Original Research Article

Clinical study of maternal and fetal outcome in pregnant women with HELLP syndrome at a tertiary hospital

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Abstract

Background: HELLP (Hemolysis, Elevated Liver enzymes, Low Platelet count) syndrome is a potentially life-threatening condition manifesting in the context of preeclampsia, which poses challenging diagnostic and management issues to the clinician. HELLP syndrome develops in 6–12% of women with preeclampsia or eclampsia accounting for 0.4–0.7% of all pregnancies. Present study was aimed to study maternal and fetal outcome in pregnant women with HELLP syndrome at a tertiary hospital. **Material and Methods:** Present study was prospective, observational and conducted in pregnant women who developed HELLP/ partial HELLP with gestational age >28 weeks, delivered at our hospital. **Results:** In present study total 51 patients satisfying study criteria were studied. Most common maternal age group was 20-25 years (47.1 %), mean maternal age was 24.1 ± 4.2 years. Most common gestational age group was 34-47 weeks (47.1 %), mean gestational age was 34.71 ± 2.89 weeks, range was 29- 38 weeks. High risk factors were pre-eclampsia (76.5 %), Previous history of HELLP (13.7 %) and eclampsia (3.9 %). In most of patients Antepartum onset of HELLLP syndrome (54.9 %) was noted. Vaginal delivery (56.9 %) was common mode of delivery. In present study malaise (90.2 %), proteinuria (86.3 %), right upper quadrant/epigastric pain (84.3 %), right upper quadrant/epigastric tenderness (82.4 %), hypertension (80.4 %), nausea/vomiting (74.5 %) and headache (64.7 %) were common signs and symptoms noted in patients of HELLP syndrome As per Mississippi triple-class system 70.59% patients had partial HELLP, 29.41% had complete HELLP. 3.92%, 9.8 % and 15.69 % patients had HELLP class I, II and III respectively. Placental abruption (35.29 %) was most common complication noted, followed by postpartum hemorrhage (29.41 %), acute kidney injury (13.73 %), pulmonary oedema (7.84 %), DIC (7.84 %), multiorgan dysfunction (7.84 %) and eclampsia (3.92 %). Maternal death was noted in 2 (3.92 %) patients. 15 neonates (29.4 %) required neonatal resuscitation. Common neonatal high-risk factors were prematurity (74.5 %), IUGR (35.3 %), Respiratory distress (60.8 %), Neonatal jaundice (11.8 %). During early neonatal period 29 neonates (56.9 %) required admission to NICU. **Conclusion:** HELLP syndrome is associated with poor outcome for the mother and fetus. Timely diagnosis and management of HELLP syndrome by induction and delivery by vaginal route or by cesarean section is beneficial and prevents complications in mother and fetus.

Keywords: HELLP syndrome, pre-eclampsia, vaginal delivery, fetomaternal outcome

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INTRODUCTION

HELLP (Hemolysis, Elevated Liver enzymes, Low Platelet count) syndrome is a potentially life-threatening condition manifesting in the context of preeclampsia, which poses challenging diagnostic and management issues to the clinician.[1] HELLP syndrome develops in 6–12% of women with preeclampsia or eclampsia accounting for 0.4–0.7% of all pregnancies. Many hypotheses have been proposed to define pathogenesis of HELLP syndrome, but the true pathology remains a mystery. Role of soluble vascular endothelial growth factor receptor-1

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(Svegfr-1) released by hypoxic placenta causing endothelial cell and placental dysfunction,[3] a placental-instigated acute inflammatory condition targeting the liver,[4] dysfunction in the complement system activation or defective regulation for a given amount of endothelial injury[5] are proposed mechanisms of HELLP syndrome. Patients with HELLP syndrome have increased risk of complications like diffuse intravascular coagulation (DIC), abruptio placenta, acute renal failure, pulmonary edema, rupture of liver hematoma, retinopathy, cerebral haemorrhage, multi organ dysfunction syndrome (MODS), maternal death.[6,7] Fetal complications are mainly due to uteroplacental insufficiency leading to IUGR (Intrauterine Growth Restriction), low birth weight babies, IUFD (Intrauterine Fetal death) and complications due to prematurity. Perinatal mortality appears to be primarily related to the gestational age at the time of delivery.[8] Present study was aimed to study maternal and fetal outcome in pregnant women with HELLP syndrome at a tertiary hospital

MATERIAL AND METHODS

Present study was prospective, observational and conducted in department of Obstetrics and Gynaecology, at XXX medical college and hospital, XXX, India. Study duration was of 1 years (July 2019 to June 2020). Institutional ethics committee approval was taken for study.

