

# HELLP SYNDROME – A diagnostic dilemma

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## Introduction

HELLP Syndrome is a life threatening obstetrical condition usually a variant or complication of pre-eclampsia. It is characterized by hepatic endothelial disruption followed by platelet activation, aggregation and consumption, ultimately resulting in ischemia and hepato cellular death.

HELLP syndrome usually begins during third trimester. Rare cases have been reported as early as 21 weeks or early post partum period<sup>1,2,3</sup>. HELLP Syndrome and pre-eclampsia both occur in latter stage of pregnancy or sometimes after childbirth.

The acronym of HELLP was coined by Weinstein in 1982 to describe this syndrome. HELLP is an abbreviation of the three (3) main features:

H- Haemolysis

EL- Elevated Liver Enzyme

LP- Low Platelet Count.<sup>4</sup>

HELLP syndrome was identified as a distinct clinical entity (as opposed to severe pre-eclampsia) by Dr. Louis Weinstein in 1982.<sup>5</sup>

In a 2005 article, Weinstein wrote that the unexplained postpartum death of a woman who had haemolysis, abnormal liver function, thrombocytopenia, and hypoglycemia motivated him to review the medical literature and to compile information on similar woman.<sup>6</sup>

## Epidemiology

Its incidence is reported as 0.5-0.9% of all pregnancies, and 10-20% of women with severe preeclampsia.<sup>1</sup> HELLP develops in approximately 0.1 to 0.8 percent of pregnancies overall and in 10 to 20 percent of women with severe preeclampsia/eclampsia.<sup>7</sup> HELLP usually occurs in Caucasian women over the age of 25.<sup>8</sup>

HELLP Syndrome occurs in 0.2% to 0.6% of all

pregnancies. This syndrome may be the first warning of preeclampsia which may be confused with Hepatitis or thrombotic thrombocytopenic purpura. Maternal Mortality is estimated to be high as 2%-24%. Perinatal Mortality is also high ranging from 9%-65%.<sup>9</sup>

## Risk Factors

There is no single cause for this condition. Instead, the medical community widely recognizes various risk factors that may increase the chances of developing HELLP syndrome.

Preeclampsia is the greatest risk factor. This condition is marked by high blood pressure, and it occurs during the last trimester of pregnancy. However, not all pregnant women with preeclampsia will necessarily develop HELLP syndrome.

Other risk factors include: Age of 25, Caucasian, multi para, obesity, poor diet, lack of exercise, diabetes.<sup>10</sup>

## Pathophysiology

The exact pathological mechanism is unknown, but general activation of the coagulation cascade is considered the main underlying problem. Fibrin forms cross linked networks in the small blood vessels. This leads to a micro angiopathic hemolytic anemia: the mesh causes destruction of red blood cells as if they were being forced through a strainer. Additionally, platelets are consumed. As the liver appears to be the main site of this process, downstream liver cells suffer ischemia, leading to periportal necrosis. Other organs can be similarly affected. HELLP syndrome leads to a variant form of disseminated intravascular coagulation (DIC), leading to paradoxical bleeding, which can make emergency surgery a challenge.<sup>11</sup>

The Elevated Liver Enzyme levels in the syndrome are thought to be secondary to obstruction of hepatic blood flow by fibrin

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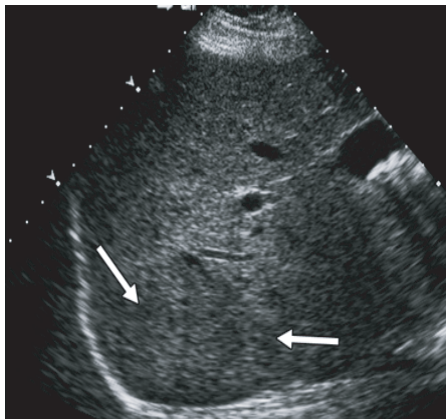
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deposits in the sinusoids. This obstruction leads to periportal necrosis and, in severe cases, intrahepatic hemorrhage, subcapsular hematoma formation or eventual rupture of Glisson's capsule.

