

## The Effect of Corticosteroid Administration on Maternal Outcomes in Patients with HELLP Syndrome

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### ABSTRACT

*HELLP syndrome is a hemolysis syndrome with microangiopathic blood smears, increased liver enzymes, and low platelets in pregnant and postpartum patients. HELLP syndrome may be a complication or progression of severe preeclampsia. The death rate due to HELLP syndrome is relatively high. The use of corticosteroids is expected to increase platelet counts, reduce LDH values, and reduce liver function parameters to speed up the duration of healing and reduce mortality. Corticosteroids inhibit endothelial activation, reduce vascular endothelial injury, increase hepatic blood flow, prevent thrombotic microvascular hemolysis, and reduce platelet consumption. Objective: To evaluate the effectiveness of corticosteroids in patients with HELLP syndrome. Method: This research was conducted using a literature review method by searching articles from Google Scholar, PubMed, and Science Direct. Results: Administration of corticosteroids can increase platelet counts, reduce AST/ALT values, and reduce the need for blood product transfusions. Conclusion: Corticosteroids effectively increase platelet counts in patients with HELLP syndrome.*

**KEYWORDS** HELLP syndrome, Corticosteroids, Dexamethasone, Platelets.



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### INTRODUCTION

HELLP syndrome is a disease characterized by hemolysis syndrome with microangiopathic blood smears, elevated liver enzymes, and low platelets in pregnant and postpartum patients. HELLP syndrome may be a complication or progression of severe preeclampsia (Mendrick et al., 2018);(Manaf et al., 2021);(Fahed et al., 2022). HELLP syndrome has a prevalence of 0.5% to 0.9% (Rus et al., 2023). About 70% of cases occur in the third trimester of pregnancy, and 30% occur within 48 hours of delivery. The mortality rate of women with HELLP syndrome is 0 - 24%, with a perinatal mortality rate of up to 37% (Van et al., 2019).

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The pathophysiology of HELLP syndrome is caused by abnormal placental development, leading to abnormal maternal immune tolerance during placentation in early pregnancy, resulting in numerous membrane lesions that will separate maternal and fetal circulation (Rochlani et al., 2017);(Mohamed et al., 2023);(Huang et al., 2021). In addition, there is a release of inflammatory products causing a systemic inflammatory response in the mother by activating coagulation pathways and complement pathways. This leads to microvascular endothelial activation, which also causes microvascular endothelial dysfunction and damage (Herlin et al., 2020);(Alkorashy et al., 2021);(Niesłuchowska-Hoxha et al., 2018).

Such microvascular damage leads to platelet activation, platelet aggregation, microthrombin formation and fibrin deposits so that circulating red blood cells become damaged as they pass through the narrowed small blood vessels and cause intravascular hemolysis (Al Shehri et al., 2022);(Rodrigues et al., 2021). Therefore, the patient had signs of microangiopathic hemolytic anemia which is the destruction of red blood cells so that there were some elevations or decreases in the complete blood examination (Wasyluk et al., 2019);(Ananthy et al., 2021). Hemolysis is characterized by the presence of schistocytes on peripheral blood smears, low serum haptoglobin levels, low hemoglobin levels, elevated lactate dehydrogenase (LDH) levels, and elevated indirect bilirubin levels (van Runnard *et al.*, 2004; England, 2019).

Patients with HELLP syndrome have microvascular damage or dysfunction, leading to accumulation of microthrombin in the liver (Nilsson et al., 2019);(Aziz et al., 2023);(Jha et al., 2023);(Suastika, 2020). Therefore, patients with HELLP syndrome experience damage to hepatocytes which will result in an increase in liver enzymes. In addition, FaSL polymorphism can also mediate apoptosis which can cause liver damage (Aziz et al., 2023). Microvascular endothelial damage also causes aggregation and decreased agglutination of platelets leading to low platelet counts in patients. Low platelet levels increase the risk of bleeding and disrupt normal hemostasis (England, 2019).

HELLP syndrome usually occurs between 27 and 37 weeks of gestation (Wallace *et al.*, 2018). It rarely occurs before 27 weeks of gestation and in certain cases only appears after delivery. HELLP syndrome patients between 27-34 weeks gestation receive fetal lung maturation therapy with corticosteroids and undergo delivery within 48 hours of corticosteroid administration. At 34 weeks gestation, immediate delivery is the standard of care. Patient stabilization is always the top priority, antihypertensive therapy such as nifedipine, hydralazine and/or labetalol is used to help control severe hypertension. Magnesium sulfate should be given to reduce the risk of seizures in all women with HELLP syndrome (Duley *et al.*, 2010).

Treatment options other than immediate delivery include administration of corticosteroids or plasma exchange. In addition to the use of corticosteroids, psidii syrup can also help increase platelet values. Until now, the use of corticosteroids in HELLP syndrome is still *off-label*. The anti-inflammatory and immunosuppressive properties of corticosteroids have some beneficial effects on thrombotic microangiopathic anemia and on the maternal systemic inflammatory response.

