A Review Article of Cases with Thrombocytopenia Diagnosed as HELLP Syndrome

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ABSTRACT

Introduction: The complications HELLP syndrome consists of preeclampsia- eclampsia for decades. Recognition and further management of HELLP syndrome in pregnant women with preeclampsia is increasing because of the frequency of blood tests results that reveals unexpected thrombocytopenia or elevated liver enzymes. The diagnosis of HELLP syndrome requires on peripheral smear examination, elevated liver enzymes and a platelet count below 100,000/cumm, after ruling out causes of hemolysis and thrombocytopenia. This study is to identify such patients for early intervention and management.

Material and Methods: It is a retrospective and prospective study done for Three years (May 2012-June 2015) at Department of Pathology and Biochemistry, MGMH/ OGH, Hyderabad Platelet counts were done on Sysmex and confirmed on microscopy. Biochemistry parameters were done in a semiautomatedanalyzer.

Results: More in multigravida women with 20-25 years age group 37 weeks of pregnancy and 100% correlation with pre eclampsia was observed. Haemoglobin levels were <10 gm/ dl with elevated liver enzymes, Platelet counts were between 50,000/cumm to 1 lakh/cumm. We had three maternal deaths 5%, 20% intrauterine deaths, 55% of normal babies, 25% of Intrauterine growth retardation. HELLP syndrome cases were 75% according to Tenesse Classification and 50% cases belong to Class III according to Mississippi classification

Conclusion: The global mortality rate of HELLP syndrome is 25%, it is important for expecting mothers to be made aware of this condition and treat early.

Keywords: Thrombocytopenia, Preeclampsia, Hemolysis

INTRODUCTION

HELLP syndrome[1-8], is characterized by Hemolysis, Elevated liver enzymes and Low Platelet count. It is a life-threatening condition complicating pregnancy. In patients with preeclampsia, it may lead to fetal and maternal death. In the early 20th century, HELLP was diagnosed as edema-proteinuria-hypertension gestosis type B. The term 'HELP syndrome' was coined by Louis Weinstein[1] in 1982.

Thrombocytopenia is, after anemia, the second most common abnormality of the complete blood count in pregnancy, with a reported frequency of 6.6% to 11.2%.[2,9-10]

Weinstein identified around 30 cases of severe preeclampsia–eclampsia complicated

by thrombocytopenia, abnormal peripheral blood smear and abnormal LFT - liver function test. He identified that these abnormalities constituted a separate entity from the general observed eeclampsia and hence gave the name HELLP syndrome (H - hemolysis; EL - elevated liver enzymes; and LP - low platelets).[3]

The pathophysiology of HELLP syndrome is unclear. Some authors describe HELLP as a variant of preeclampsia[11], as both seem to have a common pathophysiology. Preeclampsia is characterized by defective placental vascular remodeling during 16th-22nd weeks of pregnancy with the second wave of trophoblastic invasion into the decidua resulting in decreased placental perfusion. Various factors such as soluble vascular endothelial growth factor receptor-1 (sVEGFR-1), are released which then binds vascular endothelial growth factor (VEGF) and placental growth factor (PGF). This causes dysfunction of endothelial cell along with placental dysfunction. It there by prevents the binding of endothelial cell receptors with the placenta, resulting in hypertension, proteinuria, and increased platelet activation and aggregation.[1]

The endothelial cells, when activated may release von Willebrand factor multimers. They are highly reactive with platelets. HELLP syndrome shows increased amount of active VWF leading to thrombocyto-penic and thrombotic microangiopathy.[4,12-17]

In recent studies have shown that fetal complications of mitochondrial fatty acid oxidation is assosiated with obstetric complications like placental bed infarct, pre-eclampsia, acute fatty liver of pregnancy and also the HELLP syndrome. Among some patients who are heterozygous with a defect in the long chain hydroxylacyl – co- A dehydro-genase (LCHAD) enzyme and who also have a defect in fetushomozy-gous, these disorders have shown to have occured.[5] The pathogenesis of HELLP syndrome is still unknown.[1]

Pregenacy in fourth decade i.e, after 30 years of age and multiparity are considered to be the high-risk factors of HELLP syndrome. Statistics show that HELLP syndrome occurs in 0.5% of all pregnancies and among 8% of preeclampsia cases. This syndrome has shown to have occurred typically between third trimester of preganncy and delivery. In around 15-30% of the cases, HELPP syndrome

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had occurred in immediate postpatum period.[1]

The most life threatening complication in HELPP syndrome is DIC – Disseminated intravascular coagulation which needs aggressive management. Other complications include pleural effusion, pulmonary edema and ascites. Prematurity, IUGR- Intrauterine growth retardation and Thrombocytopenia are the most common neonatal complications. A very small percentage of infants also suffer with IVH-Intraventricular Hemorrhage in the brain.[1]

Two common classifications used to predict maternal morbidity and mortality were described in and are known as the 'Mississippi'[18] and the 'Tennessee[10]' classifications. Hence the study was done to identify such patients for early intervention and management.

