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MATERNAL AND FETAL OUTCOMES IN HELLP SYNDROME AT 23 WEEKS GESTATION: SYSTEMATIC REVIEW

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ABSTRACT

Introduction*: Hypertensive disorders, affecting 5-10% of pregnancies, are a leading cause of maternal and perinatal mortality. Preeclampsia-eclampsia, a syndrome contributing to significant global deaths, demands prompt identification and management, particularly in resource-limited settings. Detecting and addressing early and late-onset preeclampsia are crucial for maternal and neonatal well-being. HELLP syndrome, a severe complication of preeclampsia, presents diverse symptoms and risks, with a maternal mortality rate as high as 24%. Understanding its outcomes in pregnancies before 23 weeks is essential to guide better management strategies for improved maternal and neonatal health in such critical cases.*

Methods*: The researchers in this study followed the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to ensure that their work met the required standards. This was done to ensure the precision and reliability of the conclusions derived from the research.*

Result*: Our search produced 15 results. After looking at the titles and summaries, we found 6 papers that fit our criteria. At first, we excluded one articles because they were written in a review style. But after reading the full papers carefully, we included four papers in our final analysis. These papers included a retrospective observational study and several case reports.*

Conclusion*: Occurrences of HELLP syndrome without associated hypertensive disorders and recurrent intrahepatic ruptures at extremely premature gestational ages are rare but pose significant risks to mothers and newborns. Swift diagnosis, pregnancy termination, and continuous monitoring are crucial to address early-onset HELLP syndrome, emphasizing the need for immediate attention and prompt management.*

Keywords: *early gestation, HELLP syndrome, maternal hypertension, preeclampsia*

INTRODUCTION

Hypertensive disorders complicate a significant percentage of pregnancies, accounting for 5–10% and stand as a leading cause of maternal and perinatal mortality. The International Society for the Study of Hypertension in Pregnancy (ISSHP) classifies these disorders into "chronic" (existing before pregnancy or diagnosed before 20 weeks) or "de novo" (preeclampsia/eclampsia or gestational hypertension). Preeclampsia-eclampsia is considered a syndrome, with preeclampsia potentially arising independently or overlying chronic hypertension. This syndrome contributes to an estimated 60,000–80,000 maternal deaths annually and significantly impacts maternal, fetal, and neonatal health, particularly in low-resource nations. In resource-limited settings, the combination of pre-eclampsia-eclampsia syndrome, obstetric hemorrhage, and sepsis leads to preventable maternal and neonatal deaths.[1,2]

Numerous factors influence the morbidity and mortality associated with PE syndrome, including the timing of disease onset, distinguishing between early-onset (EO-PE) occurring before 34 weeks, and late-onset (LO-PE) manifesting at or after 34 weeks. These two forms are considered distinct in terms of their underlying processes and clinical outcomes.[3] Detecting and managing both types of preeclampsia promptly are critical. Delayed identification and treatment adversely impact both maternal and neonatal well-being.[4]

Weinstein introduced the HELLP syndrome—comprising hemolysis, elevated liver enzymes, and low platelets—as an additional marker for severe preeclampsia back in 1982. The American College of Obstetricians and Gynecologists specifies the HELLP criteria, including lactate dehydrogenase (LDH) levels ≥600 IU/L, significantly elevated aspartate transaminase and alanine transaminase (more than twice the upper limit of normal), and a platelet count <100×109/L. Other indicators such as schistocytes and echinocytes in a peripheral smear, low haptoglobin (≤25 mg/dL), and elevated bilirubin (≥1.2 mg/dL) are also used to confirm hemolysis.[5]

This syndrome arises in 0.5% to 0.9% of all pregnancies and in 10% to 20% of severe preeclampsia cases. Its presentation varies widely, often quickly emerging with symptoms like right upper quadrant (RUQ) pain, hypertension, proteinuria, general discomfort, nausea, and vomiting. However, some cases develop slowly, and approximately 15% might lack signs of hypertension or proteinuria. HELLP syndrome can be highly perilous, with reported maternal mortality rates as high as 24%. Affected mothers face increased risks of conditions such as abruptio placentae, premature delivery, disseminated intravascular coagulation (DIC), subcapsular hepatic hematoma, acute renal failure, and pulmonary edema. The primary treatment for confirmed cases is delivery. This syndrome typically occurs in the third trimester, with around 68% of cases between 27 and 37 weeks gestation. Postpartum onset is observed in about 25% of cases, while occurrences before 23 weeks are rare and not extensively understood.[5] The objective of studying HELLP syndrome outcomes on pregnancies of less than 23 weeks gestation is to understand the rarity, severity, and potential complications associated with this condition, aiming to guide timely and effective management strategies to improve maternal and neonatal outcomes in these critical situations.

METHODS

Protocol

The researchers in this study followed the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to ensure that their work met the required standards. This was done to ensure the precision and reliability of the conclusions derived from the research.

