A 5-Year Clinical Experience of Haemolysis, Elevated Liver Enzymes and Low Platelet Count (HELLP) Syndrome at a Tertiary Care Teaching Hospital in North Karnataka – A Retrospective Analysis

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ABSTRACT

BACKGROUND

Haemolysis (H), elevated liver enzymes (EL) and low platelet count (LP) i.e., HELLP syndrome is a vaguely understood condition of pregnancy which can present with rapid onset. It is commonly associated with pre - eclampsia. HELLP is also known to manifest itself without the clinical features of pre - eclampsia. The present study aims to assess the maternal and foetal complications associated with HELLP syndrome.

METHODS

This retrospective study included all the pregnant women who developed HELLP / partial HELLP with gestational age of ≥ 28 weeks. The variables analyzed were obstetric history, menstrual history, antenatal complications, laboratory investigations (haemolysis, ALT / AST, LDH, CBC), mode of delivery, postnatal complications, maternal outcomes and perinatal outcomes.

RESULTS

72 patients were included in the present study. The mean age of pregnant women with HELLP syndrome was 23.6 ± 4.15 years. The average age of gestation was 33.17 ± 4.02 weeks. 58 % patients were primigravida. As per Mississippi triple-class system 82 % patients had partial HELLP, 18 % had complete HELLP. 4 %, 4 % & 10 % patients had HELLP class I, II & III respectively. Among the total cases, 74 % patients had antepartum onset, 10 % had intrapartum & 17 % postpartum onset of HELLP syndrome respectively. 65 % patients delivered vaginally & rest 35 % underwent caesarean section. High risk factors such as pre - eclampsia (65 %), eclampsia (3 %) & previous history of HELLP (8 %) were noted in study cases. Abruptio placentae (18 %), postpartum haemorrhage (17 %), pulmonary oedema (14 %), renal failure (14 %) & DIC (7 %) were the maternal complications noted. Maternal mortality was 7 %. The major perinatal morbidities noted were prematurity (67 %) & FGR (42 %). Intrauterine death was noted in 19 % babies. Neonatal intensive care (NICU) was required for 58 % babies, of which 42 % had respiratory distress. Neonatal death was noted in 17 %.

CONCLUSIONS

HELLP syndrome is a life threatening condition of pregnancy which has serious maternal and perinatal morbidities. Prompt referral, timely and appropriate interventions can save lives. Availability of Intensive Care Units (ICU) facilities, dialysis units and blood and its components along with Neonatal Intensive Care Unit (NICU) facilities can remarkably reduce the maternal and neonatal complications.

KEY WORDS

HELLP Syndrome, Preeclampsia, Maternal Mortality, Neonatal Mortality, Mississippi Triple - Class System

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BACKGROUND

Haemolysis (H), elevated liver enzymes (EL) and low platelet count (LP) is a group of laboratory indices which is abbreviated as HELLP syndrome. It is a vaguely understood condition of pregnancy which can present with an expeditious onset. It is commonly associated with pre - eclampsia though few cases can occur without the clinical features of pre - eclampsia.[1]

The exact aetiology remains unknown. The disease process is said to start from the time of implantation. There is incomplete invasion of the trophoblastic cells into the decidua. The defective maternal spiral arteries remodelling in turn results in activation of the coagulation system. This further results in vascular ischemia, fibrin deposits, vasospasm and activation of clotting cascade. This triggers the release of angiogenic factors which in turn cause hypertension and proteinuria.[2] Microvasular injury can cause multiple organs to be affected. In the Liver, raised liver enzymes are noticed.[3]

Another theory is that the foetus is the cause of the maternal disease. Abnormal oxidation of the fatty acids in the foetus and the transfer of these metabolites to the mother can cause the vascular defects and further multiorgan involvement.[4]

The diagnosis of HELLP syndrome is based on laboratory findings. Clinical suspicion of the disease is illusive as the symptoms of nausea and vomiting, headache or malaise are non - specific and manifest in other conditions such as viral hepatitis or acute fatty liver of pregnancy. Some patients will present with epigastric pain or right hypochondriac pain which is an unfavourable symptom.[5]

Laboratory diagnosis of HELLP syndrome is done on the following laboratory criteria.[2]