MATERIAL AND METHODS

It was a retrospective and prospective study donefor a period of Three year (May 2012-June 2015) at Department of Pathology and Biochemistry, Modern Government Maternity Hospital, Osmania Medical College, Hyderabad. Out of 500 cases of thrombocytopenia 57 cases of HELLP Syndrome were diagnosed.

Platelet counts were done on Hematology analyser and confirmed on microscopy. Biochemistry parameters were done in asemiautomated analyzermodel number.

We had ruled out other causes of thrombocytopenia. Parity and gestational age was taken into consideration among these women. Serious complications including maternal morbidity and perinatal mortality was studied.

STATISTICAL ANALYSIS

Statistical analysis was done with the help of Microsoft office 2007. Descriptive statistics were used to analyse the data.

RESULTS

Most common age group observed was 20-25years, common age at presentation is < 37 wks of pregnancy. 65% of cases were multigravidae. There was a 100% correlation with preeclampsia [Figure 1].

80% of cases were presented with Hb levels < 10gm/dl. Platelet count observed were 50,000 / cumm to 1 lakh / cumm. liver enzymes were elevated in all the cases [Figure 2]. Peripheral smear findings showed schistocytes, fragmented RBCs and low platelet count [Figure 3].

Fetal complications like intra uterine growth retardation comprising 25% and intrauterine death was observed in 20% of cases. In our cases we have 3 maternal deaths (5%) and most of the mothers were with no morbidity. [Figure 4]

It is observed that 75% of the cases presented with full HELLP according to Tenesse classification. 50% of the cases are in class II, followed by class III and class I according to Missisipi classification. [Figure 5]

The most common symptoms were general malaise, epigastric pain, headache and vomiting. [Figure 1]

DISCUSSION

HELLP is an obstetric complication that is frequently missed at initial presentation as most of the symptoms like general malaise, headache and vomiting. It is considered as a variant of pre eclampsia[16] and can be misdiagnosed as viral hepatitis, ITP, Gallbladder disease or TTP.[9,10]

The underlying disease of thrombocytopenia has to be identified in order to give targeted treatment. Differential diagnosis is hence important. For example, in gestational thrombocytopenia, no complications for mother and child arise. But autoimmune thrombocytopenia leads to maternal

