



HELLP Syndrome Diagnostic and Management Approach, Literature Review

Hayfa Ziyad Alotaibi^{1*}, Lama Abdullah Aljuaidan¹, Shouq Rafat Elmokid¹, Wessam Abdullah Al Ghamdi¹, Ahmed Dhaifallah Alghamdi², Samaher Ali Alshehri³, Leyan Riyad Bakedo⁴, Omar Mousa Kadhem⁵, Marwa Mohammed Al Jumaiah⁶, Maria Talal Kufyah⁷

¹Faculty of Medicine, Alfaisal University, Riyadh, KSA.

²Faculty of Medicine, King Khalid University, Abha, KSA.

³Faculty of Medicine, Ibn Sina National College of Medicine, Jeddah, KSA.

⁴Faculty of Medicine, King Abdulaziz University, Jeddah, KSA.

⁵Department of Quality, Al Meeqat General Hospital, Madinah, KSA.

⁶Faculty of Medicine, King Faisal University, Al Ahsa, KSA.

⁷Maternity and Child Hospital, Makkah, KSA.

ABSTRACT

HELLP syndrome is a fatal complication in pregnancy it consists of 3 major conditions which are hemolysis, elevated liver enzymes, and low platelet count 10% to 20% of patients with preeclampsia will develop HELLP syndrome, and 0.5% to 0.9% of all pregnancies this paper will discuss the pathophysiology, diagnosing, complications and management of this syndrome. PubMed database was used for articles selection, and the following keys were used in the mesh ("HELLP syndrome" [Mesh]) AND ("Preeclampsia" [Mesh]). In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: HELLP syndrome, Preeclampsia, Management of HELLP syndrome. Exclusion criteria were all other articles, which did not have one of these topics as their primary endpoint. The incidence, etiology, and management options were analyzed. HELLP syndrome is a very serious illness and it should be managed carefully and diagnosed correctly to save maternal and fetal lives.

Keywords: HELLP syndrome, Preeclampsia, Management of HELLP syndrome, Evaluation

Corresponding author: Hayfa Ziyad Alotaibi

e-mail ✉ Hayfa973@gmail.com

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INTRODUCTION

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) syndrome is considered one of the complications and extension of severe Preeclampsia, it highly increases the level of morbidity and mortality in the prenatal period and peripartum period also, the pathophysiology is not well understood but still, there are some theories we will mention them in this paper, in addition to the clinical presentation of this syndrome and the laboratory criteria to diagnose it, In the management of HELLP syndrome the best evidence is for aggressive management since this will lower the risk of mortality a lot, and the conservative management has shown a huge failure since the mortality and morbidity level is very high. After delivery, the laboratory tests will back to the baseline after a few days and the patient is stable again.

The purpose of this review is to discuss the HELLP syndrome, and how to manage it and its complications

MATERIALS AND METHODS

PubMed database was used for articles selection, and the following keys were used in the mesh ("HELLP syndrome" [Mesh]) AND ("Preeclampsia" [Mesh]).

In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: HELLP syndrome, Preeclampsia, Management of HELLP syndrome. Exclusion criteria were all other articles, which did not have one of these topics as their primary endpoint.

Around 90 publications were chosen as the most clinically relevant out of 1,202 articles indexed in the previous two decades, and their full texts were evaluated. A total of 31 of the 90 were included after a thorough examination. Additional research and publications were found using reference lists from the recognized and linked studies. Expert consensus recommendations and commentary were added where relevant to help practicing physicians assess chest pain most simply and practically.

Pathogenesis

As we described above HELLP syndrome is considered as one of the complications of severe preeclampsia so everything starts with abnormal placentation as the researchers postulated and this will lead to placental ischemia and so production of toxic and inflammatory factors will affect the endothelial cells (Van

Beek & Peeters, 1998; Salman *et al.*, 2021). Injury of endothelial cells causes vasoconstriction, increased capillary permeability, and platelet aggregation and this will show the clinical presentation of preeclampsia which is hypertension, proteinuria, edema, and thrombocytopenia (Paternoster *et al.*, 1995; Gondo, 2021).