1. Haemolysis is defined by abnormal peripheral blood smear and increased bilirubin levels (1.2 mg / dL or more); Haemolysis characterised by microangiopathic haemolytic anaemia. This is diagnosed by the presence of histocytes and Burr cells in the peripheral smear.
2. Elevated liver enzymes, defined by aspartate aminotransferase (AST) of 70 IU / L or more and lactate dehydrogenase (LDH) above 600 U / L
3. Decreased platelet count (< 100,000 mm^3). Increased serum lactate dehydrogenase level, decreased haptoglobin concentration and the presence of unconjugated bilirubin (>1.2 mg / 100 mL) all shows sign of haemolysis. Liver enzyme elevation shows liver involvement and also haemolysis. The activated platelets adhere to the damaged vascular endothelial cells which causes the circulating count of platelets to decrease.

It is associated with serious maternal morbidity, as renal failure, disseminated intravascular coagulation (DIC), consumptive coagulopathy, sub capsular liver haematoma, abruption-placenta, pulmonary and cerebral edema, hypovolemic shock and subsequent severe postpartum bleeding. Prematurity, foetal growth retardation (FGR), thrombocytopenia and perinatal death are the most common foetal complications.[6] This condition is often underdiagnosed.

The aim of treatment of HELLP syndrome patients is to terminate pregnancy at 34 weeks or to terminate the pregnancy in view of presence of maternal complications such as multiorgan dysfunction, non - reassuring foetal conditions or other obstetric catastrophies like placental abruption.[7]

The present study aims to evaluate the maternal and foetal outcomes in pregnancies with HELLP syndrome.

METHODS

The study was conducted in the Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College Hospital and Research Centre, BLDE (Deemed to Be) University, Vijayapura, Karnataka, India from April 1st 2015 to 31st March 2020. The study had been approved by the Institutional ethics committee with reference number BLDE (DU) / IEC / 410 / 2019-20.

All pregnant women who developed HELLP / partial HELLP with gestational age ≥ 28 weeks were included in the study. Woman with other medical disorders like cholecystitis, viral hepatitis were excluded as these patients will have deranged hepatic parameters that confound the findings of HELLP syndrome. As period of viability in India is taken as 28 weeks, hence the cases with gestational age ≤ 28 weeks were excluded.

The diagnosis of HELLP syndrome was made when the following laboratory investigation were present, haemolysis, abnormal liver enzymes and low platelets. (Table 1)[8]

Maternal outcomes were measured in terms of age of mother, parity, period of gestation, severity of preeclampsia, eclampsia, class of HELLP syndrome, mode of delivery, need for blood and its components, pulmonary edema, acute renal failure, abruption placenta, disseminated intravascular coagulation, postpartum haemorrhage and maternal mortality. Perinatal outcome were measured in terms of prematurity, FGR, intrauterine foetal demise (IUD), birth asphyxia, NICU admission and early neonatal death. After complete stabilization patients were discharged.

Statistical Analysis

Data was collected & analyzed. Statistical analysis. All characteristics were summarized descriptively for continuous variables; the summary statistics of mean ± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Data were analyzed using SPSS software v.23.0.

RESULTS

72 patients were included in the present study. The average maternal age of the patients was 23.6 ± 4.15 years. The mean gestational age was 33.17 ± 4.02 weeks; ranging between 29-38 weeks? Mean parity of patients was 1.82 ± 1.01. 58 % patients were primigravida. The mean systolic blood pressure (SBP) was 154 ± 22.9 mmHg & diastolic blood pressure (DBP) was 102.1 ± 21.4 mmHg. Mean Proteinuria was 2.3 ± 1.2 (semi quantitative analysis) (Table 2).

