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Review Article

HELLP SYNDROME: A BRIEF REVIEW

Dinesh Kumar Yadav[1*], Ajay Kumar Shah[1]

[1]Pharm.D, Department of Pharmacy Practice, Krupanidhi College of Pharmacy, Carmelaram Post, Varthur Hobli, Bangalore-560035, Karnataka, India.

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ABSTRACT

HELLP is an abbreviation of hemolysis (H), elevated liver enzyme (EL), and low platelet count (LP) which is a serious complication in pregnancy and also described as a severe form of preeclampsia and which is also associated substantial maternal and perinatal morbidity and mortality which is usually misdiagnosed at initial presentation. The patients with HELLP syndrome may present complain of malaise (90%), epigastric or right upper quadrant pain (90%), and nausea or vomiting (50%) and the healthcare should be alert to provide possible diagnosis. Hypertension and protein urea may be absent or inappreciable. The pathophysiology of HELLP syndrome is exactly imprecise. HELLP syndrome is also caused due to coagulation cascade activation leading to platelets consumption is due to adherence onto a damaged and activated endothelium. Laboratory investigation includes a low platelet count and increased hepatic enzymes. HELLP syndrome patients require plasmapheresis and corticosteroids therapy.

Keywords: HELLP syndrome, preeclampsia, thrombocytopenia, management, corticosteroids.

INTRODUCTION:

HELLP is an abbreviation of hemolysis (H), elevated liver enzyme (EL), and low platelet count (LP) which is a serious complication in pregnancy and also described as a severe form of preeclampsia. The HELLP syndrome word is the name given by Louis Weinstein in 1982 (1).HELLP syndrome was believed to be a severe form of preeclampsia further it was known that it usually occurs only 10% to 20% cases without preeclampsia (2). HELLP syndrome is believed that its influence is about 0.5% to 0.9% of all pregnancies and its ubiquity is high in patients having preeclampsia (3). Preeclampsia is a complication of a pregnancy that is distinguished by high blood pressure (systolic blood pressure >140mm Hg and diastolic blood pressure >90 mm Hg, and in severe preeclampsia systolic blood pressure >160 mm Hg and diastolic blood pressure >110 mm Hg, respectively and proteinuria (excretion of protein >300 mg collection of urine within a 24 hours), and the women who have normal blood pressure can develop after 20 weeks of pregnancy and up to 6 weeks after delivery (4).

The HELLP syndrome treatment is based on the age of the gestational but termination of pregnancy is the treatment of choice to prevent any impediment for the mother and the baby. When disseminated intravascular coagulation occurs, conservative treatment is prohibited to the patients (18). When the symptoms of HELLP syndrome starts to aggravate after the supportive treatment, delivery should be done (3). HELLP syndrome patients should know that conservative treatment may increases the rate of acute renal failure, placental abruption, acute renal failure, disseminated intravascular coagulation, pulmonary oedema and increasing risk of maternal or fetal death (19).

Pathophysiology:

HELLP syndrome is a syndrome that is denoted by thrombocytopenia, liver dysfunction and hemolytic anemia which shows the result from activation of microvascular endothelial cells and cell injury and platelet activation after the release of serotonin and thromboxane A and cause cascade of vasospasm, platelet agglutination and endothelial damage (12, 13).

*Corresponding author: Dinesh Kumar Yadav | E-mail: yadavdineshkumar509@gmail.com

The pathophysiology of HELLP syndrome is exactly imprecise. HELLP syndrome is also caused due to coagulation cascade activation leading to platelets consumption is due to adherence onto a damaged and activated endothelium. And also microangiopathic hemolysis is caused due to shearing of erythrocytes as they forcely travel through capillaries laden with deposit of platelet-fibrin. Necrosis of hepatic and Multiorgan microvascular injury leads to liver dysfunction and contribute to the development of HELLP syndrome (5, 6, 7, 8, 9, 10).

HELLP is a variation of preeclampsia. Normally during pregnancy, the spiral arteries dilate 5-10 times normal size and developing large central arteries which deliver lots of blood to the fetus but during preeclampsia, the spiral arteries are fibrous causing them narrow which means less blood to the fetus. The hypoxic placenta releases different placental factors including soluble vascular endothelial growth factor receptor-1 (sVEGFR-1), after that it binds vascular endothelial growth factor (VEGF) and placental growth factor (PGF), which then causes dysfunction of placental and endothelial cell and then prevents them from binding endothelial cell receptors. This result shows proteinuria, hypertension and increased platelet activation and aggregation.

HELLP syndrome may also be due to the maternal-fetal immune balance alternation, which leads to arterial hypertension and platelet activation and aggregation and endothelial dysfunction (11). This leads to inflammation which targets the liver (13, 14).

