13% class II, and 24% class III, contrasting with our findings (15).

The present study found that 76.4% of mothers with HELLP syndrome developed adverse outcomes. These findings are higher compared to a study in India by *Anita et al.* in 2020 which revealed that 60% of women with HELLP syndrome developed complications. This

may be explained by late diagnosis and referral to our facility. The adverse maternal outcomes in our study included 64.9% of eclampsia, 44.7% need for blood/blood products transfusion, 34.5% renal failure, 18.2% bleeding disorders, 18.1% ICU admission, 4.7% brain edema, 7% stroke/CVA and 6% placental abruption. We found an elevated rate of adverse maternal outcomes, particularly eclampsia in this study as compared to *Haddad et al.* in a study conducted in the USA in which eclampsia was present only in 6% of women had eclampsia, placental abruption in 10% and the need for transfusion of blood products was 22% (16). However, a high rate of eclampsia was also found at 52% in a study with a small sample size by *Cavkaytar et al*. in Turkey, with 73% of caesarean deliveries higher than 61.3% found in our study (24). The same study showed a similar rate of caesarean deliveries to our findings.

In another investigation in Saudi Arabia by *Gasem et al.* (2009), maternal complications included 84.4% blood product transfusion, 36.4% Abruptio placentae, and 31.8% DIC, higher than the results of our study (49). The sample size may be the reason for this difference. In Canada, *Lisonkova et al.* found as less as 8.6% of eclampsia but 17.6% of severe hemorrhage comparable to our finding of 18.2% of bleeding disorders (7). Renal failure was as lesser as 22.9% in the same study compared to 34.5% found in our current results. *Chidanandaiah et al.,* also demonstrated 18.75% of ARF (46) while *Cavkaytar et al. (2007) Turkey* found 15% (24). Early diagnosis and prompt delivery may avoid the progression of HELLP syndrome to such complications. Another study conducted in Thailand by *Kongwattanakul et al.* identified that 9% of patients developed acute kidney failure (18). *Liu et al.* also found that the likelihood of acute renal failure among patients with HELLP syndrome was 5 five times higher while maternal death in patients with HELLP syndrome was two times higher (21).

The results in this study showed that maternal death occurred in 9.1%, which is comparable to the studies conducted by *Erdemoğlu et al.* which found 7.9% mortality (25), and by

Chidanandaiah et al. with 11.3% of maternal death. The little difference could be attributed to the difference in sample size and study settings. However, higher maternal mortality, up to 25%, has been reported (50).

Our investigation established that 81.3% of the infants developed an adverse outcome. The identified adverse outcomes included 66.5% prematurity, 72.2% low birth weight, 43.4% of low Apgar score, 35% stillbirths, 21% FGR, 26.2% RDS, 49.4% admission to NICU, and 28.8% neonatal death at 7th-day post-delivery. However, in a study conducted in India *by Anitha et al.* in 2020, the perinatal complications included 42.5% perinatal death, 40% NICU admission, 37% fetal growth retardation, and 20% stillbirth (19). Stillbirths were less in their but FGR was elevated compared to our findings. *Gasem et al. (2009)* also found as higher as 79.7% prematurity and 28% FGR (49). The study settings, late referral, and quality of perinatal care may explain the higher rates of IUFD and perinatal death in our study.

Gestational age at diagnosis < 37 weeks, absent or irregular ANC attendance, creatinine≥137 micromol/L, ALT ≥ 154 IU/L, AST ≥ 170 IU/L, and total bilirubin ≥ 30 micromol/L (1.75 mg/dL) were significantly associated with maternal adverse outcome. Women diagnosed with HELLP before term were more likely to develop adverse outcomes compared to those who were diagnosed at term. These findings are comparable to *Erkilinc* and *Eyi* in a study conducted in Turkey assessing clinical and laboratory parameters and adverse maternal outcomes in women with HELLP syndrome where the findings revealed that AST > 316 U/L, ALT > 217 U/L, total bilirubin >2.0 mg/dL, LDH > 1290 U/L, blood urea nitrogen (BUN) > 44 mg/dL, and low platelets (<50,000/mm3) were risk factors for unfavorable maternal outcomes (26).