Corticosteroids are known to show beneficial effects in endothelial dysfunction disorders. Glucocorticoids inhibit various events associated with endothelial

activation and platelet activation. Corticosteroids are known to decrease platelet consumption of antibodies by the spleen, decrease antibody production by the spleen, decrease antibody production by the bone marrow, and increase marrow platelet production. Glucocorticoids can also inhibit platelet aggregation caused by arachidonic acid, ADP, collagen, and thrombin. Corticosteroids are known to inhibit cytokine production of endothelial cells, macrophages, eosinophils, T lymphocytes, and mast cells, thereby inducing anti-inflammatory effects (van Runnard *et al.*, 2004).

Various studies have been published in the literature regarding the use of corticosteroids for the treatment of HELLP syndrome. There are two different results regarding the use of corticosteroids for the treatment of HELLP syndrome, namely corticosteroids can significantly increase platelet counts and overall laboratory parameters. While other results state that corticosteroids do not reduce overall maternal morbidity and mortality so that further literature review is needed regarding the effect of corticosteroids on maternal *outcomes*.

## RESEARCH METHOD

This literature study used a phased and structured approach and selection process. The sources used were databases such as Google Scholar, PubMed and Science Direct. The search technique used specific keywords from the research question and boolean operators (AND, OR, NOT or AND NOT). This aims to facilitate the search for articles that are specific to the *literature review* compiled. The keywords used were "*HELLP Syndrome*" AND "*Corticosteroids*". The article search was limited to articles published in the last 10 years, from 2015 to 2024. Language limits were also applied to limit the search to articles published only in English and Indonesian. The type of data used in this *literature review* is secondary data. Secondary data is data obtained from journals, textbooks, and scientific articles.

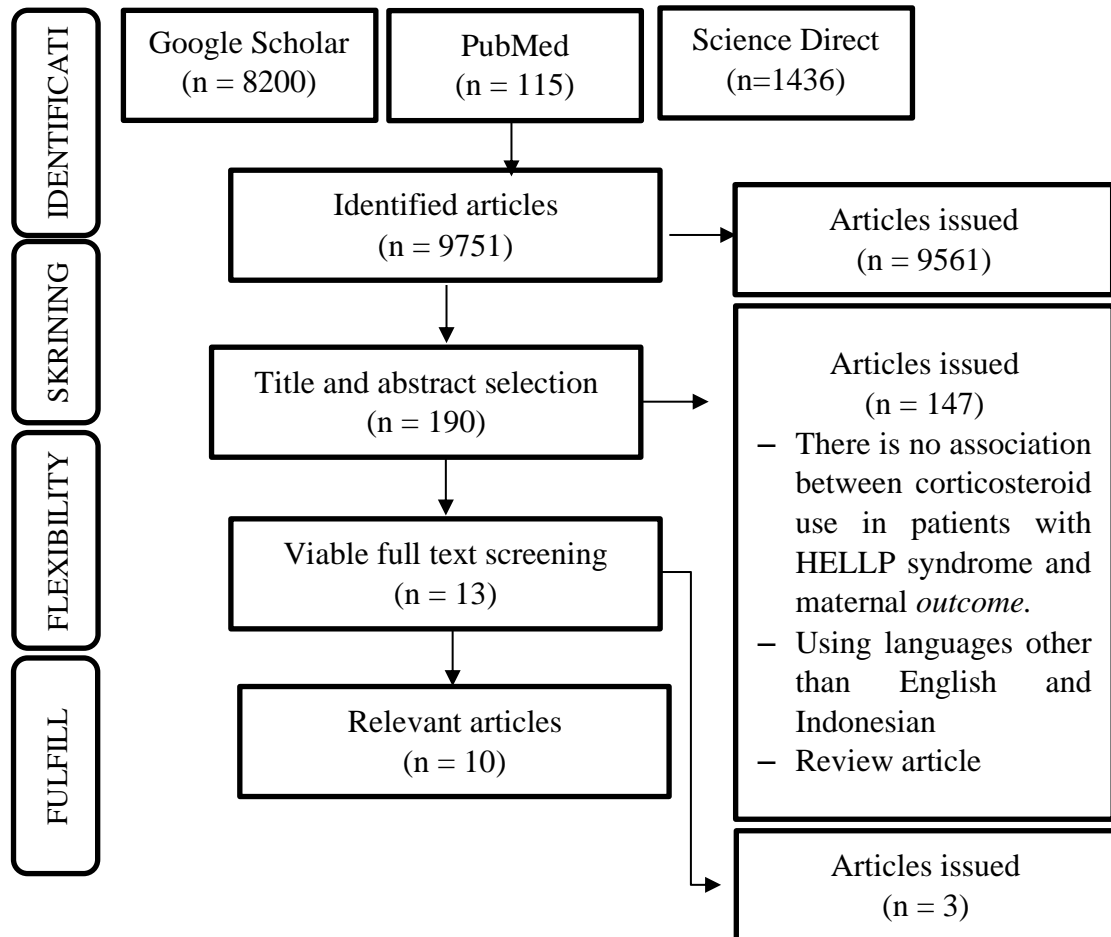
Relevant articles were screened and analyzed according to the inclusion criteria using the PRISMA diagram. The inclusion criteria for writing this *literature review* are original articles, articles in Indonesian and English, research published in the last 15 years, namely from 2010-2024. While the exclusion criteria for writing this literature review are articles that cannot be accessed (*no open access*), review articles, articles that only contain abstracts, articles with foreign languages other than Indonesian and English. All articles that are relevant and in accordance with the inclusion criteria are collected into one folder. The next step is to ensure that there is no duplication obtained from the database, screening the titles and abstracts of journals that have been stored in a special folder to ensure whether the journal can be used or not. The next step was to read the *full text* of the journal.