<20 years of age	2
20-25 years age	29
26-30 years age	23
31-35 years age	3

Figure-1: Part A: Age at presentation: Total cases: 57

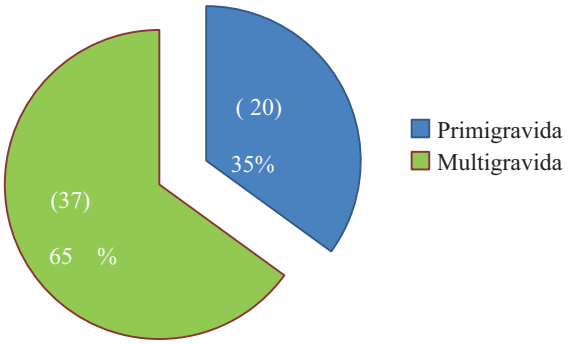

Figure-1: Part B: Parity

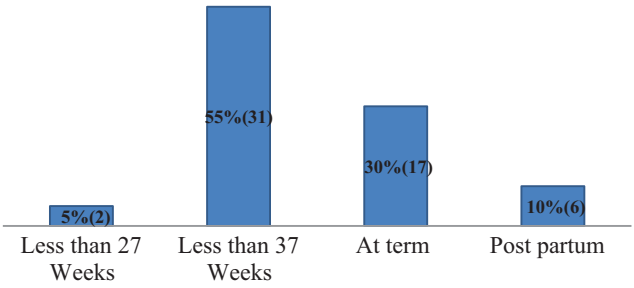

Figure-1: Part C: Gestational age at presentation

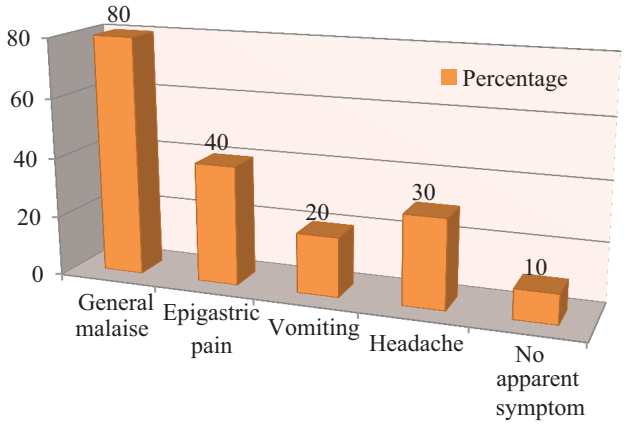

Figure-1: Part D: Clinical signs and symptoms

Haemoglobin level in gm/dl	Percentage of cases
1.0-5.0	30%
6.0-10.0	50%
11.0-15.0	20%

Figure-2: Part A: Haemoglobin level in gm/dl

	Elevated liver enzymes(14-40 IU/L)		Bilirubin levels		
Levels	(40-70IU/L)	(>70IU/L)	<1.2mg/dl	1.2-4.0mg/dl	>4.0 mg/dl
No of cases	37(65%)	20(35%)	6(10%)	31(55%)	20(35%)

Figure-2: Part B: Elevated liver enzymes and bilirubin levels

Study	<50,000/cumm	50,000-1 Lakh/cumm	1Lakh-1,50,000/cumm
Cases	17	29	11

Figure-2: Part C: Platelet count

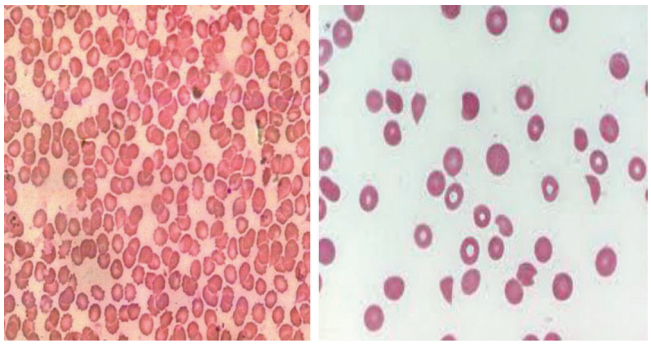

Figure-3: Microscopy findings

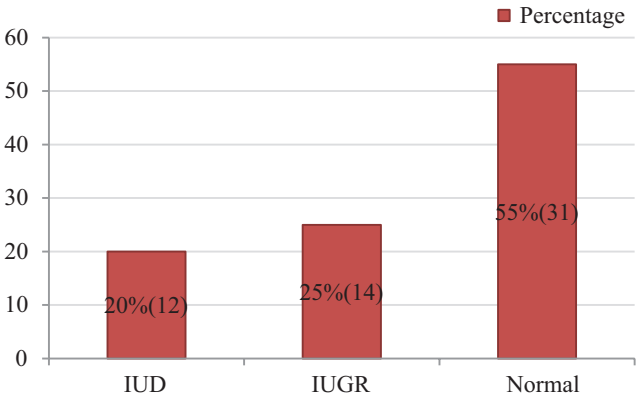

Figure-4: Part A: Fetal complications

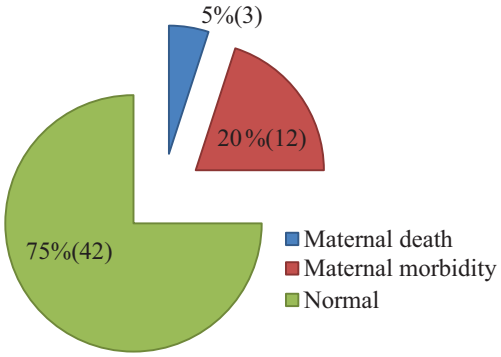

Figure-4: Part B: Maternal mortality and morbidity

bleeding and severe neonatal haemorrhage as the antibodies cross the placenta. Hence HELLP syndrome[15] should be differentiated from other autoimmune anemia by proper laboratory investigations.