Spontaneous rupture of a Subcapsular liver haematoma in pregnancy is a rare, but life threatening complication. Rupture most often occurs in the right liver lobe.<sup>9</sup>



### Clinical features

Feeling generally unwell or fatigued 80%-90%, abdominal pain especially upper right side/below ribs, nausea, vomiting 30%-90%, headache 33-61%, may also have swelling in the hands or face, weight gain, blurring vision/ visual disturbance 17%, heart burn or indigestion, shoulder tip pain, pain when breathing deeply. In rare cases nose bleeds or other bleeding and seizures.

On physical examination - Right upper quadrant tenderness present in 90%, edema is not a useful marker, increase blood pressure (82-88%) and proteinuria found in (86-100%)<sup>12</sup>

### Classification

#### TENNESSEE classification

Based on laboratory criteria ● Platelet count <100,000/μL, ● AST 70 IU/L & ● LDH 600 IU/L. Hemolysis on peripheral smear.

Partial HELLP includes presence of any 2 of the 3 criteria – can be managed by conservative treatment.

Full HELLP includes all of the 3 criteria<sup>13,14</sup> - high risk group for complications like DIC and should be considered delivery within 48 hours.

#### MISSISSIPPI classification (2006)

##### CLASS I –

- Platelet 50,000/μL, ● AST 70 IU/L
- LDH 600 IU/L, Hemolysis on smear – are at higher risk for maternal morbidity and mortality.

##### CLASS II-

- Platelet 50,000/μL-100,000/μL, ● AST 70 IU/L, ● LDH 600 IU/L, Hemolysis on smear.

##### CLASS III-

- Platelet 100,000/μL -150,000/μL, ● AST 40 IU/L, ● LDH 600 IU/L, Hemolysis on smear.

CLASS II & III are considered as clinical significant transitional stage.

Haemolysis - Peripheral smear shows Spherocyte, Schistocyte, Triangular cell, Barr cell.

Liver function test- Total bilirubin->1.2mg%, LDH->600 IU/Litre. Level of AST or ALT->150 IU/L associated with increased maternal morbidity or mortality.

##### Low platelet count

Platelet count <150000/cu mm, Leukocytosis. Coagulation Factors- If DIC is not present – PT, APTT, S. Fibrinogen will be normal. If fibrinogen is <300 mg/dl along with other laboratory abnormality DIC is suspected. Positive D-dimer test is more sensitive indicator of subclinical coagulopathy. S Uric Acid– Increased.

Hypoglycemia–Persistent, Profound hypoglycemia inspite of repeated glucose transfusion is peculiar to H. Syndrome Proteinuria<sup>12</sup>.

##### Differential Diagnosis

Disease related to pregnancy- Acute fatty liver of pregnancy, Gestational thrombocytopenia, Benign thrombocytopenia of pregnancy, Acute Exacerbation of SLE. Haemolytic uraemic syndrome

Infection and inflammatory diseases not related to pregnancy- Viral Hepatitis. Cholecystitis, Upper UTI, Gastric Ulcer, Acute Pancreatitis.

##### Maternal Complications-

- Acute Renal Failure,
- DIC,
- Severe Ascites,
- Cerebral Oedema,
- Pulmonary Oedema,
- Abruptio Placenta,
- Eclampsia,
- Sub capsular liver haematoma,
- Liver Rupture,
- Hepatic Infarction,
- Retinal Detachment,
- Cerebral Haemorrhage,
- Maternal Death.

### **Fetal/Neonatal Complication-**

- Pre-term delivery,
- IUGR,
- Neonatal Thrombocytopenia,
- RDS,
- Perinatal Death.<sup>13</sup>

**HELLP Syndrome can be managed** by Corticosteroid, Magnesium Sulfate, Hypotensive Drug, Blood Product and delivery.

**Eligibility to Conservative Management** includes

- Controlled Hypertension at less than 160/110 mm hg.
- Oliguria responds to fluid management .
- Class II –III (platelet count) >50000

### **Corticosteroids**

Corticosteroid therapy should be instituted in patients with HELLP syndrome who have a platelet count of less than 100,000 per mm<sup>3</sup> and should be continued until liver function abnormalities are resolving and the platelet count is greater than 100,000 per mm.<sup>3,15</sup>

The antenatal administration of dexamethasone (Decadron) in a high dosage of 10 mg intravenously every 12 hours has been shown to markedly improve the laboratory abnormalities associated with HELLP syndrome.<sup>14</sup>