## RESULT AND DISCUSSION

Based on the results of a literature search through Google Scholar, PubMed, and Science Direct publications. The author found 9751 related articles published in 2005-2024. Articles obtained from the Google Scholar database amounted to 8200 articles, from the Pubmed database amounted to 115 articles, and from the

## The Effect of Corticosteroid Administration on Maternal Outcomes in Patients with HELLP Syndrome

Science Direct database amounted to 1436 articles. The research articles were then screened by considering the inclusion and exclusion criteria. There were 13 included in the next stage, namely by reading the full text of the article, so that 10 relevant articles were obtained.



The articles that have been screened and extracted are presented in Table I. Detailed descriptions of the study title, study design, study sample, administration dose and study results are summarized in the table.

**Table I. List of Articles Reviewed in the Literature Review**

<b>No.</b>	<b>Researcher</b>	<b>Title Research</b>	<b>Research Design</b>	<b>Research Sample</b>	<b>Dosage Giving</b>	<b>Research Results</b>
1	Heimel <i>et al.</i> , 2005 Netherlands	A randomized placebo-controlled trial of prolonged prednisolone administration to patients with HELLP syndrome remote from term	A randomized, double-blind trial	31 patients	Prednisolone 50 mg twice daily	Long-term administration of prednisolone reduces the risk of recurrent exacerbations of HELLP syndrome. Platelet count recovered faster in the prednisolone group compared to the placebo group.
2	Wallace <i>et al.</i> , 2013	Seeking the Mechanism(s) of action for corticosteroids in HELLP syndrome: SMASH study	single-center prospective study	17 patients	Dexamethasone 10 mg every 12 hours IV	Dexamethasone significantly decreased hemolysis and liver parameters, and significantly increased platelets within 24 hours of administration.
3	Oruc <i>et al.</i> , 2015 Turkey	Impact of Postpartum Dexamethasone on Postpartum Disease Stabilization in Women with HELLP Syndrome	Randomized prospective study	38 patients	Dexamethasone 8 mg, 4 mg and 2 mg IV twice daily, on days 1, 2 and 3 postpartum	Dexamethasone significantly increased platelet count within 24 hours and significantly decreased AST and ALT within 18 hours.
4	Aguayo and Gracia, 2018 Bolivia	Dexamethasone in HELLP syndrome: experience in Bolivia	Cross-sectional study	97 women with HELLP syndrome, 43 (44.3%) received dexamethasone.	Dexamethasone is given immediately after delivery at a dose of 8 mg every 8 hours for 72 hours, for a total of 72 mg	This study showed that postpartum administration of dexamethasone at a dose of 8 mg every 8 hours for 72 hours in HELLP syndrome was associated with a significant increase in platelet count.
5	Takahashi <i>et al.</i> , 2018 Japan	Effects of high-dose dexamethasone in postpartum women with class 1	Retrospective Study	18 women with grade 1 HELLP syndrome	The high-dose dexamethasone regimen consists of two doses. 10 mg IV dexamethasone	Administration of dexamethasone significantly improved platelet count recovery in postpartum women with grade 1 HELLP

## The Effect of Corticosteroid Administration on Maternal Outcomes in Patients with HELLP Syndrome

		haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome			e bolus every 12 hours, followed by 5 mg IV dexamethasone bolus every 12 hours	syndrome, and did not increase the rate of postpartum maternal complications.
6	Kang <i>et al.</i> , 2019 China	Effectiveness of high-dose glucocorticoids on hemolysis, elevating liver enzymes, and reducing platelets syndrome	Retrospective study	A total of 151 patients	Methylprednisolone is given intravenously by infusion at 80 to 120 mg/day for a total of 3 to 7 days.	High-dose glucocorticoids cannot significantly improve maternal and fetal prognosis and laboratory indices.
7	Ozdogan <i>et al.</i> , 2019 Turkey	The Effect of Dexamethasone Treatment on Maternal Outcome in HELLP Syndrome	Retrospective study	20 patients admitted to the ICU with a diagnosis of HELLP syndrome.	Dexamethasone treatment at a dose of 2 × 10 mg IV	Patients receiving dexamethasone treatment showed increased platelet count, but the difference was not statistically significant. And there is no statistically significant differences in ICU length of stay, mortality rates, and transfusion needs between Group.
8	Fonseca <i>et al.</i> , 2019 Colombia	Dexamethasone for the treatment of class I HELLP syndrome: A double blind, placebo-controlled, multicenter, randomized clinical trial	A double blind, placebo-controlled, multicenter, randomized clinical trial	87 patients	Pregnant women in the experimental group received a 10 mg dose of dexamethasone IV every 12 hours until delivery. Postpartum women received three 10 mg doses after delivery.	More blood products (platelets, plasma and red blood cells) were required for women in the placebo group, but this was not significant. the results of this study failed to show the benefit of using dexamethasone in patients with HELLP syndrome class I.