Criteria for Eligibility

For inclusion in the study, published articles had to meet particular requirements. They had to be research papers written in English, focusing maternal and fetal outcomes in HELLP syndrome at 23 weeks gestation. The studies had to meet the following criteria: they needed to have been published after 2017 but within the applicable timeframe for this systematic review. Articles falling into categories like editorials, lacking a DOI, review articles that were already published, or duplicating previously published journal papers were excluded from the assessment.

Search Strategy

We conducted a comprehensive literature search using PubMed and Google Scholar, focusing on studies published from 2017 to 2023. The search terms employed were as follows: ("maternally"[All Fields] OR "maternities"[All Fields] OR "maternity"[All Fields] OR "mothers"[MeSH Terms] OR "mothers"[All Fields] OR "maternal"[All Fields]) AND ("fetale"[All Fields] OR "fetally"[All Fields] OR "fetals"[All Fields] OR "fetus"[MeSH Terms] OR "fetus"[All Fields] OR "fetal"[All Fields] OR "foetal"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields]) AND ("hellp syndrome"[MeSH Terms] OR ("hellp"[All Fields] AND "syndrome"[All Fields]) OR "hellp syndrome"[All Fields]) AND "23"[All Fields] AND "Weeks"[All Fields] AND ("gestate"[All Fields] OR "gestated"[All Fields] OR "gestates"[All Fields] OR "gestating"[All Fields] OR "gestational"[All Fields] OR "gestations"[All Fields] OR "pregnancy"[MeSH Terms] OR "pregnancy"[All Fields] OR "gestation"[All Fields]) Furthermore, we conducted cross-referencing of pertinent articles to uncover any supplementary research. The assessment of study quality, methodology, interventions, and outcomes was conducted separately by the researchers, and any disparities were addressed through discussion and consensus. Additionally, both researchers extracted and compared findings from all studies, with the possibility of conducting a meta-analysis if it was found to be viable.

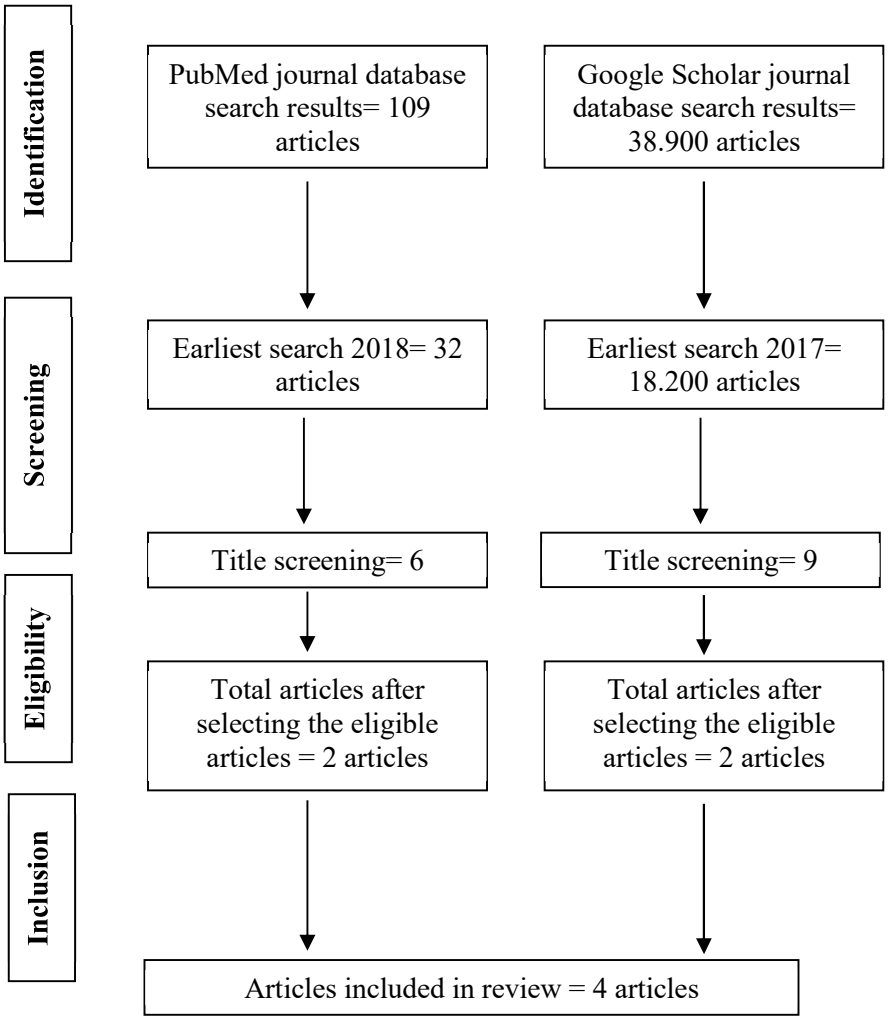

Figure 1. Article search flowchart

Inclusion and exclusion criteria

Inclusion criteria for the studies were as follows: (1) original research that assesses the maternal and fetal outcomes in HELLP syndrome at 23 weeks gestation; (2) Randomized Controlled Trials (RCTs) or observational studies (cohort or case-control studies); (3) availability of relevant data. Exclusion criteria were as follows: (1) ongoing studies or studies without available data; (2) duplicate publications. In cases of duplicate publications, the most recent article was chosen; (3) Non-English language studies were excluded.