Nevertheless, these findings are in contrast to those from *Haddad et al.* in a study conducted in the United States which revealed that a nadir platelet count of <50, 000/microL, a peak

serum AST >150 U/L, and an LDH level >1400 U/L were not independent risk factors for an adverse outcome (16). Thus, in their study, laboratory characteristics were not independent risk factors for adverse maternal outcomes. This may be explained by the difference in sample size between the two studies. However, the influence of laboratory parameters on adverse maternal outcomes among patients with HELLP syndrome needs to be more investigated to ascertain their extent or exact influence on the severity of outcomes.

The present study found that gestational age at diagnosis and ANC attendance were significantly associated with the perinatal adverse outcome although only gestational age at diagnosis was a significant independent factor associated with perinatal adverse outcome. These findings are consistent with *Kim et al.* (2006/Korea) who found that diagnosis of HELLP before 34 weeks of gestation was associated with increased fetal concerns and increased risk of perinatal adverse outcomes (10). Before 34 weeks of gestation, there exist fetal concerns related to prematurity and delay in the decision-making of delivery. Mississippi classification of HELLP syndrome did not influence perinatal adverse outcomes in our study. This is similar to a study conducted in Spain by *Miranda et al.* who found that the severity of the condition, as per Mississippi classification, was correlated with the rate of poor maternal outcomes but did not influence the fetal results (17).

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1. Conclusion

HELLP syndrome is a pregnancy complication associated with a higher rate of maternal and perinatal morbidity/mortality and may present with unspecific symptoms like epigastric/RUQ pain, headache, and blurred vision in the context of abnormal BP, particularly in the late second trimester and 3rd trimester.

The complications include among others eclampsia, renal failure, hemorrhagic disorders, need for blood/blood products transfusion, abruptio placentae, CVA, prematurity, FGR, RDS, IUFD, and maternal and perinatal mortality.

The gestational age at diagnosis, blurred vision, and BP levels are associated with adverse maternal outcomes in HELLP syndrome. Moreover, biological parameters such as ALT≥ 154 U/L, AST≥ 170U/L, and total bilirubin≥ 30 micromol/L (≥1.75 mg/dL) may be useful in predicting maternal complications without anticipating adverse perinatal outcomes. Only the gestational age at diagnosis was found to be significantly associated with perinatal complications.

6.2. Recommendations

To promote early and regular ANC attendance and screening for early diagnosis of HELLP syndrome particularly in patients presenting with epigastric/RUQ pain, headache, or blurred vision, particularly in the context of elevated BP.

To ensure close monitoring of maternal-fetal well-being, serial lab parameters (ALT, AST, Total bilirubin, LDH, and renal function test) assessment and multidisciplinary management of patients admitted with HELLP syndrome in view to plan for the timing of delivery accordingly to prevent progression to maternal and fetal complications.

To conduct further studies for more evidence on predictors of maternal and perinatal complications in HELLP syndrome that might be used to improve maternal outcomes and increase infant survival.

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APPENDICES

Appendix I: Data Abstraction tool

Section A: Sociodemographic data

1. What is the patient's age (years)? _____
2. What is the level of education?
   a) Primary [ ] c) Secondary [ ]
   b) Tertiary [ ] d) None [ ]
3. Does the patient gave employment history?
   a) Employed [ ] c) Self-employed [ ]
   b) Unemployed [ ]
4. What is the patient marital status?
   a) Married [ ] c) Separated [ ]
   b) Single [ ]

Section B: Clinical Characteristics

Please provide information on the following as documented on the patient file:

5. Parity……
6. Gravidity……..
7. Gestational age at diagnosis……..
8. Does the patient have a history of previous preeclampsia?
   Yes [ ] No [ ]
9. Does the patient have any history of HELLP syndrome?
   Yes [ ] No [ ]
10. Does the patient have a history of chronic hypertension?
    Yes [ ] No [ ]
11. Does the patient have a history of diabetes?
    Yes [ ] No [ ]
12. Did the patient attend an antenatal Clinic?
    Yes [ ] No [ ]
13. If yes, How many…….