As per Mississippi triple - class system 82 % patients had partial HELLP syndrome and 18 % had complete HELLP syndrome. The HELLP syndrome was classified into three

classes depending upon platelet count; AST or ALT and LDH levels. In our study 4 % of the patients were in class I and II each and 10 % of the patients were in class III of HELLP syndrome. Antepartum onset was observed in 74 % of the patients, another 10 % had intrapartum onset and 17 % had postpartum onset of the disease. In our study, 65 % patients delivered vaginally and 35 % underwent cesarean section. High risk factors such as pre - eclampsia (65 %), eclampsia (3 %) & previous history of HELLP syndrome (8 %) were noted in study patients (Table 3). Abruptio placentae (18 %), postpartum haemorrhage (17 %), and pulmonary edema (14 %), acute kidney injury (AKI) (14 %), DIC (7 %) and maternal mortality (7 %) were the maternal complications observed in the present study. (Table 4)

HELLP Class	Platelet Count (in µL)	AST or ALT (in IU / L)	Total LDH (in IU / L)
1	≤ 50,000	≥ 70	≥ 600
2	≥ 50,000 & ≤ 1,00,000	≥ 70	≥ 600
3	> 1,00,000 & ≤ 1,50,000	≥ 40	≥ 600
Partial HELLP Syndrome	Presence of Severe Preeclampsia – Eclampsia in Association with two of three Laboratory Criteria for HELLP Syndrome		

Table 1. HELLP Syndrome - Mississippi Triple - Class System.[4]

HELLP: Haemolysis, Elevated Liver enzymes, Low Platelet count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase.

Characteristic	Mean (± 2SD)
Maternal Age (Years)	23.6 ± 4.15
Gestational Age (Weeks)	33.17 ± 4.02
Parity	1.82 ± 1.01
Systolic BP (mmHg)	154 ± 22.9
Diastolic BP (mmHg)	102.1 ± 21.4
Proteinuria (1+ to 4+)	2.3 ± 1.2

Table 2. Demographic and Clinical Characteristics

Parameters	Partial HELLP	HELLP	Total
Mississippi Classification			
No. of Cases	59 (82 %)	13 (18 %)	72 (100 %)
HELLP Class I		3 (4 %)	
HELLP Class II		3 (4 %)	
HELLP class III		7 (10 %)	
Time of Onset			
Antepartum	45 (63 %)	8 (11 %)	53 (74 %)
Intrapartum	6 (8 %)	1 (1 %)	7 (10 %)
Postpartum	8 (11 %)	4 (6 %)	12 (17 %)
Mode of Delivery			
Vaginal Delivery	39 (54 %)	8 (11 %)	47 (65 %)
Caesarean Delivery	20 (28 %)	5 (7 %)	25 (35 %)
High Risk Factors			
Pre - Eclampsia	40 (56 %)	7 (10 %)	47 (65 %)
Eclampsia	1 (1 %)	1 (1 %)	2 (3 %)
Previous History of HELLP	2 (3 %)	4 (6 %)	6 (8 %)

Table 3. Clinical Characteristics of the Patients with HELLP Syndrome

Maternal Complications	No. of Cases (%)		
	Partial HELLP	HELLP	Total
Postpartum Haemorrhage	8 (11 %)	4 (6 %)	12 (17 %)
DIC	2 (3 %)	3 (4 %)	5 (7 %)
Abruptio Placentae	11 (15 %)	2 (3 %)	13 (18 %)
Pulmonary Edema	5 (7 %)	5 (7 %)	10 (14 %)
Acute Kidney Injury	6 (8 %)	4 (6 %)	10 (14 %)
Maternal Death	2 (3 %)	3 (4 %)	5 (7 %)

Table 4. Maternal Complications

In terms of perinatal morbidity, prematurity (67 %) & FGR (42 %) were major outcomes. Intrauterine death was noted in 19 % babies. Post - delivery NICU admission was required in 58 % babies and among them 42 % had respiratory distress. Early neonatal death was observed in 17 % of the babies (Table 5).

Perinatal Complications	No. of Cases (%)		
	Partial HELLP	HELLP	Total
Prematurity	39 (54 %)	9 (13 %)	48 (67 %)
FGR	25 (35 %)	5 (7 %)	30 (42 %)
Respiratory distress	13 (18 %)	3 (4 %)	16 (22 %)
IUD	11(15 %)	3 (4 %)	14 (19 %)
NICU admission	35 (49 %)	7 (10 %)	42 (58 %)
Early neonatal death	8 (11 %)	4 (6 %)	12 (17 %)

