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MANAGEMENT OF HELLP SYNDROME BEFORE DELIVERY: A SYSTEMATIC REVIEW

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ABSTRACT

Background: *HELLP syndrome, named for 3 features of the disease (hemolysis, elevated liver enzyme levels, and low platelet levels), is a life-threatening condition that can potentially complicate pregnancy. HELLP was once known as edema-proteinuria-hypertension gestosis type B in the early 20th century and was later renamed in 1982 by Louis Weinstein.*

The aim: *This study aims to show management of HELLP syndrome before delivery.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search on SagePub brought up 110 articles. The results of the search conducted for the last year of 2013 yielded a total 23 articles for PubMed and 75 articles for SagePub. The result from title screening, a total 8 articles for PubMed and 28 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.*

Conclusion: *HELLP syndrome is an important complications in pregnancy which increases maternal and fetal mortality. This disease usually remits with supportive treatment which includes prescription of corticosteroid, magnesium sulfate, stabilization of mother and pregnancy termination. Plasmapheresis is a treatment of choice which improves clinical outcomes in complicated cases.*

Keyword: *HELLP, proteinuria, hypertension.*

INTRODUCTION

Haemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a life-threatening complication of pregnancy. HELLP syndrome is a severe variant of preeclampsia that occurs in 10–20% of women who have preeclampsia with severe features. Partial HELLP syndrome, which has one or two elements of the triad of HELLP syndrome, is not considered a separate disorder from HELLP syndrome. Although HELLP/partial HELLP syndrome usually occurs in the third trimester of pregnancy or peripartum period, women with preeclampsia can also develop HELLP/partial HELLP syndrome at a periviable gestational age (22–24 weeks of gestation).[1,2]

The only definitive treatment for HELLP syndrome is termination of pregnancy. However, an obstetrician will face the dilemma of decision-making regarding the optimal timing for delivery of the foetus and the placenta in the management of HELLP syndrome remote from term, especially in the periviable period. Delaying the termination of pregnancy increases the risk of maternal organ dysfunction and mortality, but is beneficial to foetal maturation. The Mississippi protocol (MP), which is used to treat HELLP syndrome and involves high doses of dexamethasone (Antepartum: 10 mg intravenously every 12 hours within 24–72 hours after diagnosis; Postpartum: two 10-mg doses 12 hours apart followed by two additional doses of 5 mg at 12-hour intervals) in combination with antihypertensives and magnesium sulphate, is known to prevent disease progression and maternal morbidity.[1]

Delivery is the only cure for preeclampsia, eclampsia, and HELLP syndrome. Indications, timing, and method of delivery largely depend on clinical acumen. If eclampsia or HELLP syndrome develops before 24 weeks of gestation, termination of pregnancy should be considered. Cesarean delivery should be considered in the patients with HELLP syndrome and eclampsia <32–34 weeks of gestation where long induction with cervical ripening agents is expected. Most often, fetal bradycardia occurs during and immediately after a seizure. However, the fetal heart rate pattern improves with therapeutic interventions in the mother and fetus. In these cases, surgery can be delayed for a short period of time to allow for in utero resuscitation before delivery.[3,4]

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we compare and contrast of the management of HELLP syndrome before delivery. It is possible to accomplish this by researching or investigating management of HELLP syndrome before delivery. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about the management of HELLP syndrome before delivery. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used " Management of HELLP syndrome before delivery" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *(("HELLP"[MeSH Subheading] OR "HELLP syndrome"[All Fields] OR "Incident of HELLP syndrome [All Fields]) AND ("HELLP syndrome before delivery"[All Fields] OR " HELLP syndrome during pregnancy"[All Fields]) AND ("The impact of HELLP syndrome"[All Fields]) OR ("Complication of HELLP syndrome [All Fields]))* used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