It is unclear which patient will develop HELLP syndrome after preeclampsia and which one will not but Paternoster *et al.* (1995) showed that there is a level of compensated DIC in all patients with HELLP syndrome when compared with normotensive patients and patients with preeclampsia without HELLP syndrome, there is a statistically significant increase in the level of fibrinogen degradation products, D-dimer and plasma fibronectin, also there is a decrease in the level of protein C and S, in addition, to decrease in the level of Antithrombin III, The routine laboratory hematological tests (PTT, PT, DIC, fibrinogens) were not a good predictor or indicator of which patient will develop this syndrome.

Immunological factors could be one of the initiators causes to develop Preeclampsia and HELLP syndrome, since Haeger *et al.* (1996) noticed an elevation in the level of tumor necrosis factor-alpha at the time of delivery inpatient with HELLP syndrome, this factor affects the endothelial cells and the coagulation cascade inside the body.

Fibrin deposition in the periportal sinusoids and hemorrhage in the space of Disse leads to the histological pattern of liver injury in HELLP syndrome, and hepatocellular necrosis as a result. If this hemorrhage continues it will dissect the connective tissue and progress to a subcapsular liver hematoma, Needle biopsy of HELLP syndrome patients show also fatty deposition in the liver in addition to fibrin deposition and this led to a theory that says HELLP syndrome, acute fatty liver of pregnancy, and preeclampsia are all part of the same disease (Minakami *et al.*, 1988).

Clinical symptoms and occurrence

The incidence of HELLP syndrome is 0.5%-0.9% in all pregnancies and 10%-20% inpatient with severe preeclampsia, the peak period of HELLP syndrome is from 27th and 37th gestational weeks, Onset of HELLP syndrome usually is very rapid and the patient already has hypertension and proteinuria, weight gain and generalized edema proceed the HELLP syndrome in 50% of patients (Sibai, 1990).

Typical clinical presentation of HELLP syndrome is right upper quadrant pain or epigastric pain, nausea, and vomiting, The pain is colicky and fluctuant, exacerbates during the night, and relieved during the day.

Hemolysis in HELLP syndrome is due to microangiopathic hemolytic anemia (MAHA), RBCs are fragmented due to high-velocity passage through the injured endothelium, presence of schizocytes and Burr cells in the blood smear is highly suggestive for hemolysis, increasing in the reticulocytes count will suggest a compensatory mechanism of MAHA, also increasing in LDH and low hemoglobin concentration will also be noticed (Rath *et al.*, 2000).

Elevated liver enzymes may reflect liver involvement in hemolysis increasing in LDH, but AST and ALT elevation mostly will be due to liver injury.

Thrombocytopenia or low platelet (less than 150×10^9) may be explained by a lot of etiologies, gestational thrombocytopenia, immunological reaction, DIC, Preeclampsia or HELLP syndrome,

but in the case of HELLP syndrome it is due to overconsumption of platelets due to endothelial injury, platelets will be activated and aggregation is turned on (Visser & Wallenburg, 1995; Nilesh *et al.*, 2021).

Diagnostic criteria and differential diagnosis

In diagnosing help syndrome, we have mainly two classifications, Tennessee and Mississippi, the first defines help syndrome as pathological peripheral blood smear shows schistocytes and HAMA in addition to low platelets count (less than $100 \times 10^9/L$), elevated LDH more than 600 IU/L, and elevated AST more than 70 IU/L, the latter divides HELLP syndrome into 3 classes (Sibai, 1990; Sibai, 2004):

class 1: low platelets count (less than $50 \times 10^9/L$), AST or ALT more than 70 IU/L, elevated LDH more than 600.

class 2: low platelets count (less than $100 \times 10^9/L$ and more than $50 \times 10^9/L$), AST or ALT more than 70 IU/L, elevated LDH more than 600.

class 3: low platelets count (less than $150 \times 10^9/L$ and more than $100 \times 10^9/L$), AST or ALT more than 40 IU/L, elevated LDH more than 600 (Sibai, 1990; Sibai, 2004).

Differential diagnoses of HELLP syndrome can be viral hepatitis or cholangitis since both of them have right upper quadrant abdominal pain and elevated liver enzymes also.

less commonly but more seriously are: idiopathic thrombocytopenic purpura (ITP), Fatty liver in pregnancy, systemic lupus erythematosus, those diagnoses could be mistaken with HELLP syndrome either due to similar presentation or similar lab values.