Table 5. Perinatal Complications

DISCUSSION

HELLP syndrome is a devastating maternal complication. Patients are usually diagnosed in late stages with multiorgan dysfunction. Aggressive treatment with multispecialty approach is required in many of the cases. Facilities like ICU, blood bank with component therapy and round the clock services of obstetricians, neonatologists and intensivists are required to treat such cases. In 4 - 12 % of the cases of severe pre - eclampsia, HELLP syndrome has been diagnosed. It causes high percentage of maternal (24 %) and perinatal (up to 40 %) mortalities even with timely decision of delivery.[9]

The chance of pre - eclamptic women developing HELLP is 0.5-0.9 %. The presentation of the syndrome may be complete wherein all the three components of the HELLP manifest, or partial where at least two of the three components manifest.[10] presentation of the disease has seen to be acute and often dramatic. Hypertension and proteinuria is seen in 10-20 % of the cases with HELLP.[5] The clinical profile of preeclampsia can affect the mother by causing multiorgan disorders and can affect the foetus by causing foetal growth restriction.[11]

Mean maternal age in our study was 23.6 ± 4.15 years. Various other studies conducted in India observed that the mean maternal age was 27.31 ± 5.0 years[11] and 24.25 ± 3.05.[12] The mean gestational age at presentation in our study was 33.17 ± 4.02, in other Indian studies, the mean gestational age was 32.89 ± 2.66 weeks[12], 36.34 ± 3.75 weeks,[13] 36.06 ± 3.50 weeks by.[14] In the present study, 58 % patients were primigravida, which was comparable with a study done in south India (60.7 %).[15] In another study in India showed 63.64 % were primigravida.[16]

In the present study, 65 % delivered vaginally and 35 % underwent cesarean section. The results are comparable with a study done in Kolkata, India, where in 27.27 % of the patients had vaginal delivery and 72.72 % underwent cesarean section.[17] Hypertensive disorders of pregnancy were the most common risk factor noted in 68 % patients in our study. Two (3 %) patients had eclampsia, which is far less than the study conducted in Mumbai, India where in 23 % had eclampsia with HELLP syndrome.[18]

Abruptio placentae (18 %), postpartum haemorrhage (17 %), and pulmonary edema (14 %), acute kidney injury (AKI) (14 %), DIC (7 %) and maternal mortality (7 %) were the maternal complications observed in the present study. In a study conducted in Andhra Pradesh[17] maternal mortality was higher than that observed in our study 61.66 %. In a study conducted in Kerala, out of 55 cases with HELLP syndrome, no maternal deaths were observed[18] and the study had reported

that most maternal complications were due to DIC and Abruptio placenta. A study conducted in Delhi[12] reported maternal mortality of 12.5 % due to pulmonary edema, liver haematoma and DIC. Another study in Andhra Pradesh reported that the maternal mortality in their study was 4.5 %.[14]

The maternal mortality in HELLP syndrome averages from 1 to 25 %. The leading causes of maternal mortality in HELLP are sepsis, disseminated intravascular coagulation (DIC), acute respiratory distress syndrome, liver failure, acute kidney injury, stroke or cardiopulmonary arrest.

In present study NICU admission was required in 58 % of the babies and among them 42 % had respiratory distress. Early neonatal death was noted in 17 % in the present study. A study done in Kerala reported that prematurity with FGR accounts for most common complications among HELLP syndrome patients.[18] Perinatal morbidity was 46.6 % in a study done in Andhra Pradesh.[17] A study done in Delhi reported a perinatal mortality of 45.8 % cause due to prematurity and FGR.[12] Another study in Andhra Pradesh showed reported prematurity as the major cause for perinatal mortality of 24 %.[13]

Adverse maternal and perinatal outcomes stresses upon the need for early recognition of the disease with prompt antenatal care (ANC) registration, regular antenatal follow up and monitoring of clinical symptoms and laboratory parameters.

In HELLP syndrome, it has been noticed that there is no correlation between the level of hypertension and the severity of the disease. The biochemical laboratory values carry more importance in the diagnosis. The hypertensive complications are considered as a major risk factor for recurrence and may also be responsible for adverse outcomes like FGR and placental abruption.

CONCLUSIONS

HELLP syndrome is a serious complication of pregnancy. A standardized protocol to diagnose and manage HELLP syndrome is the need of the hour. Prompt referral, timely and appropriate intervention can save lives. Availability of intensive care units (ICU), dialysis units and blood and its components along with NICU facilities can significantly improve the maternal and neonatal outcomes.

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