Data Retrieval

The authors conducted a thorough examination of relevant studies, specifically selecting those that met precise inclusion criteria. They focused on original, unpublished papers in English to ensure a refined and high-quality selection. The analysis covered essential information, such as study particulars, authors, publication dates, locations, and research methodologies, aligning with the study's objectives.

Author	Origin	Method	Sample Size	Result
Mark et al., 2021.[6]	US	Retrospective observational study; case series.	Total 11 women.	This retrospective case series examines the outcomes of women who had abortions due to severe preeclampsia or eclampsia before reaching 24 weeks of gestation. The study observed 11 women who underwent abortion for these reasons, with 9 having dilation and evacuation procedures and 2 undergoing labor induction. Most opted for dilation and evacuation, and among those who chose either induction of labor or dilation and evacuation, there were no severe complications directly linked to the abortion.

Kascak et al., 2017.[7]	US.	Case report	Single patient.	a case of a woman who presented with HELLP syndrome in two subsequent pregnancies (age 36 and 40), at gestational age of 22 weeks in both pregnancies with a rapid onset and progression. She presented with characteristic clinical symptoms and laboratory findings. Both pregnancies were delivered by caesarean sections due to deterioration in the mother's condition, although neither pregnancy progressed into the 1st stage of the syndrome according to Mississippi classification.
Okorie et al., 2022.[8]	South Africa	Case Report	Single patient.	A 29-year-old woman, pregnant for the third time after one miscarriage, began prenatal care at 10 weeks. Her only identified preeclampsia risk was being pregnant for the first time with her current partner. She had one mid-trimester scan but no comprehensive screening for preeclampsia using ultrasound or biomarkers. At 18 weeks, she went to a clinic with headache, epigastric pain, and a high blood pressure reading of 169/71 mmHg. She received alpha-methyldopa as an outpatient but suffered two seizures the next day. She was then transferred to a specialized hospital and diagnosed with atypical eclampsia and HELLP syndrome. After treatment and stabilizing with MgSO4, her pregnancy was safely terminated, and she had a full recovery.
GH Han et al., 2018 [9]	South Korea.	Case reports	Single patient.	34-year-old multiparous woman without hypertension was admitted at 21 weeks' gestation because of a spontaneous hepatic rupture with hemoperitoneum. Four years previously, the patient had undergone an exploratory laparotomy during her first pregnancy that involved the ligation of bleeders, because a hepatic capsule rupture had caused hemoperitoneum development. Interventions: Unlike the first pregnancy, she was managed nonsurgically and conservatively during the second pregnancy, and she underwent frequent laboratory analyses and magnetic resonance imaging follow-up. On day 11 of the patient's hospital admission, we decided to deliver the baby at 23 weeks' gestation, because her condition had deteriorated

RESULT

Our search produced 15 results. After looking at the titles and summaries, we found 6 papers that fit our criteria. At first, we excluded one articles because they were written in a review style. But after reading the full papers carefully, we included four papers in our final analysis. These papers included a retrospective observational study and several case reports.

In retrospective study conducted by Mark et al (2021) on the case series period, the University of Maryland Medical Center recorded 7941 deliveries. Among these, 256 cases of severe preeclampsia were identified, including 32 instances of HELLP syndrome, with 11 cases (4.3%) diagnosed before 24 weeks of gestation (including 6 HELLP syndrome cases). These early cases represented 0.01% of all deliveries at the institution during the study period. Table 1 outlines the maternal outcomes for these cases. Conservative management wasn't recommended for the 6 women meeting HELLP syndrome criteria. Among the additional 5 cases, 2 had fetal demise at presentation. Labor induction was performed in 2 cases, with one experiencing intrapartum fetal demise and another delivering a neonate already demised at birth. The average hospital stay for these cases was 4.6 days (ranging from 3 to 8 days). Three of the 9 patients encountered significant disease-related complications. One patient experienced postabortal endomyometritis, postoperative pulmonary edema, and Clostridium difficile enterocolitis. Another patient had an eclamptic seizure during diagnosis confirmation and remained hospitalized due to elevated blood pressures and liver function tests. The third patient had dilated cardiomyopathy and was hospitalized for cardiac management postoperatively.[6]