9	Dejene <i>et al.</i> , 2021 Dawa	The Effect of Dexamethasone Treatment on the Outcome of Patients with Antepartum HELLP Syndrome: A Prospective Cohort Study	Prospective cohort study design	86 patients were involved in the study, 43 patients in the treated group and 43 patients in the control group	Dexamethasone was administered intravenously in 4 doses of 10 mg, 10 mg, 5 mg, and 5 mg at 12-hour intervals.	Administration of dexamethasone to patients with antepartum HELLP syndrome increased platelet counts and reduced the overall need for blood product transfusions, but there was no significant difference in duration of hospitalization and development of complications.
10	Hosten <i>et al.</i> , 2023 Germany	Prolongation of Pregnancy in Patients with HELLP Syndrome Using Methylprednisolone: A Retrospective Multicentric Analysis	A Retrospective Multicentric Analysis	138 pregnant women with HELLP syndrome	Each patient in the treatment group was given 64 mg of methylprednisolone intravenously for 10 days, with the dose reduced by 50% every day	In a group of patients with HELLP syndrome, prolongation of pregnancy with methylprednisolone treatment improved maternal and neonatal outcomes.

## Discussion

HELLP syndrome is characterized by the presence of hemolysis with microangiopathic blood smears, elevated liver enzymes, and low platelet count. HELLP syndrome is one of the most severe complications of preeclampsia. It is associated with increased frequency of complications such as death, eclampsia, acute renal failure, as well as longer duration of hospital stay. Women affected by HELLP syndrome can be classified based on the degree of thrombocytopenia, including HELLP syndrome class 1 ( $\leq 50,000$  platelets/mm<sup>3</sup>); HELLP syndrome class 2 (between 50,000 and 100,000 platelets/mm<sup>3</sup>); and HELLP syndrome class 3 (between 100,000 and 150,000 platelets/mm<sup>3</sup>) (Wallace *et al.*, 2018; Fonseca *et al.*, 2019).

The hemolysis seen in HELLP syndrome is a microangiopathic hemolytic anemia that results from fragmentation of red blood cells as they move through blood vessels with damaged endothelium and fibrin strands. Hemolysis is defined by the presence of schistocytes on peripheral blood smears, low serum haptoglobin levels, low hemoglobin levels, elevated lactate dehydrogenase (LDH) levels, and elevated indirect bilirubin levels. Elevated liver enzymes often refer to elevated aspartate aminotransferase (AST) levels, abnormal alanine aminotransferase (ALT) levels, and/or elevated bilirubin levels. Liver enzymes are elevated in women with HELLP syndrome due to microangiopathy with sinusoidal obstruction leading to hepatocyte necrosis. The diagnosis of thrombocytopenia is based on a low platelet

count and is believed to result from a high rate of platelet consumption in areas where there is vascular damage. In the case of HELLP syndrome, platelets are activated leading to their attachment to damaged vascular endothelial cells, resulting in increased platelet turnover (Wallace *et al.*, 2018).

HELLP syndrome is most commonly diagnosed in late pregnancy with a peak incidence between 27 and 37 weeks of gestation. However, some cases do not develop until the postnatal period. Signs and symptoms of HELLP syndrome include elevated blood pressure, abdominal or epigastric pain in the right upper quadrant, headaches that do not resolve with acetaminophen, visual disturbances, significant weight gain, nausea and vomiting. Unlike preeclampsia, HELLP syndrome (15-20% of cases) may or may not be associated with elevated blood pressure (> 140/90 mmHg) or proteinuria (> 300 mg/day or urine protein:creatinine ratio > 30 mg/mmol) (Robert *et al.*, 2003).

Currently, the main treatment for HELLP syndrome is symptomatic treatment. This treatment includes regular spasmolysis and blood pressure lowering, use of glucocorticoids to treat the patient's condition and promote fetal lung maturation, addition of appropriate blood products, improvement of coagulation disorders, and close monitoring of the patient's condition. In addition, evaluation of the fetal condition in utero and timely termination of pregnancy are performed in HELLP syndrome (Li *et al.*, 2016; Gabor *et al.*, 2016).

The main mechanisms of glucocorticoid treatment are inhibiting endothelial activation, reducing vascular endothelial injury, increasing hepatic blood flow, preventing thrombotic microvascular hemolysis, and reducing platelet consumption. Corticosteroids work by decreasing platelet adhesion, decreased platelet disposal in the spleen, direct endothelial effects or rheological mechanisms, and finally increased platelet activation (Magann *et al.*, 1994). Several studies have shown that glucocorticoids can significantly increase BPC, LDH, ALT, and AST levels, blood pressure, and urine volume. The lower the primary BPC, the greater the significant improvement after glucocorticoid treatment (Kang *et al.*, 2019). Corticosteroids are thought to prevent platelet consumption and erythrocyte damage by stabilizing the vascular endothelium and effectively reducing the need for blood product administration. Platelet recovery is reported to begin 12 hours after corticosteroid administration (Mao and Chen., 2015).