The maternal who has HELLP syndrome and the child with long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency (LCHA) and acute fatty liver of pregnancy (AFLP). This inherited autosomal recessive abnormality of fatty-acid oxidation which causes liver damage due to insufficient mitochondrial oxidation of fatty acids which is used for ketogenesis (15, 16).

HELLP syndrome include serious complicatiofor the mother such as Disseminated intravascular coagulation, bleeding, hematoma, Cardiac arrest, myocardial ischemia, Pulmonary edema, respiratory failure, pulmonary embolism, adult respiratory distress syndrome , Hemorrhage/stroke, cerebral edema, central venous thrombosis, seizures, retinal detachment, Acute renal failure, chronic renal failure requiring dialysis, Hepatic hematoma, ascites, diabetes insipidus, Infection. HELLP syndrome also leads serious complication to the neonates such as Prematurity, Intrauterine growth retardation (39%), Thrombocytopenia (3).

Diagnosis:

The clinical presentation of HELLP syndrome is often unclear which leads to initial misdiagnosis and also leads to delayed treatment (8, 22). The patients with HELLP syndrome may present complain of malaise (90%), epigastric or right upper quadrant pain (90%), and nausea or vomiting (50%) and the healthcare should be alert to provide possible diagnosis (22).

It was found that patients with HELLP syndrome may also present with respiratory, gastrointestinal, or hematologic symptoms in relation with elevated liver enzymes or low platelet count when there is no hypertension or proteinuria. It is also found that HELLP syndrome is misdiagnosed as hepatitis upper respiratory infection, pancreatitis, and cholecystitis, acute fatty liver of gestational or immune thrombocytopenic purpura (2).

The platelet count which is used first for finding the HELLP syndrome. The D-dimer test which may be used for identifying the preeclampsia to the patients with severe HELLP syndrome (12). The preeclampsia patients with positive D-dimer test shows HELLP syndrome and which is more sensitive towards subclinical coagulopathy (12). Proteinuria and an increased uric acid concentration play vital role for diagnosing preeclampsia but it is not helpful for diagnosing HELLP syndrome (23).

Hemolysis is also used for finding the HELLP syndrome and it is presented by an elevation of serum lactic dehydrogenase (LDH), anaemia with peripheral smear for schistocytes and low level of haptoglobin concentration. Hepatic lesion leads to increase in both aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Low platelet count shows the result of a higher use of activated platelets following with reduced life span of endothelial cells (17, 27).

Laboratory investigation which is done for finding HELLP syndrome should include, complete blood cell (CBC) count, Coagulation studies, Peripheral

smear for schistocytes, helmet cells, and burr cells. Liver function tests such as serum aspartate aminotransferase, alanine aminotransferase (AST/ALT) levels and Lactate dehydrogenase (LDH) level, complete metabolic panel, Bilirubin level, Haptoglobin level and Fibrinogen levels.

Special diagnostic test such as computed tomography, magnetic resonance imaging or hepatic ultra sound are only done when there is serious problem in the liver that is not detected cannot by liver function tests (12).

The HELLP syndrome is measured according to the blood platelet count and protein urea of the gestation and is classified as Class A (severe thrombocytopenia): platelets under 50,000/mm3, Class B (moderate thrombocytopenia): platelets between 50,000 and 100,000/mm3 and Class C (AST > 40 IU/L, mild thrombocytopenia): platelets between 100,000 and 150,000/mm3 (17).

Treatment:

The diagnosis and treatment which is done early is critical during the management of HELLP syndrome if it is delayed its intervention leads to increase in the mortality and morbidity rates. The highest maternal mortality rate has been found to be 25% (12, 20).

The supportive care should be recommended for the treatment of HELLP syndrome including seizure prevention and blood pressure control (1). Delivery should be recommended for the women who has HELLP syndrome because it is one of the effective treatment (19, 20). Maternal morbidity will not increase when conservative management like bed rest, fluids and close observation will be used in patients who were at less than 34 weeks of gestation (12).

The one most effective and lifesaving method to treat HELLP syndrome is plasmapheresis which will decrease the maternal mortality rate from 23.1% to 0% (21).

The magnesium sulphate 4gm to 6gm intravenously should be used for treatment to prevent the seizures and loading dose should be over 20 minutes and then 2gm should be given per hour as maintenance dose and this should be used until 24 hours after delivery (12).

Treatment of hypertension:

The main aim is to monitor the blood pressure and is to keep the systolic blood pressure <160 and the diastolic blood pressure <105. Methyldopa 250mg each 8 hours should be given if proteinuria is present during pregnancy due to hypertension. Labetalol and hydralazine are the most commonly recommended drugs. The hydralazine 2.5 mg to 5 mg intravenously should be used every 15 to 20 minutes until the blood pressure becomes normal (12).