Case report conducted by Kascak revealed a case of 36-year-old woman pregnant for the first time, admitted at 21 weeks and 3 days of gestation, was diagnosed with preeclampsia and HELLP syndrome. Initially presenting with nausea and epigastric pain, she had normal blood pressure and standard laboratory results upon admission. However, her condition rapidly deteriorated two days later, marked by severe epigastric pain, vomiting, and a blood pressure spike to 220/110 mmHg. The clinical team promptly initiated anticonvulsive therapy, intravenous antihypertensive therapy, and low molecular weight heparin (LMWH). Although her blood pressure stabilized after treatment, her lab results worsened significantly within six to twelve hours, with a steep drop in platelet count and hemoglobin, while liver enzymes soared to 30-80 times the upper limit of normal (ULN). Despite stable renal function and normal blood electrolyte levels, she exhibited signs of severe illness, including headache and vomiting. In light of her rapidly deteriorating condition, immediate pregnancy termination was recommended due to the imminent threat to her life. A cesarean section was

performed due to her swiftly worsening state, resulting in the delivery of a female fetus weighing 280 g. Postoperatively, her condition improved steadily, with declining aminotransferase levels and stable hemocoagulation parameters. Although her urine protein temporarily spiked after termination, it eventually returned to normal levels. She was discharged eight days after the procedure, continuing antihypertensive and LMWH therapy and receiving treatment to cease lactation, as well as a referral for a thrombophilia screening.[7]

In a subsequent occurrence in 2013, at 40 years old and pregnant for the second time, the same patient presented at 21 weeks and 2 days of gestation, reporting epigastric pain, headache, chills, and continuous vomiting. She had a history of a previous termination in 2009 due to severe preeclampsia and HELLP syndrome, which was confirmed to be associated with a heterozygous factor V Leiden mutation. Since then, she had received antihypertensive treatment until the 12th week of her pregnancy in 2013. Prophylactic LMWH had been initiated from the beginning of this second pregnancy. Upon admission, she exhibited hypertension, significant proteinuria, and abdominal tenderness, but no uterine tenderness. Laboratory tests showed elevated liver enzymes, D-dimer, and LD levels, while coagulation parameters were abnormal. Despite initial improvement with treatment, her pain intensified, and blood pressure rose, necessitating a second termination of pregnancy via cesarean section. This time, a nonviable male fetus weighing 455 g was delivered. The postoperative period was uncomplicated, with gradual improvements in coagulation parameters and normalization of liver enzyme levels. Since this second termination, the patient has not attempted pregnancy again and remains childless.

In 2022 Okorie et al reported a case regarding 29 years old women who was pregnant for the third time, this woman, who had experienced one previous miscarriage and a caesarean section due to cephalopelvic disproportion, began antenatal care at 10 weeks gestation with a blood pressure of 119/66 mmHg and a body mass index of 25 kg/m2. She had been managing human immunodeficiency virus (HIV) infection for 7 years with a consistently undetectable viral load and a CD4 count of 434 cells/µl. Her primary risk factor for hypertensive disorders in pregnancy was identified as being pregnant for the first time with her current partner. Managing her HIV with a fixed-dose combination of tenofovir, efavirenz, and emtricitabine (TEE), she encountered no complications. As per national guidelines, she did not undergo full blood count (FBC) or liver function tests at her initial appointment and was not screened for preeclampsia using ultrasound or biomarkers due to their unavailability. She underwent only one mid-trimester scan during her pregnancy.[8]

At 18 weeks, she reported headache, epigastric pain, and an elevated blood pressure of 169/71 mmHg at the primary healthcare clinic. Alpha-methyldopa was prescribed, and despite her perceived low risk for preeclampsia, she was discharged home. However, a day later, she experienced two witnessed seizures lasting approximately 2 minutes each. Rushed back to the clinic, her blood pressure was 133/87 mmHg with 2+ proteinuria, but her Glasgow Coma Scale score was normal. She received magnesium sulfate and was immediately referred to a tertiary hospital. Upon arrival at the tertiary hospital, her blood pressure was 161/96 mmHg, but her overall vital signs and clinical assessments, including a cardiovascular check and symphysio-fundal height measurement, were normal, corresponding to an 18-week gestational stage. Admitted to an obstetric high-care unit, she received prompt medications including nifedipine, alpha-methyldopa, and maintenance doses of magnesium sulfate. Blood tests revealed abnormalities consistent with HELLP syndrome: platelet count at 35 × 109/L, AST at 130 U/L, ALT at 66 U/L, and LDH at 1638 U/L. Renal function assessments were within normal ranges. Due to the severity of her condition, medical termination of pregnancy ensued using a combination of vaginal misoprostol doses and a trans-cervical Foley catheter bulb, resulting in the delivery of a 200 g fetus. Before the termination, a brain computerized tomography scan showed signs of posterior reversible encephalopathy syndrome. Following her recovery, counseling, and a 6-day postpartum hospital stay, she underwent a normal 12-week postnatal clinic visit with stable blood pressure and negative connective tissue screening.[8]

This case presentation by Hee Han and Kim in 2018 had received approval from the Ethics Committee of Gangnam Severance Hospital, and the patient provided written informed consent. At 30 years old and pregnant for the first time, a woman presented symptoms of right upper quadrant pain and nausea at 182/7 weeks' gestation in September 2013. Though initially stable, her condition rapidly deteriorated, revealing major abnormalities in laboratory tests and confirming the presence of hepatic rupture and extensive liver necrosis. Urgent surgery was imperative, and during the procedure, an extensive capsular rupture and a hepatic laceration were identified and treated. Unfortunately, the fetus succumbed, and the patient faced a complex recovery, eventually stabilizing after several days in the ICU.[9]