Based on research conducted by Wallace *et al* (2013), clinical findings showed that systolic and diastolic blood pressure decreased significantly at 12 and 24 hours after IV dexamethasone administration. Based on laboratory values, significantly increased platelets after 12 and 24 hours of dexamethasone administration. Hematocrit decreased significantly in response to dexamethasone at 12 hours and after 24 hours. Serum LDH and AST levels both decreased 12 and 24 hours after dexamethasone administration and continued to decrease significantly after treatment of additional doses of dexamethasone. There were no significant changes in creatinine levels due to dexamethasone use. Uric acid increased ( $P<0.05$ ) 24 hours after dexamethasone administration but did not change significantly during the first 12 hours of dexamethasone treatment.

Research conducted by Oruc *et al* (2015), the treatment group was given dexamethasone therapy 8 mg, 4 mg and 2 mg intravenously twice a day, on days 1, 2



and 3 postpartum. The results showed a significant decrease in AST or ALT laboratory values at 18 hours postpartum. The treatment group had higher mean platelet counts for all time intervals and the difference between groups was significant after 42 hours postpartum. In the steroid-treated group, platelet counts were over 50,000/mm<sup>3</sup> after 12 hours postpartum and began to steadily increase after the 18th hour.

The study of Heimel *et al* (2005) conducted in a *randomized placebo controlled manner*, the treatment group was given 50 mg prednisolone therapy twice a day. It was found that daily administration of prednisolone for a long period of time did not result in prolongation of pregnancy. However, prednisolone significantly reduced the recurrence of antepartum HELLP exacerbations and accelerated the recovery of biochemical abnormalities. The anti-inflammatory properties of prednisolone may have a beneficial effect on HELLP syndrome by stabilizing the activated endothelium by inhibiting cytokine synthesis by endothelial cells, macrophages, eosinophils, T lymphocytes, and mast cells. In addition, the results of this study found significantly faster platelet recovery in the group receiving prednisolone therapy.

Research conducted by Aguayo and Grace (2018), showed that the administration of dexamethasone doses of 8 mg every 8 hours for 72 hours in postpartum patients with HELLP syndrome, was associated with a significant increase in platelet count. The average increase in platelets in the group without corticosteroids was 27,448 and in the corticosteroid group 88,408. On average within 3 days there was a 3.2-fold greater increase in the corticosteroid group ( $p = 0.001$ ). When viewed from the results of mortality and morbidity, the use of high-dose corticosteroids does not reduce maternal and perinatal morbidity and mortality with HELLP syndrome. Based on research conducted by Kang *et al* (2019), the duration of hospitalization in patients who received dexamethasone was faster than the placebo group, but not statistically significant.

Research conducted by Hosten *et al* (2023), which was conducted with a retrospective observational study on HELLP syndrome patients with stable maternal and fetal conditions for pregnancy extension. Patients were given methylprednisolone therapy starting with a dose of 64 mg and reducing the dose by 50% every day. The result was that HELLP syndrome patients who were given methylprednisolone therapy could extend the pregnancy by an average of four days. Pregnancies with gestational age less than 34 weeks were extended by 6 days, while pregnancies with gestational age less than 29 weeks were extended by 10 days.

In addition, methylprednisolone also affects laboratory results, in the first three days of treatment with methylprednisolone, there was a significant increase in platelet count in the group that received methylprednisolone compared to the control group. Platelet count increased from  $76,060 \pm 22,900/\mu\text{L}$  to  $117,430 \pm 39,065/\mu\text{L}$  in the treated group compared to the control group 1 there was an increase from  $66,500 \pm 25,852/\mu\text{L}$  to  $83,430 \pm 34,608/\mu\text{L}$  and from  $78,890 \pm 19,100/\mu\text{L}$  to  $131,080 \pm 50,900/\mu\text{L}$  in control group 2 ( $p < 0.001$ ). Analysis of other laboratory values showed a decrease in aspartate transaminase (AST) levels in the treatment group within the first three days.

## The Effect of Corticosteroid Administration on Maternal Outcomes in Patients with Hellp Syndrome

On average, normalization of AST values in the treatment group was achieved after 6.2 days. The LDH value decreased in the treatment group within the first three days to 205.8 U/L and in the control group to 706.2 U/L ( $p = 0.121$ ). Both groups still showed values above the normal range. This study also showed that severe neonatal complications including sepsis, ventilation, and infant mortality were significantly reduced in the corticosteroid-treated group ( $p < 0.05$ ). There were no cases of intrauterine fetal death in the treatment group, while two fetuses in control group 1 died intrauterine (4.4%).

Like other cases of preterm birth, babies born to women with HELLP syndrome have high stillbirth and mortality rates after the first week of life. Perinatal morbidity and mortality rates in pregnancies complicated by HELLP syndrome are between 7.4-34%, and depend on gestational age at diagnosis and delivery. In addition to being small for gestational age, babies born to mothers with HELLP syndrome often suffer from respiratory distress syndrome, perinatal asphyxia, intraventricular hemorrhage, and long-term morbidity. Several studies have shown that mothers diagnosed with HELLP syndrome late in their pregnancy have a reduced rate of perinatal morbidity, most likely due to a reduced incidence of prematurity (Wallace *et al.*, 2018).