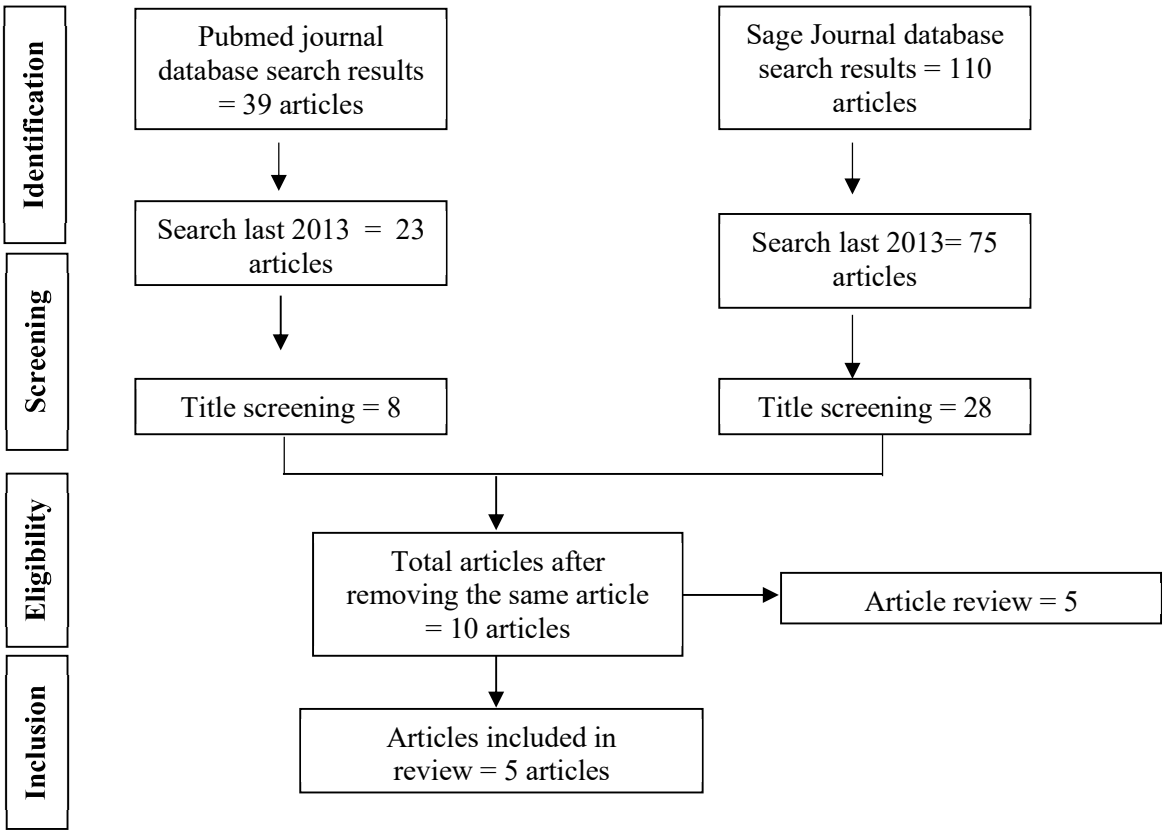

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 39 articles, whereas the results of our search on SagePub brought up 110 articles. The results of the search conducted for the last year of 2013 yielded a total 23 articles for PubMed and 75 articles for SagePub. The result from title screening, a total 8 articles for PubMed and 28 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

Sungkar, A *et al* (2021)[5] showed there is association in gestational age at delivery, nullipara, blood pressure, and laboratory findings (urea, creatinine, uric acid, albumin) between preeclampsia and HELLP syndrome group. History of hypertension in previous pregnancy is a significant risk factor for HELLP syndrome. Regarding neonatal outcome, baby born from HELLP syndrome has lower median birth weight.