Complications of HELLP syndrome

Maternal mortality

Maternal mortality is ranging between 1.1% up to 25%, HELLP syndrome is a very serious condition and life-threatening to both mother and fetus and it should be managed aggressively 26% of deaths in HELLP syndrome are reported due to cerebral hemorrhage and strokes (Isler *et al.*, 1999), and maternal mortality due to subcapsular hematoma is ranging from 18% up to 86% (Mihu *et al.*, 2007).

Perinatal morbidity and mortality

The rate of Perinatal mortality in HELLP syndrome patients is between 5%-20% (Harms *et al.*, 1995).

Gestational age and birth weight at delivery determines the neonatal survival rate in patients with HELLP syndrome, Weinstein reported hematological abnormalities and he refers this due to the ability of toxic substances and inflammatory factors to cross the placenta, neonatal thrombocytopenia has been reported in 50% of cases, Leukopenia and neutropenia had been reported in 40% of cases with HELLP syndrome and 92% of pregnancies with HELLP syndrome the neonates have abnormal peripheral blood smear, and for liver enzymes in the neonates, they found that there is no correlation between elevated liver enzymes in the mothers and the neonates (Koenig & Christensen, 1989).

DIC

The cascade of HELLP syndrome is very similar and looks the same as DIC both have endothelial damage and platelet adhesion and aggregation and due to this fact 38% of pregnant women with HELLP syndrome will develop DIC (FDP more than 40mg/L, and low serum fibrinogen concentration less than 3g/L) and this is mostly associated with placental abruption and also maybe due to increased consumption of these products in case of DIC and liver dysfunction with decreased synthesis (Sibai et al., 1986).

Management of a patient with HELLP syndrome

In managing patients with HELLP syndrome or severe preeclampsia our decision mainly depends on the gestational age, so if the gestational age is 34 weeks or more the treatment of choice is immediate delivery and this will save the life of the fetus and mother at the same time and this is considered the mainstay treatment of HELLP syndrome (Gul et al., 2005).

Inpatient with a gestational age of less than 34 weeks and more than 27 weeks the mainstay treatment is conservative for 48h, stabilizing the patient condition and corticosteroid could be given for ensuring lung maturation within this period and then delivery should take a place and this is the case in the majority of patients (Sibai et al., 1994).

For patients with gestational age, less than 27 weeks conservative management for more than 72 hours and corticosteroid could be considered but this regimen is differ according to the hospital protocols and country guidelines, and repeated dose of corticosteroid is not advised since there is a study of randomized control trial suggests that the long term and repetitive dose of corticosteroids will lead to fetal growth restriction, adrenal suppression and increase perinatal mortality so the only initial dose is required (Vincer et al., 2006).

CONCLUSION

Contrasting definitions and classification have up now been used in the diagnosis of HELLP syndrome. The functionality of many results has been limited because of this. The Mississippi and Tennessee classifications are suitable to provide comparisons. In future reports, Classifications used should be restricted to one of these. Neither Cochrane evaluations nor randomized trials regarding delivery in women with HELLP syndrome have been carried out. There is a consensus that early delivery is indicated when the HELLP syndrome develops after 34 weeks of pregnancy to reduce the risk of potentially serious complications, The two main controversial issues, before 34 weeks of gestation are expectant management and the use of CS in the HELLP syndrome. About the timing of delivery and the best method of delivery, there is no general agreement. A standard CS course is usually recommended after stabilization of the maternal condition during deliveries in the time-span between 24 and 34 weeks gestation, which is followed by delivery, 24 hours afterward. This effect seems to be limited or lacking in patients with HELLP syndrome even though a maternal benefit has been demonstrated for patients with severe preeclampsia. High-dose dexamethasone treatment and repeated CS dosage cannot be recommended instantly. Both antepartum and post-partum HELLP patients need adequately sized, randomized, placebo-controlled trials regarding the dosage of CS, as well as high-dose dexamethasone versus standard CS dosage. New treatment alternatives and improved

clinical management will be as a result of better insight into the complex pathophysiology of the HELLP syndrome. The establishment of a well-designed multicenter study testing the benefit of antithrombin to counteract DIC in the HELLP syndrome should be promoted (Haram et al., 2009).

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