In a subsequent pregnancy in October 2017, after thorough counseling, the patient was prescribed low-dose aspirin. Until 21 weeks' gestation, the pregnancy progressed uneventfully. However, at 215/7 weeks, she experienced symptoms similar to her previous liver complication, leading to another admission. Imaging confirmed an extensive hematoma within the liver, but surgical intervention wasn't necessary initially. However, as her condition deteriorated days later, conservative management ensued, leading to premature delivery via induction due to the mother's worsening state. Although challenging, the patient's condition stabilized post-delivery, and she was discharged after a significant recovery period. The newborn, a premature male, is under medical care, while the mother continues her recuperation. Throughout her postpartum phase, her health gradually improved, leading to her eventual discharge. [9]

DISCUSSION

Diagnoses of severe preeclampsia and eclampsia before 24 weeks of gestation are exceedingly rare; in related institution, these cases accounted for just 0.01% of all deliveries over a five-year span. Previous evidence indicates that conservative

management in such situations yields little benefit, with high rates of neonatal mortality and maternal morbidity. Consequently, the usual recommendation is abortion in these exceptional cases. However, the specific risks associated with abortion, particularly dilation and evacuation, in this context have not been thoroughly investigated. The small case series involving 11 patients revealed that abortion generally led to swift recovery from these severe and potentially life-threatening conditions. During study period, labor induction protocol did not involve mifepristone, and the dosing and frequency of misoprostol administration were below the World Health Organization's recommended levels.[11]

Nevertheless, both women undergoing labor induction had successful abortions within 24 hours. Most complications observed, such as cardiomyopathy and the need for transfusions due to severe thrombocytopenia or hemolytic anemia, were primarily related to the disease itself rather than the abortion process. One significant concern regarding abortion in women with severe preeclampsia, particularly those with HELLP syndrome, is the risk of blood loss. In this case series, only one woman experienced post-abortion hemorrhage, and she did not have significant thrombocytopenia before the procedure. However, she did have a fetal demise, which is associated with an increased risk of hemorrhage.[12]A prior case series similarly demonstrated that dilation and evacuation procedures can be safely conducted in women on anticoagulation therapy with a low risk of substantial bleedin. Providing women the choice of abortion method may aid in their grieving process, especially when aborting a desired pregnancy is advised. This limited case series provides supporting data for offering women the option of dilation and evacuation or labor induction when abortion is necessary due to severe preeclampsia or eclampsia.[6]

In Kascak et al documented case, we report a rare recurrence of preeclampsia and HELLP syndrome, both occurrences manifesting at an early gestational age.[7] Previous investigations illustrate the rarity of HELLP syndrome before 28 weeks of gestation, with no instances reported in a study analyzing 34 pregnancies in Ostrava, Czech Republic.[13] Another ten-year analysis in a tertiary maternity center in the Netherlands documented 26 cases of preeclampsia occurring before 24 weeks, wherein 65% experienced severe maternal morbidity, including HELLP syndrome, eclampsia, pulmonary edema, and a single maternal death.[14] Similarly, a study involving 35,937 deliveries in the United States identified only 39 cases (1%) of preeclampsia occurring earlier than 25 weeks, treated as severe preeclampsia, with associated complications such as placental abruption, HELLP syndrome, acute renal insufficiency, and eclampsia. Notably, the perinatal mortality rate was 99.4%.[15]

This case involved a patient who experienced recurring severe HELLP syndrome in both pregnancies, a situation scarcely reported in literature, with only one similar case found. This patient, aged 42 and 45 during her pregnancies, suffered from severe HELLP syndrome combined with superimposed preeclampsia. Her situation aligns with tbe case and that of a 41-year-old primigravida experiencing severe HELLP syndrome at 17 weeks of gestation.[7]

The management of HELLP syndrome aims to prevent severe maternal morbidity and mortality. In instances with a nonviable fetus, vaginal termination of pregnancy is preferred, but various factors, including cervix score, disease progression speed, symptom severity, and feasibility of early delivery, must be considered. In the case, we opted for expedited delivery via cesarean section due to minimal chances of rapid vaginal termination. Prompt intervention in the initial pregnancy potentially averted the progression of HELLP syndrome to its severe stage and prevented further maternal complications. Rapid deterioration in lab results and clinical symptoms correlates with heightened maternal morbidity, especially in early HELLP syndrome cases. The decision for cesarean section in the second pregnancy was influenced by the previous surgery.[7]

In some cases, expectant observation with corticosteroid therapy can be considered, especially nearing fetal viability, although this could lead to adverse outcomes for both the fetus and the mother. In a case report by Merz and Gembruch, stabilizing the disease at 21 weeks was followed by the development of severe preeclampsia at 22 weeks and intrauterine fetal death.[16] Although conservative management in a strictly selected subgroup (GA 24–34 weeks) led to better outcomes, it did not improve prognosis in cases before 24 weeks, increasing maternal morbidity.[7]