Research conducted by Takahashi *et al* (2018), this study was conducted on patients diagnosed with HELLP syndrome class 1. This study showed that dexamethasone significantly increased platelet recovery. Dexamethasone was also associated with a significant decrease in AST levels, although it had no impact on LDH and total bilirubin levels. In this study using dexamethasone therapy 10 mg IV bolus every 12 hours for two doses, followed by dexamethasone 5 mg IV bolus every 12 hours, a prospective study showed that this regimen improved laboratory results and clinical parameters. Corticosteroid administration in HELLP syndrome can improve platelet levels, SGOT, SGPT, LDH, mean arterial blood pressure and urine production. *Postpartum* corticosteroid administration has no effect on platelet levels. Corticosteroid administration has no effect on maternal and perinatal/neonatal morbidity and mortality (Ministry of Health, 2017).

Research conducted by Ozdogan *et al* (2018), there was a tendency to increase platelet count from the first day to the third day in the group given dexamethasone 10 mg intravenous therapy immediately after induction of anesthesia and 2 additional dexamethasone with the same dose every 12 hours after delivery, but the difference was not statistically significant. In addition, there was a decrease in ALT and bilirubin values in the group receiving dexamethasone compared to the placebo group, but the difference was not statistically significant.

This study also showed that in the group given dexamethasone therapy and in the control group, there was one patient suffering from eclampsia who died due to multiple organ failure. Two intrauterine deaths and one premature death occurred. Two of the cases were diagnosed with postpartum HELLP after spontaneous vaginal delivery. Analysis of the pregnant and postpartum groups showed no difference in the occurrence of complications, recovery of laboratory parameters, transfusion requirements, combined morbidity or duration of hospitalization.

HELLP syndrome is a disease that affects multiple organs, including the liver, spleen, kidneys and brain. In addition to multisystem involvement, there are various

morbidities associated with HELLP syndrome. Some women may experience renal dysfunction, which is partly due to glomerular endotheliosis and will manifest into acute kidney injury or even renal failure. Although rare, some women have reported eye complications during pregnancy and immediately after delivery. More commonly reported are cases of intracerebral hemorrhage, posterior reversible encephalopathy or eclampsia. In addition, there are some reports of women experiencing cerebral infarction or cerebral edema (Paul *et al.*, 2013).

Dejene *et al* (2021), conducted research on antepartum patients who were given dexamethasone therapy in 4 doses, namely 10 mg, 10 mg, 5 mg, 5 mg with a 12-hour interval. The administration of dexamethasone to antepartum HELLP syndrome patients significantly increased platelet counts. The platelet count ranged from 18,000 to 94,000/mm<sup>3</sup> while the platelet count in the comparison group was 11,000 to 92,000/mm<sup>3</sup>. The average duration of days required to reach a platelet count of 100,000 cells/mm<sup>3</sup> was significantly faster in the dexamethasone-treated group. However, there was no statistically significant difference in the duration required to reach an AST level of <70 U/L between the dexamethasone-treated group (M=4.40, SD=1.72) and the comparison group (M=4.77, SD=1.70).

When observed from the parameters of hospitalization duration, there was no statistically significant difference in the mean duration of hospitalization between patients receiving dexamethasone therapy (M=5.40, SD=1.43) and the placebo group (M=5.67, SD=1.74),  $t(84) = -.811$ ,  $p=0.420$ . There were 14 (32.6%) women in the control group who received platelet transfusion, but only one patient (2.4%) in the treated group received transfusion [RR, 0.07; 95% CI, 0.01-0.52]. A total of 21 (48.8%) women in the control group received whole blood transfusion, but only 4 (9.3%) women in the treated group received whole blood transfusion [RR, 0.19; 95% CI, 0.07-0.51].

Fonseca *et al* (2019), a study conducted with a *double blind, placebo-controlled, multicenter, randomized clinical trial* in patients with class I HELLP syndrome. Based on the time required to reach platelet count >100,000/mm<sup>3</sup>, it was found that there was no statistically significant difference between patients who received dexamethasone and the control group. When observed from the LDH and AST values, it was found that there was no statistically significant difference between patients receiving dexamethasone and the control group who reached LDH below 600 U/L and AST below 70 U/L before hospital discharge. In addition, it was found that more blood products, namely platelets, plasma, and red blood cells were required by women in the control group. Based on the morbidity and development of complications in patients treated with dexamethasone, there was no significant difference between the treated and control groups.

Based on these studies, corticosteroids have the activity of inhibiting endothelial activation, increasing hepatic blood flow, preventing thrombotic microvascular hemolysis, and reducing platelet consumption that can be used in patients with HELLP syndrome. This *literature review* is expected to be useful in providing optimal therapy for pregnant and postpartum women with HELLP syndrome.

## CONCLUSION

Administration of corticosteroids in patients with HELLP syndrome can improve laboratory parameters including platelet count, AST/ALT levels, and LDH levels, and can reduce the overall need for blood product transfusions.