Hosten, AK *et al* (2023)[6] showed the results of the present study are of interest in the routine use of MP for prolongation of pregnancy. This holds true in perinatal centers with the possibility of optimal monitoring of maternal and fetal conditions and the prerequisite of immediate readiness for C-section in case of sudden complications. The results indicate that MP therapy not only improves the clinical and laboratory outcomes of mother and child, it also reduces the number of postpartum complications. For example, fewer red blood cells and platelet concentrates have to be transfused. The therapy also reduces the risk of complications from blood transfusion. From an economic point of view, MP therapy is clearly superior to transfusion or alternative HELLP syndrome therapies such as plasmapheresis. Plasmapheresis may give results similar to MP therapy; however, it is more invasive, dangerous and, above all, expensive.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Sungkar, A *et al*., 2021[5]	Indonesia	Cross-sectional study	113 patients	There were 676 deliveries which was complicated by preeclampsia without or with severe features and 113 patients with HELLP syndrome. Gestational age, history of hypertension systolic and diastolic blood pressure, hemoglobin, hematocrit, urea, creatinine, uric acid, and albumin are different significantly between HELLP and preeclampsia patients. History of hypertension in previous pregnancy is considered as a significant risk factor for HELLP syndrome (p=0.001); RR 2.33 (95% CI 1.41–3.9). Based on data of gestational age at delivery which lower in HELLP syndrome, it showed lower median birth weight in HELLP syndrome (1442.5 g) compared with preeclampsia (1442.5 g vs 2400 g, p=; 95%CI There is significant difference in gestational age at delivery, nullipara, blood pressure, and laboratory findings (urea, creatinine, uric acid, albumin) between preeclampsia and HELLP syndrome group. History of hypertension in previous pregnancy is a significant risk factor for HELLP syndrome. Regarding neonatal outcome, baby born from HELLP syndrome has lower median birth weight.
Hosten, AK *et al*., 2023[6]	Germany	A Retrospective Multicentric Analysis	146 patients	Pregnancies in the treatment group were prolonged by 4 days (median 1–55 days). The platelet counts increased from 76,060 ± 22,900/µL to 117,430 ± 39,065/µL in the MP group compared with an increase from 66,500 ± 25,852/µL to 83,430 ± 34,608/µL in control group 1 and from 78,890 ± 19,100/µL to 131,080 ± 50,900/µL in control group 2 ($p < 0.001$). Severe neonatal complications were significantly reduced in the treatment group ($p < 0.05$): sepsis, 9.25% vs. 24%; ventilation, 44.6% vs. 46.5%; and infant death, 1.6% vs. 8.6%.

Li, B & Yang, H., 2022[7]	China	A retrospective study	83 patients	In total, 31.9% and 63.9% of women in the EO-PE with HELLP and LO-PE with HELLP groups, respectively, were asymptomatic at diagnosis ($P = 0.004$, OR = 0.265 (0.106–0.662)). Headache or visual symptoms were more frequent in the EO-PE group than in the LO-PE group (48.9% vs. 25%, $P = 0.026$, OR = 0.348 (0.135–0.896)). Women in the EO-PE with HELLP group had higher SBP and DBP than those in the LO-PE with HELLP group. Laboratory tests, including platelets, liver function, and hemolysis, which are the main indicators for the diagnosis of HELLP syndrome, showed almost no significant differences between the two groups, with kidney function being the only difference observed. Women in the EO-PE with HELLP group had higher Scr than those in the LO-PE with HELLP group. The degree of proteinuria was higher in the EO-PE group than in the LO-PE with HELLP group. The incidence of severe maternal complications was significantly higher in the EO-PE group than in the LO-PE with HELLP group (25.5% vs. 5.6%, $P = 0.016$, OR = 0.172 (0.036–0.824)). In total, 57.4% and 8.3% of neonates in the EO-PE and LO-PE with HELLP groups were admitted to the NICU, and the difference was statistically significant, even after adjustment for the delivery week ($P = 0.009$, OR = 0.830 (0.729–0.944)). Postpartum HELLP syndrome was more common in the LO-PE group than in the EO-PE group (30.6% vs. 4.3%, $P = 0.001$, OR = 9.9 (2.031–48.256)).
Cadoret, F *et al* ., 2019[8]	France	A retrospective	61 patients	Ninety-nine patients were included in our study. Among them, 61 were managed expectantly. At baseline, the active management group was more likely to suffer from persistent hyperreflexia (p < .001), headache (p ¼ .006) and confusion (p < .01). Moreover, this group was associated with

				worst biological and ultrasound features, namely decreased prothrombin ratio (p ¼ .04), increased creatinine value (p ¼ .01), and increased rates of pathological umbilical cord flow (p ¼ .05) and abnormal ductus venosus flow (p ¼ .007). After logistic regression, baseline significant prognostic factors were hyperreflexia (RR ¼ 12.35; CI ¼ 3.8 39.9), creatinine level (RR ¼ 1.03; CI ¼ 1002 1058) and abnormal umbilical cord flow (RR ¼ 3.95; CI¼ 1.05 14.81). Last, expectant management leads to longer gestation time after diagnosis with an average value of 7.75 days without increasing maternal nor fetal mortality.
Rimaitis, K *et al*., 2019[9]	Lithuania	A retrospective observational cohort study	77 patients	The means of diagnosis and treatment outcomes within those groups were analysed statistically. There was insufficient statistical evidence of the blood pressure levels corresponding to the severity of patients' condition ($p > 0.05$ in all of the groups). The clinical presentation varied within all of the classes, and the only objective means of diagnosis and evaluation of progression of the condition were laboratory tests. Even though HELLP syndrome is considered a hypertensive multi-organ disorder of pregnancy, the level of hypertension does not correlate to the severity of the condition; hence, the diagnosis should be based on biochemical laboratory evidence. Vigilance in suspicion and the recognition of HELLP syndrome and appropriate treatment are essential in order to ensure better maternal and neonatal outcomes.