Despite the suggestion that HELLP syndrome before 26 weeks may only occur in the presence of superimposed preeclampsia or positive antiphospholipid antibodies, the case contradicts these assumptions. We ruled out antiphospholipid syndrome, and the patient was not hypertensive before the onset of the disease in her first pregnancy. However, post-termination, we confirmed she had a heterozygous factor V Leiden mutation. Corticosteroid therapy in HELLP syndrome is under intense research, with emerging evidence supporting its benefits. Though steroid treatment was not administered during the study, we've included it in departmental guidelines given the mounting evidence base. Withdrawal of antihypertensive therapy and the outpatient prescription of low-dose aspirin in her second pregnancy are subjects open for debate and consideration.[7]

In investigation conducted by Warih Angesti et al in 2022, HELLP syndrome occurred in 7% of severe preeclampsia cases. Contrarily, Khumsat et al (2008) reported a higher prevalence of 12.5% in severe preeclampsia patients. This disparity in HELLP syndrome occurrences between this study and Khumsat's could be attributed to differences in the duration of sample collection. While this study spanned one year, Khumsat's research extended over two years. Additionally, variations in sample collection locations might have contributed to the differing results.

The gestational age at which delivery occurs significantly impacts outcomes. Studies suggest that about 64% of babies from HELLP syndrome cases are delivered around 32 weeks of gestational age.[17] However, in this study, the HELLPs group had deliveries occurring at an average of 33-34 weeks, while the non-HELLPs group had a later average of 36-37 weeks. Prolonging the pregnancy duration potentially reduces maternal mortality but increases neonatal morbidity. They propose optimizing the maternal condition while minimizing perinatal risks associated with premature birth.[11] The mortality rates in HELLPs cases vary but can range from 0 to 24%. Concerning neonatal outcomes, this study observed stillbirth rates of 25% among HELLPs group neonates and 6.2% in non-HELLPs. The management focus on optimizing maternal conditions and preventing maternal mortality could contribute to the higher stillbirth rates in HELLP syndrome cases. Erkilinc & Eyi's (2013) study on neonatal outcomes in HELLP syndrome found that neonates' birth weights were commonly below 1500 g, with a majority delivered before 34 weeks of gestation. Similarly, this study reported an average birth weight of 1994.4 g for HELLPs and 2656.3 g for non-HELLPs neonates. Prematurity, often occurring in gestational ages under 34 weeks, can significantly impact birth weight and first-minute Apgar scores.

In case report by Okarie, it would have been valuable to ascertain whether low platelet count and abnormal liver enzymes were evident during the initial booking, especially given the patient's history of HIV infection and ongoing anti-retroviral therapy (ART). However, routine assessments of liver function tests (LFT) and full blood count (FBC) are not standard during the first antenatal visit in public healthcare facilities in South Africa. Instead, mandatory tests include haemoglobin concentration, rapid plasma regain, Rhesus D factor, and HIV counselling and testing. For HIV-positive individuals on ART without complications, additional checks at booking encompass viral load, CD4 count, and serum creatinine, which aids in evaluating tenofovir-related renal side effects. Typically, primary HIV care facilities in South Africa administer fixed-dose combinations like TEE or TLD, known for their rare association with liver toxicity compared to nevirapine-based regimens prevalent in the early HIV epidemic.[8]

Diagnosing preeclampsia before 20 weeks of gestation poses a challenge, particularly concerning accurately recorded blood pressure (BP) readings. It's crucial to employ validated devices and correct measurement techniques when taking BP readings, recording the average of the final two readings. In pregnancy, a diastolic pressure of 110 mmHg and/or systolic pressure of 160 mmHg signifies severe hypertension, necessitating repeated measurements and prompt administration of antihypertensive medication. Patients displaying severe features of preeclampsia ought to receive MgSO4 therapy to prevent eclampsia. In instances of incomplete diagnostic features, measuring sFlt-1 and placental growth factor (PIGF) blood concentrations after 20 weeks' gestation can aid in confirming or excluding preeclampsia. However, the use of sFlt-1/PIGF ratio for diagnosing preeclampsia earlier in pregnancy lacks substantial evidence and remains contentious.[19,20]

Placental histology might provide insights into placental-mediated disorders like fetal growth restriction and preeclampsia. It's unfortunate that the placenta wasn't subjected to histological examination due to logistical constraints in this case.[8] Utilizing history, physical examination, ultrasound, and biomarkers could help identify high-risk individuals for preeclampsia, offering preventive therapies such as aspirin and calcium supplementation where necessary. However, due to resource limitations, such screening is often unavailable in public healthcare facilities in South Africa. Nonetheless, implementing a comprehensive multimodal screening strategy in future pregnancies might be beneficial for early identification and management of preeclampsia risk. Universal aspirin prophylaxis for preeclampsia in low- and middle-income countries has been a subject of debate due to concerns regarding pill burden, treatment compliance, and potential side effects for both the mother and offspring.[19-22]