## REFERENCES

- Al Shehri, H. A., Al Asmari, A. K., Khan, H. A., Al Omani, S., Kadasah, S. G., Horaib, G. B., Al Buraidi, A., Al Sharif, A. A., Mohammed, F. S., & Abbasmanthiri, R. (2022). Association between preventable risk factors and metabolic syndrome. *Open Medicine*, 17(1), 341–352. <https://doi.org/10.1515/med-2021-0397>
- Alkorashy, M., Al-Ghamdi, B., Tulbah, S., Al-Numair, N. S., Alhadeq, F., A Takroni, S., & Al-Hassnan, Z. N. (2021). A novel homozygous SCN5A variant detected in sick sinus syndrome. *Pacing and Clinical Electrophysiology*, 44(2), 380–384.
- Ananth, V., Priyadharsini, R. P., & Subramanian, U. (2021). Pathogenesis, Diagnosis, and Management of Metabolic Syndrome: A Comprehensive Review. *J Basic Clin Appl Health Sci*, 4(2), 39–45.
- Aziz, Z., Shareef, H., Afridi, E., Kashif, M., Hussain, M., Waseem, M., Shahid, T., Khan, M. A., Muntaha, S. T., & Silro, H. H. (2023). Combating Metabolic Syndrome through Non-Pharmacological Strategies: A Literature Review: Combating Metabolic Syndrome. *Pakistan Journal of Health Sciences*, 20–28. <https://doi.org/10.54393/pjhs.v4i11.1145>
- Aguayo, M.Y.A., & Gracia, P.V.D. 2018. Dexamethasone in HELLP syndrome: experience in Bolivia. *The Journal of Maternal-Fetal & Neonatal Medicine*. ISSN: 1476-7058 (Print) 1476-4954 (Online)
- Dejene, T.J., Assefa, D., Gezahegn, M. 2021. The Effect Dexamethasone Treatment On The Outcome of Patients With Antepartum HELLP Syndrome: A Prospective Cohort Study. *Lancet Journal*, Available at SSRN: <https://ssrn.com/abstract=3807319> or <http://dx.doi.org/10.2139/ssrn.3807319>
- Duley, L.A., Gulmezoglu, D., Henderson, S., & Chou, D. 2010. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. *Cochrane Database Syst Rev* :11, CD000025.
- England. 2019. HELLP Syndrome: Pathogenesis and Clinical Findings. *The Calgary Guide to Understanding Disease*. <https://calgaryguide.ucalgary.ca/hellp-syndrome-pathogenesis-and-clinical-findings/>
- Fonseca, J.E., Otero, J.C., & Messa C. 2019. Dexamethasone for the treatment of class I HELLP syndrome: A double-blind, placebo-controlled, multicenter, randomized clinical trial. *Pregnancy Hypertension*, Volume 17 Pages 158-164
- Fahed, G., Aoun, L., Bou Zerdan, M., Allam, S., Bou Zerdan, M., Bouferraa, Y., & Assi, H. I. (2022). Metabolic syndrome: updates on pathophysiology and management in 2021. *International Journal of Molecular Sciences*, 23(2), 786.
- Gabor, M., Drab, M., & Holoman, K. 2016. Postpartum corticosteroids in HELLP syndrome - standard to prompt recovery. *Bratislavské Lekárske Listy*, 117: 418–424

- Heimel, P.J.V.R., Huisjes, A.J.M., Franx, A., Koopman, C., Bots, M.L., & Bruinse, H.W. 2005. A Randomised Placebo-Controlled Trial of Prolonged Prednisolone Administration to Patients with HELLP Syndrome Remote from Term. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 128, 187-193
- Hosten, A.K., Bonitz, J., Thale, V., & Tchirikov, M. 2023. Prolongation of Pregnancy in Patients with HELLP Syndrome Using Methylprednisolone: A Retrospective Multicentric Analysis. *Life*, 13,1013.<https://doi.org/10.3390/life13041013>
- Herlin, M. K., Petersen, M. B., & Brännström, M. (2020). Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome: a comprehensive update. *Orphanet Journal of Rare Diseases*, 15(1), 1–16.
- Huang, R., Yan, L., Lei, Y., & Li, Y. (2021). Hypothyroidism and complicated sick sinus syndrome and acute severe psychiatric disorder: A case report. *International Medical Case Reports Journal*, 171–176.
- Jha, B. K., Sherpa, M. L., Imran, M., Mohammed, Y., Jha, L. A., Paudel, K. R., & Jha, S. K. (2023). Progress in Understanding Metabolic Syndrome and Knowledge of Its Complex Pathophysiology. *Diabetology*, 4(2), 134–159. <https://doi.org/doi.org/10.3390/diabetology4020015>
- Kang, S., Zhou, L., Wang, X., Li, Y., & Wang, Y. 2019. Effectiveness of High-Dose Glucocorticoids on Hemolysis, Elevating Liver Enzymes, and Reducing Platelets Syndrome. *Journal of International Medical Research*, Vol. 47(2) 738-747
- Kemenkes RI. 2017. Pedomam Nasional Pelayanan Kedokteran Tata Laksana Komplikasi Kehamilan. Jakarta: Menteri Kesehatan Republik Indonesia.
- Li, Y., Ren, C., & Mao M. 2016. Prognostic factors of the efficacy of high-dose corticosteroid therapy in hemolysis, elevated liver enzymes, and low platelet count syndrome during pregnancy: a meta-analysis. *Medicine*, 95: e3203
- Magann EF, Bass D, Chauhan SP, Sullivan DL, Martin RW, Martin JN. 1994. Antepartum corticosteroids: disease stabilization in patients with the syndrome of hemolysis, elevated liver enzymes and low platelets (HELLP). *Am J Obstet Gynecol*. 171: 1148-1153. 10.1016/0002-9378(94)90054-X.
- Mao M, & Chen C. 2015. Corticosteroid Therapy for Management of Hemolysis, Elevated Liver Enzymes, and Low Platelet Count (HELLP) Syndrome: A Meta-Analysis. *Med Sci Monit*, 21: 3777-3783 DOI: 10.12659/MSM.895220
- Manaf, M. R. A., Nawi, A. M., Tauhid, N. M., Othman, H., Rahman, M. R. A., Yusoff, H. M., Safian, N., Ng, P. Y., Manaf, Z. A., & Kadir, N. B. A. (2021). Prevalence of metabolic syndrome and its associated risk factors among staffs in a Malaysian public university. *Scientific Reports*, 11(1), 8132. <https://doi.org/10.1038/s41598-021-87248-1>
- Mendrick, D. L., Diehl, A. M., Topor, L. S., Dietert, R. R., Will, Y., La Merrill, M. A., Bouret, S., Varma, V., Hastings, K. L., & Schug, T. T. (2018). Metabolic syndrome and associated diseases: from the bench to the clinic. *Toxicological Sciences*, 162(1), 36–42. <https://doi.org/10.1093/toxsci/kfx233>
- Mohamed, S. M., Shalaby, M. A., El-Shiekh, R. A., El-Banna, H. A., Emam, S. R., & Bakr, A. F. (2023). Metabolic syndrome: risk factors, diagnosis,