Differential Diagnoses[13]

Other conditions causing thrombocytopenia are:

Acute fatty liver pregnancy,
TTP,

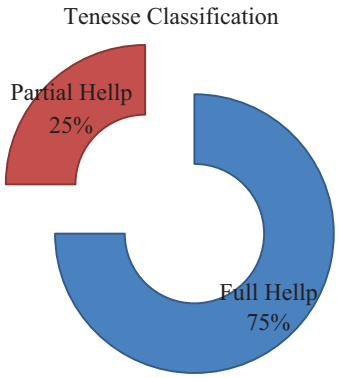

Figure-5: Part A:Tenesse Classification

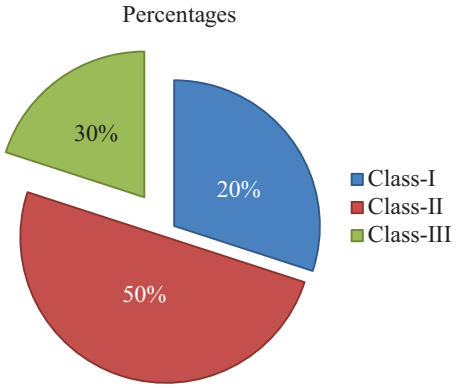

Figure-5: Part B:Missisippi Classification

HUS,
Acute liver failure,
DIC,
Sepsis and drug induced thrombocytopenia.
Abruptio Placentae
Acute Fatty Liver of Pregnancy
Anemia and Thrombocytopenia in Pregnancy
Antiphospholipid Antibody Syndrome and Pregnancy
Eclampsia
HemolyticAnemia
Hemolytic-Uremic Syndrome
Hepatitis, Viral
Hyperemesis Gravidarum
Hypertension and Pregnancy
Nephrolithiasis, Acute Renal Colic
Peptic Ulcer Disease
Preeclampsia
Thrombocytopenia in Pregnancy
Thrombotic Thrombocytopenic Purpura

Laboratory evaluation should include the following:

- Proper screening and Typing
- CBP count - Complete blood Picture: To rule out anemia and Thrombocytopenia.
- Coagulation studies: Normal prothrombin time and majority of cases may have prolonged APTT.

- Peripheral smear: Schistocytes, helmet cells, and burr cells secondary to MAHA-microangiopathichemolyticanemia.
- Serum aspartate aminotransferase/alanine aminotransferase (AST/ALT) levels: Elevated secondary to liver dysfunction.
- LDH - Lactate dehydrogenase level: Due to hemolysis, LDH is increased secondary to liver dysfunction or hemolysis.
- CMP- Complete metabolic panel: Creatinine [BUN] levels are increased due to acute renal failure.
- Bilirubin level are increased and Haptoglobin level are decreased secondary to hemolysis.
- Fibrinogen levels: Low secondary to increased coagulation.
- D-dimer: In cases of DIC, fibrinolysis, this is a useful parameter to detect increased fibronolysis.
- The hemolysis in HELLP syndrome is microangiopathichemolyticanemia.
- As RBCs pass through small blood vessels with endothelial damage and fibrin deposits, they get fragmented.
- The peripheral smear reveals spherocytes, shistocytes and burr cells.
- The increase in bilirubin and liver enzyme levels is due to secondary to obstruction of fibrin deposits in the liver sinusoids.This obstruction may lead to periportal necrosis and in severe cases intrahepatic hemorrhage, subcapsular hematoma or hepatic rupture.
- The thrombocytopenia has been attributed to increased consumption or destruction of platelets.
- With platelet activation, thromboxane A and serotonin are released vasospasm,plateletagglutination and aggregation and further endothelial damage.[1]

Management

Early disgnosis and aggressive management is must in cases of HELPP syndrome.[13,14] High risk patients who have elevated hypertension and low platelet count have to be followed regularly.

Timing of delivery is important. If gestation period is >34 weeks, then deliver. If<34 weeks gestation, administer corticosteroids and then deliver in 48hours.[1]

Patients who are at a risk of developing preeclampsia should be identified as it is a preventable disorder.[7] However, in high risk cases, termination of pregnancy is recommended.

CONCLUSION

The presence of HELLP syndrome is associated with life threatening maternal and fetal complications. The diagnosis of HELLP syndrome is critical and the importance lies in early diagnosis by hematologists and input by the clinicians in the management of pre eclampsia. Maternal Platelet count is considered the best and reliable marker in the diagnosis of HELLP.

HELLP syndrome with pre eclampsia of early onset is associated with poor prognosis.Any case of pregnant women who have preeclampsia, thrombocytopenia, elevated BP and proteinuria must be regularly followed up and checked for any manifestations of HELLP syndrome.

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