Steroids given antenatally do not prevent the typical worsening of laboratory abnormalities after delivery. However, laboratory abnormalities resolve more quickly in patients who continue to receive steroids postpartum.<sup>16</sup>

Intravenously administered dexamethasone appears to be more effective than intramuscularly administered betamethasone for the antepartum treatment of mothers with HELLP syndrome.<sup>17</sup>

### **Proposed mechanism of action of steroids**

Diminish oedema, inhibit endothelial activation and reduce endothelial dysfunction. Prevents thrombotic microangiopathic anaemia. Inhibits cytokine production. Induce anti-inflammatory effects in the HELLP syndrome. In addition to accelerate foetal lung maturity, antenatal steroid has been used to reduce the risk of IVH and NEC in selected cases of the HELLP syndrome.

Dosing Schedule For most of patient with HELLP syndrome- 10 mg IV dexamethasone every 12 hrs until delivery & then 10 mg IV dexamethasone every 12 hrs for additional 3 doses post partum.

For selected high risk cases with profound thrombocytopenia with CNS dysfunction.

20mg IV dexamethasone every 6hrs up to 4 doses

### **Magnesium Sulphate**

Patients with HELLP syndrome should be treated prophylactically with magnesium sulphate to prevent seizures.

Antihypertensive therapy should be initiated if blood pressure is consistently greater than 160/110 mm Hg despite the use of magnesium sulfate. The goal is to maintain diastolic blood pressure between 90 and 100 mm Hg.

The most commonly used antihypertensive agent has been: Hydralazine, Labetolol, Nifedipine

### **Blood Products**

Between 38 -93 % of patients with HELLP syndrome receive some form of blood product. Patients with a platelet count greater than 40,000 per mm<sup>3</sup> are unlikely to bleed. Patients who undergo cesarean section should be transfused if their platelet count is less than 50,000 per mm.<sup>3</sup>

Prophylactic transfusion of platelets at delivery does not reduce the incidence of postpartum hemorrhage or hasten normalization of the platelet count. Patients with DIC should be given fresh frozen plasma and packed red blood cells.

### **Management of post-partum HELLP syndrome**

In most women with a HELLP syndrome, the maternal Platelet counts continue to decrease immediately post-partum with an increasing trend on the third day.

About 30% of the HELLP syndromes develop after birth.

The time of onset ranged from few hours to 7 days; the majority within the first 48 hours after delivery.

In post-partum HELLP syndrome, risk of renal failure and pulmonary oedema is significantly increased.

Since early post-partum administration of high-dose corticosteroids might accelerate recovery , its routine administration is highly advocated (10 mg of dexamethasone every 12 hours) Women with a HELLP syndrome who demonstrate progressive elevation of bilirubin or creatinine for more than 72 hours after delivery may benefit from plasma exchange with fresh frozen plasma. In the case of continuing haemolysis, persistent thrombocytopenia and hypoproteinaemia, post-partum erythrocyte and thrombocyte substitution, as well as albumin supplementation are standard treatment regimens.

### Risk of Recurrence and Preconception Counselling

Sibai has shown that oral contraceptives are safe in women with a prior HELLP syndrome.<sup>7</sup> Women with a history of the HELLP syndrome carry an increased risk of at least 20% (range 5–52%) that some form of gestational hypertension will recur in a subsequent gestation.

If someone wants contraception, Oral Contraceptive Pill is safe with history of HELLP syndrome.

Women with a history of HELLP syndrome at or before 28 weeks' gestation during the index pregnancy are at increased risk for several obstetric complications (preterm birth, pregnancy-induced hypertension and increased neonatal mortality) in a subsequent pregnancy.<sup>13</sup>

### Conclusion

HELLP Syndrome and its management still poses a problem in modern obstetrics as exact etiology of this disease is unknown. Initially symptoms are more like flu so we obstetricians must be very alert if any pregnant women visit at her 2<sup>nd</sup> or 3<sup>rd</sup> trimester with flu like syndrome. Those patients should be evaluated by two simple tests CBC and Liver Enzyme. This is the only way for early diagnosis and for starting early management and thereby we can decrease the fatality of the disease.

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