Spontaneous hepatic rupture during pregnancy is a rare and life-threatening complication, and its exact cause remains relatively unclear. It primarily affects individuals with HELLP syndrome and is often linked to underlying issues such as acute fatty liver, adenomas, malignancies, or hemangiomas. When occurring in patients with preeclampsia and HELLP syndrome during pregnancy, its incidence is less than 1% to 2%. The recurrence rate of HELLP syndrome varies from 2% to 19%. The specific mechanisms behind spontaneous hepatic rupture associated with HELLP syndrome are not entirely understood. In cases related to hypertensive disorders, it's believed that microvascular clot formation due to blood clotting abnormalities leads to subcapsular hematomas. However, the development of spontaneous hepatic rupture without hypertension remains unclear.[9]

Clinical indicators of spontaneous hepatic rupture include right upper quadrant pain, epigastric pain, severe right shoulder pain, nausea, vomiting, abdominal distension, and hypovolemic shock, presenting in 30% to 90% of patients. However, these symptoms can be mistaken for gastrointestinal issues or acute fatty liver of pregnancy. Laboratory findings in HELLP syndrome cases with liver hematoma typically show elevated aspartate aminotransferase and alanine aminotransferase levels, reduced haematocrits, and thrombocytopenia. Differential diagnosis between acute fatty liver of pregnancy and HELLP syndrome can be challenging due to similar symptoms and moderate-to-severe liver dysfunction.[9]

Repeated episodes of hepatic hemorrhage, while infrequent in subsequent pregnancies, play a crucial role in diagnosing such cases. In this context, determining treatment options poses challenges due to the rarity of extremely early gestational age complications like severe preeclampsia and HELLP syndrome. When these occur, delivery becomes the primary treatment, but with extreme prematurity, the risk of neonatal mortality and morbidity increases.[9]

Comparing the patient's first and second pregnancies, the initial vital signs indicated instability during the first, demanding immediate operative measures. Conversely, in the second pregnancy, the patient's condition was relatively stable, allowing more manageable interventions. Depending on the stability of the patient, various treatment options, including surgeries and conservative management, may be considered. Prolonging a pregnancy beyond complications can benefit fetal outcomes but poses risks to maternal health. Monitoring both the fetus and mother is crucial when considering this approach. [9]

CONCLUSIONS

The occurrence of HELLP syndrome without a hypertensive disorder and the recurrence of intrahepatic rupture at an extremely premature gestational age represent rare and serious conditions linked to maternal and neonatal mortality and morbidity. While prolonging the pregnancy might be considered based on the mother's and fetus's conditions, international consensus advises against routine extension due to the high risks involved. Continuous laboratory and imaging examinations are recommended to monitor maternal health and the limits of neonatal survival amid extreme prematurity and its potential consequences. Early onset HELLP syndrome, occurring below the viability level of the fetus, is exceedingly rare but requires vigilance from obstetricians due to its rapid progression, posing a significant risk to the mother's life. Therefore, prompt diagnosis and termination of pregnancy are crucial in such cases.

Robust screening for preeclampsia in the first trimester is highly recommended to identify high-risk women and provide preventive therapy like aspirin. Timely identification is critical as atypical preeclampsia can be challenging to diagnose, potentially leading to adverse outcomes if diagnosis or treatment is delayed. Suspected cases should be referred to specialized obstetrical units for further evaluation and the exclusion of other potential diagnoses. Offering women the choice between dilation and evacuation or labor induction for necessary abortion in severe preeclampsia or eclampsia could aid their grieving process, particularly in cases where abortion of a desired pregnancy is advised.

REFERENCES

[1] Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Karumanchi SA, et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens [Internet]. 2022;27(September 2021):148–69. Available from: doi: 10.1016/j.preghy.2021.09.008

[2] Duhig K, Vandermolen B, Shennan A. Recent advances in the diagnosis and management of pre-eclampsia. F1000Res. 2018;7:242. Published 2018 Feb 28. doi:10.12688/f1000research.12249.1

[3] Khalid F, Mahendraker N, Tonismae T. HELLP Syndrome. [Updated 2023 Jul 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560615/

[4] Wadhwani P, Saha PK, Kalra JK, Gainder S, Sundaram V. A study to compare maternal and perinatal outcome in early vs. late onset preeclampsia. Obstet Gynecol Sci. 2020;63(3):270–7. doi: 10.5468/ogs.2020.63.3.270 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[5] Matthew H. Mossayebi, Neel S. Iyer, Rodney A. McLaren, Hind N. Moussa, Baha M. Sibai, Huda B. Al-Kouatly, HELLP syndrome at <23 weeks' gestation: a systematic literature review, American Journal of Obstetrics and Gynecology, Volume 229, Issue 5, 2023, Pages 502-515.e10, ISSN 0002-9378, https://doi.org/10.1016/j.ajog.2023.04.046. (https://www.sciencedirect.com/science/article/pii/S0002937823002843) Abstract: Objective

[6] Mark, K., Flanagan, N., Hurvitz, J., & Chawla, K. (2021). Abortion in women with severe preeclampsia and eclampsia prior to 24 weeks gestation. Contraception, 103(6), 420–422. doi:10.1016/j.contraception.2021.01.012 10.1016/j.contraception.2021.01.012