The use of corticosteroid (dexamethasone) is used to decrease the fetal morbidity by decreasing respiratory distress syndrome and cerebral haemorrhage (20, 22). The use of corticosteroid (dexamethasone) therapy is said to be controversial (19). It is said that the use of steroid may decrease intravascular endothelial injury and prevents from hepatic and platelet dysfunction (12, 20). It has also been shown that improvement in blood pressure, urine output, platelet count, and liver function tests (12). Corticosteroids were used in a maternal in case of severe or moderate thrombocytopenia in HELLP syndrome.

Corticosteroids therapy should be used regularly in a HELLP syndrome patient. The use of dexamethasone 10 mg intravenously to the HELLP syndrome patients by antenatal care shows improve in the laboratory abnormalities (31). The patients who are treated with dexamethasone take longer time for delivery and it shows the maternal transfer to a tertiary care hospital and postnatal maturity of the fetal lungs.
Patients are closely monitored once they are stabilized when they are in labor and delivery departments of tertiary health care centre (8, 19) .The patients who are close to 34 weeks gestation should require immediate delivery if there is no clinical or laboratory (19).

Conservative management should be recommended to the women who has HELLP syndrome if only there is controlled in hypertension, oliguria responds to fluid management, and having no right upper quadrant or epigastric pain (12).

The treatment which is used for unstable HELLP syndrome:

Postpartum curettage is used for lowering arterial pressure and improvement in urine output and thrombocytopenia (20).

Plasmapheresis is used for correcting coagulation abnormalities with platelets or plasma (8).
The treatment approach is different for each patient and should be based on the estimated gestational age and the condition of the mother and fetus (12).

Complications:

The highest maternal mortality rate has been found to be a 25% (12, 20) .The woman who is affected from 1 to 25 % may develop serious complications such as disseminated intravascular coagulopathy (DIC), placental abruption, adult respiratory distress syndrome, hepatorenal failure, subcapsular hematoma, pulmonary oedema, and hepatic rupture. The patients with HELLP syndrome may receive only a significant percentage of blood products (24).

The infant mortality and morbidity rates is 10% to 60% which will depends on the severity of maternal diseases Infant morbidity and mortality rates range from 10 to 60 percent, depending on the severity of maternal disease (25). The infants who are affected by HELLP syndrome may likely to experience intrauterine growth retardation and respiratory distress syndrome (26).

Prognosis:

The risk of developing HELLP syndrome is 19% to 27% in a subsequent pregnancy who had already been a patient of HELLP syndrome (28). There is also the risk of developing preeclampsia up to 43% during another pregnancy (28). There is a high risk of recurrence in a patient with class I HELLP syndrome (28). When HELLP syndrome reoccurs during another pregnancy, it will be less severe after two episodes. Oral contraceptive pills should be used safely in the patients who have had HELLP syndrome (29). The presence of antiphospholipid antibodies should be screened in patients who will develop atypical early onset HELLP syndrome or preeclampsia (30).

It is said that the use of acetylsalicylic acid (aspirin) or calcium will help to prevent preeclampsia, but the use of aspirin may be helpful in some patients with early onset severe preeclampsia. Calcium may be useful for preventing preeclampsia in a high risk patient.

Conclusion:

HELLP is an abbreviation of hemolysis (H), elevated liver enzyme (EL), and low platelet count (LP) which is a serious potentially life threating, complication in pregnancy and also described as a severe form of preeclampsia(1, 3). HELLP syndrome is a syndrome which leads to poor maternal and neonatal outcomes (3).

The pathophysiology of HELLP syndrome is exactly imprecise. HELLP syndrome is also caused due to coagulation cascade activation leading to platelets consumption is due to adherence onto a damaged and activated endothelium.

The clinical presentation of HELLP syndrome is often unclear which leads to initial misdiagnosis and also leads to delayed treatment (8, 22). The patients with HELLP syndrome may present complain of malaise (90%), epigastric or right upper quadrant pain (90%), and nausea or vomiting (50%) and the healthcare should be alert to provide possible diagnosis (22).
HELLP syndrome was believed to be a severe form of preeclampsia further it was known that it usually occurs only 10% to 20% cases without preeclampsia (2). Preeclampsia is denoted by gestational hypertension with proteinuria (2).

The use of dexamethasone 10 mg intravenously to the HELLP syndrome patients by antenatal care shows improve in the laboratory abnormalities (31). Labetalol and hydralazine are the most commonly recommended drugs. The hydralazine 2.5 mg to 5 mg intravenously should be used every 15 to 20 minutes until the blood pressure becomes normal (12).

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