- pathogenesis, and management with natural approaches. *Food Chemistry Advances*, 3, 100335. <https://doi.org/10.1016/j.focha.2023.100335>
- Niesłuchowska-Hoxha, A., Cnota, W., Czuba, B., Ruci, A., Ciaciura-Jarno, M., Jagielska, A., Wójtowicz, D., Kierach, R., Dąbrowski, K., & Sidorowicz, M. (2018). A retrospective study on the risk of respiratory distress syndrome in singleton pregnancies with preterm premature rupture of membranes between 24+ 0 and 36+ 6 weeks, using regression analysis for various factors. *BioMed Research International*, 2018.
- Nilsson, P. M., Tuomilehto, J., & Rydén, L. (2019). The metabolic syndrome—What is it and how should it be managed? *European Journal of Preventive Cardiology*, 26(2\_suppl), 33–46. <https://doi.org/10.1177/2047487319886404>
- Rochlani, Y., Pothineni, N. V., Kovelamudi, S., & Mehta, J. L. (2017). Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. *Therapeutic Advances in Cardiovascular Disease*, 11(8), 215–225. <https://doi.org/10.1177/1753944717711379>
- Rodrigues, M. C., Maciel, E. da S., Quaresma, F. R. P., Sesti, L. F. C., Paiva, L. da S., Macedo Junior, H., Araújo, F. A. de, Fonseca, F. L. A., & Adami, F. (2021). Prevalence and factors associated with metabolic syndrome in a vulnerable population in northern Brazil: a cross-sectional study. *Journal of Human Growth and Development*, 31(2), 291–301. <https://doi.org/10.36311/jhgd.v31.11410>
- Rus, M., Crisan, S., Andronie-Cioara, F. L., Indries, M., Marian, P., Pobirci, O. L., & Ardelean, A. I. (2023). Prevalence and risk factors of metabolic syndrome: A prospective study on cardiovascular health. *Medicina*, 59(10), 1711.
- Suastika, K. (2020). The challenges of metabolic disorders in Indonesia: focus on metabolic syndrome, prediabetes, and diabetes. *Medical Journal of Indonesia*, 29(4), 350–353. <https://doi.org/10.13181/mji.com.205108>
- Takahashi, A., Kita, N., Tanaka, Y., Tsuji, S., One, T., Ishiko, A., Kimura, F., Takahashi, K., & Murakami, T. 2018. Effect of High Dose Dexamethasone In Postpartum Women With Class 1 Haemolysis, Elevated Liver Enzymes And Low Platelets (HELLP) Syndrome. *Journal Of Obstetrics and Gynaecology*, 39(3):335-339. doi: 10.1080/01443615.2018.1525609
- Van Lieshout L.C.E.W., Koek G.H., Spaanderman M.A., van Runnard Heimel P.J. 2019. Placenta derived factors involved in the pathogenesis of the liver in the syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP): A review. *Pregnancy Hypertens*, 18:42–48. doi: 10.1016/j.preghy.2019.08.004
- Van Runnard, P.J., Frans, A., Schobben, A.F.A.M., Huisjes, A.J.M., Derks, J.B., & Bruinse, H.W. 2004. Corticosteroids, Pregnancy, and HELLP Syndrome: A Review. *Obstetrical and Gynecological Survey*: Vol 60 No 1
- Wallace, K., Harris, S., Addison, A., & Bean, C. 2018. HELLP Syndrome: Pathophysiology and Current Therapies. *Curr Pharm Biotechnol*, 19(10):816-826.
- Wasyłuk, W., Wasyłuk, M., Zwolak, A., & Łuczyk, R. J. (2019). Metabolic syndrome-diagnostics, pathophysiology and treatment. *Journal of Education, Health and Sport*, 9(8), 45–62.