[7] Kascak P, Paskala M, Antal P, Gajdosik R. Recurrent HELLP Syndrome at 22 Weeks of Gestation. Case Rep Obstet Gynecol. 2017;2017:9845637. doi:10.1155/2017/9845637

[8] Ugonna Aja-Okorie, Nnabuike Chibuoke Ngene, Atypical preeclampsia-eclampsia syndrome at 18 weeks of gestation: A case report, Case Reports in Women's Health, Volume 36, 2022, e00470, ISSN 2214-9112, https://doi.org/10.1016/j.crwh.2022.e00470. (https://www.sciencedirect.com/science/article/pii/S221491122200090X)

[9] Han GH, Kim MA. Recurrent spontaneous hepatic rupture in pregnancy: A case report. Medicine (Baltimore). 2018;97(29):e11458. doi:10.1097/MD.0000000000011458

[10] World Health Organization Safe abortion: technical and policy guidance for health systems. 2nd ed; 2012 https://apps.who.int/iris/bitstream/handle/10665/ 70914/9789241548434 _ eng.pdf?sequence=1 accessed December 17, 2020 .

[11] P, W. A., Ernawati, E., & Susanti, D. (2016). CHARACTERISTICS OF HELLP SYNDROME IN SEVERE PREECLAMPSIA PATIENTS IN DR. SOETOMO HOSPITAL SURABAYA. Folia Medica Indonesiana, 51(4), 272–276. https://doi.org/10.20473/fmi.v51i4.2858

[12] Tschann, Mary; Edelman, Alison; Jensen, Jeffrey; Bednarek, Paula; Kaneshiro, Bliss (2017). Blood loss at the time of dilation and evacuation at 16 to 22 weeks of gestation in women using low molecular weight heparin: a case series. Contraception, (), S001078241730433X–. doi:10.1016/j.contraception.2017.09.002

[13] O. Simetka, I. Michalec, H. Zewdiov´a, R. Kol´aˇrov´a, J. Proch´azkov´a, and M. Proch´azka, "Course and delivery outcomes of 34 pregnancies complicated by HELLP syndrom," Ceska Gynekologie, vol. 75, no. 3, pp. 242–247, 2010.

[14] I. P. M. Gaugler-Senden, A. G. Huijssoon, W. Visser, E. A. P. Steegers, and C. J. M. de Groot, "Maternal and perinatal outcome of preeclampsia with an onset before 24 weeks' gestation. Audit in a tertiary referral center," European Journal of Obstetrics Gynecology and Reproductive Biology, vol. 128, no. 1-2, pp. 216–221, 2006.

[15] S. M. Jenkins, B. B. Head, and J. C. Hauth, "Severe preeclampsia at <25 weeks of gestation: maternal and neonatal outcomes," American Journal of Obstetrics & Gynecology, vol. 186, no. 4, pp. 790–795, 2002.

[16] W. M. Merz and U. Gembruch, "Severe, early-onset hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome episode with spontaneous remission during pregnancy," Journal ofMaternal-Fetal and Neonatal Medicine, vol. 20, no. 8, pp. 631- 632, 2007.

[17] Roelofsen AC, van Pampus MG, Aarnoudse JG (2003). The HELLP-syndrome; maternal-fetal outcome and follow up infants. Journal Perinatal Medicine 31, 201- 208

[18] Erkilinc S and Eyi EGY (2013). Adolescent pregnancies complicated by HELLP syndrome: clinical experience of 26 cases. The Journal of Gynecology- Obstetrics and Neonatology 10, 1643-1646

[19] N.C. Ngene, J. Moodley, Blood pressure measurement in pregnancy and preeclampsia: devices, techniques, and challenges, Cardiovasc. J. Afr. 30 (20) (2019) 120–129.

[20] L.A. Magee, G.N. Smith, C. Bloch, A.-M. Cˆot´e, V. Jain, K. Nerenberg, P. von Dadelszen, M. Helewa, E. Rey, Guideline No, 426: Hypertensive disorders of pregnancy: diagnosis, prediction, prevention, and management, J. Obstet. Gynaecol. Can. 44 (5) (2022).

[21] L.A. Magee, M.A. Brown, D.R. Hall, S. Gupte, A. Hennessy, S.A. Karumanchi, L. C. Kenny, F. McCarthy, J. Myers, L.C. Poon, S. Rana, S. Saito, A.C. Staff, E. Tsigas, P. von Dadelszen, The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice, Pregnancy Hypertens 27 (2022) 148–169.

[22] Society for Maternal-Fetal Medicine (SMFM), J.M. Louis, J. Parchem, A. Vaught, M. Tesfalul, A. Kendle, E. Tsigas, (Preeclampsia Foundation), Preeclampsia: a report and recommendations of the workshop of the Society for Maternal-Fetal Medicine and the Preeclampsia Foundation, Am. J. Obstet. Gynecol. 227 (5) (2022) B2–B24.