Section C: Biological factors

Please provide information as documented in patient files on the following biological factors:

14. Alanine Transferase (ALT) ……
15. Aspartate Aminotransferase (AST)……
16. Lactate Dehydrogenase (LDH) …….
17. Platelet count……..
18. Creatinine……..
19. Urine Protein levels…….
20. Albumin levels…….
21. Uric acid …….
22. Hemoglobin levels…….
23. Total bilirubin ……..

Section D: HELLP syndrome classification

24. What is the classification of HELLP Syndrome

    Class I [ ] Class II [ ] class III [ ]

Section E: Maternal adverse outcome

25. What is the mode of delivery

    Spontaneous vaginal delivery [ ] Caesarean section [ ]

Which of the following adverse outcomes did the patient develop?

26. Eclampsia Yes [ ] No [ ]
27. Renal failure Yes [ ] No [ ]
28. Consumption coagulopathy (DIC) Yes [ ] No [ ]
29. Placental abruption Yes [ ] No [ ]
30. Pulmonary edema Yes [ ] No [ ]
31. Brain edema Yes [ ] No [ ]
32. Liver hematoma Yes [ ] No [ ]
33. Hypovolemic choc Yes [ ] No [ ]
34. Maternal death Yes [ ] No [ ]
35. Intensive Care Unit (ICU) admission Yes [ ] No [ ]

36. Hospital stay…….. days

Section F: Perinatal adverse outcome

37. Gestational age at delivery……..
38. Birth weight (grams)…….
39. Apgar score at 5 mins…….

Which of the following adverse outcomes did the patient develop?

40. Macerated Still Birth Yes [ ] No [ ]
41. Fresh still birth Yes [ ] No [ ]
42. Birth asphyxia Yes [ ] No [ ]
43. Neonatal sepsis Yes [ ] No [ ]
44. Jaundice Yes [ ] No [ ]
45. Respiratory Distress Syndrome (RDS) Yes [ ] No [ ]
46. Neonatal Intensive Care Unit (NICU) admission Yes [ ] No [ ]
47. Neonatal death [ ]
48. Other complication [ ] 49. Which? ……
50. Hospital stay…….days

UON-KNH ERC APPROVAL

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/74

25th February, 2022

Dr. Ernesto Lungena Miji
Reg. No. H58/34091/2019
Dept. of Obstetrics and Gynecology
Faculty of Health Sciences
University of Nairobi

APPROVED 25 FEB 2022

Dear Dr. Miji,

RESEARCH PROPOSAL: ADVERSE MATERNAL-PERINATAL OUTCOMES AND ASSOCIATED RISK FACTORS IN HELLP SYNDROME AT KENYATTA NATIONAL HOSPITAL; A FIVE YEAR ANALYTICAL CROSS-SECTIONAL STUDY (P837/10/2021)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P837/10/2021.** The approval period is 25th February 2022 – 24th February 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research mus: be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Protect to discover

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Chair, Dept. of Obstetrics and Gynecology, UoN
Supervisors: Dr. Alex Bosire, Dept. of Obstetrics and Gynecology, UoN
Dr. Diana Ondieki, Dept. of Obstetrics and Gynecology, UoN
Prof. Moses Obimbo, Dept. of Obstetrics and Gynecology, UoN

ADVERSE MATERNAL AND PERINATAL OUTCOMES AND ASSOCIATED RISK FACTORS IN WOMEN WITH HELLP SYNDROME AT KENYATTA NATIONAL HOSPITAL.

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