Li, B & Yang, H (2022)[7] showed Compared with LO-PE with HELLP patients, EO-PE with HELLP patients have more obvious kidney damage, higher blood pressure and a higher risk of adverse maternal and neonatal outcomes. Patients with LO-PE need to be alerted to the occurrence of HELLP syndrome after delivery.

Cadoret, F *et al* (2019)[8] showed While expectant management in HELLP syndrome might be beneficial through its reduction of prematurity, it cannot be conducted in all patients. Identification of baseline parameters predictive of disease evolution is thus of tremendous importance to define which obstetrical approach should be prioritized.

Rimaitis, K *et al* (2019)[9] showed Considering all of these factors, the implementation of standardised diagnostic criteria based on laboratory findings such as the Mississippi triple-class system for HELLP syndrome creates a possibility of

defining this disorder similarly in most cases, applying the same treatment options in the same stage of the condition, and improving maternal and perinatal outcomes.

DISCUSSION

HELLP syndrome is a serious complication in pregnancy which was described as a severe form of preeclampsia in 1982 by Weinstein. HELLP stands for: H: hemolysis; EL: elevated liver enzymes; and LP: low platelets count. There is also partial or incomplete form of the disease which includes one or two parts of the triad. This syndrome was first assumed to be a severe form of preeclampsia but later it was revealed that it occurs in 10 to 20% of cases without preeclampsia. [10,11]

Although controversial, expectant management may be acceptable before 34 weeks in a tertiary care hospital. This should include close maternal and fetal surveillance (maternal vital signs and fluid balance, cardiotocography, and Doppler examination for fetal assessment) as well as serial laboratory assessments (complete blood count, comprehensive metabolic panel, urinalysis, coagulation profile, and lactate dehydrogenase). In addition, corticosteroid (CS) therapy, parenteral magnesium sulfate therapy (for up to 48 h), and antihypertensive management are recommended for pregnancies between 24 and 34 weeks of gestation. However, conservative management must be weighed against the risk of maternal and fetal complications. Delivery is inevitable if the maternal or fetal condition worsens with the majority of these cases requiring cesarean section. [3]

The American College of Obstetricians and Gynecologists (ACOG) Task Force on Hypertension in Pregnancy recommends antenatal CS therapy to accelerate fetal lung maturity for the affected pregnant woman with severe preeclampsia between 24 and 34 weeks of gestation. Delivery is indicated after 48 h of CS therapy in specific cases. On the other hand, delivery is recommended immediately after maternal stabilization without delay for CS in cases of eclampsia, pulmonary edema, DIC, uncontrollable severe hypertension, abnormal fetal testing, nonviable fetus, intrauterine fetal demise, or placental abruption.[3,11]

The patients with severe preeclampsia and suspected HELLP syndrome should receive parenteral magnesium sulfate therapy as prophylaxis for convulsions. The magnesium sulfate regimen includes a loading dose of 6 g intravenous (IV) over 20 min followed by a continuous infusion of 2 grams/hr starting during the period of observation and continuing until 24-h postpartum. If recurrent seizures occur, an additional bolus of 2 g magnesium sulfate can be given over 3–5 min. Close monitoring for magnesium toxicity is a necessity. If seizures are not controlled after two such boluses of magnesium sulfate, other anti-seizure drugs (e.g., diazepam, lorazepam, and midazolam) can be tried. The ACOG Task Force also recommends magnesium sulfate therapy in the setting of eclampsia to prevent recurrent seizures rather than for control of the initial seizure since the initial seizure is usually self-limited.[3]

CONCLUSION

HELLP syndrome is an important complications in pregnancy which increases maternal and fetal mortality. This disease usually remits with supportive treatment which includes prescription of corticosteroid, magnesium sulfate, stabilization of mother and pregnancy termination. Plasmapheresis is a treatment of choice which improves clinical outcomes in complicated cases.

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