Inclusion criteria

• All pregnant women who developed HELLP/ partial HELLP with gestational age >28 weeks, delivered at our hospital.

Exclusion criteria

• Woman with less than 28 weeks of pregnancy

• Women with others problems like cholecystitis, gastroenteritis, viral hepatitis

The diagnosis and classification of HELLP syndrome (**He**molysis, **E**levated Liver enzymes, **L**ow **P**latelet count) was made using the criteria established by Mississippi classification —i.e., abnormal peripheral blood smear, raised lactic dehydrogenase (LDH) ([600 U/L), elevated liver enzymes [increased plasma aspartate amino transferase (AST) [70 U/L], and low platelets (platelet count \100,000/cmm).

Table 1: HELLP syndrome: Mississippi triple-class system.[1]

HELLP Class	Platelet count (in µL)	AST / 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	Evidence of severe preeclampsia–eclampsia in association with two of three laboratory criteria for HELLP syndrome		

(AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase.)

Written informed consent was taken prior to the start of the study from each patient. Pregnant women satisfying study criteria underwent detailed history taking (chief complaints, obstetric history, etc.), clinical examination and hematological/biochemical investigations. Labour was monitored as per standard operative procedures of department. All new-born babies were immediately attended by neonatologists and if required admitted in NICU. Patients were subjected to repeat biochemical investigations; hemoglobin level and platelet count in the postpartum period after 48 hours. Maternal outcome was measured in terms of age of mother, parity, socioeconomic status, period of gestation, severity of preeclampsia, eclampsia, class of HELLP syndrome, mode of delivery, need for blood products, maternal complications like pulmonary edema, acute renal failure, abruption placenta, disseminated intravascular coagulation, postpartum haemorrhage and maternal mortality. Perinatal outcome was measured in terms of prematurity, dysmaturity, intrauterine fetal demise, birth asphyxia, APGAR score, neonatal jaundice, hypoglycemia, hypocalcemia, sepsis, NICU admission and early neonatal death. After complete stabilisation patients were discharged. Follow up was kept for 28 days. All details were entered in Microsoft excel sheet and sstatistical analysis was done using descriptive statistics.

RESULTS

In present study total 51 patients satisfying study criteria were studied. Most common maternal age group was 20-25 years (47.1 %), mean maternal age was 24.1 ± 4.2 years. Most common gestational age group was 34-47 weeks (47.1 %), mean gestational age was 34.71 ± 2.89 weeks, range was 29- 38 weeks. High risk factors were pre-eclampsia (76.5 %), Previous history of HELLP (13.7 %) and eclampsia (3.9 %). In most of patients Antepartum onset of HELLLP syndrome (54.9 %) was noted. Vaginal delivery (56.9 %) was common mode of delivery.

Table 2: Demographic and clinical characteristics

Characteristic	Number of patients/ Mean ± SD)	Percentage
Maternal age (years)	24.1 ± 4.2	
< 20	3	5.9
20-25	24	47.1
26-30	15	29.4
31-35	5	9.8
>35	4	7.8
Gestational age (weeks)	34.71 ± 2.89	
28-34	18	35.3
34-37	24	47.1
>37	9	17.6
Parity	1.56 ± 1.21	
Clinical findings on admission		
Systolic BP (mmHg)	150.4 ± 20.9	
Diastolic BP (mmHg)	100.1 ± 14.4	
Proteinuria (1+ to 4+)	2.6 ± 1.3	
High risk factors		
Pre-eclampsia	39	76.5
Eclampsia	2	3.9
Previous history of HELLP	7	13.7
Time of onset		
Antepartum	28	54.9
Intrapartum	16	31.4
Postpartum	7	13.7
Mode of delivery		
Vaginal delivery	29	56.9
Caesarean delivery	22	43.1

In present study malaise (90.2%), proteinuria (86.3 %), right upper quadrant/epigastric pain (84.3 %), right upper quadrant/epigastric tenderness (82.4 %), hypertension (80.4 %), nausea/vomiting (74.5 %) and headache (64.7 %) were common signs and symptoms noted in patients of HELLP syndrome

Table 3: Sign and symptoms of HELLP syndrome.

Sign and symptoms	Percentage	
Malaise	46	90.2
Proteinuria	44	86.3
Right upper quadrant/epigastric pain	43	84.3
Right upper quadrant/epigastric tenderness	42	82.4
Hypertension	41	80.4
Nausea vomiting	38	74.5
Headache	33	64.7
Visual changes	11	21.6
Ascites	6	11.8
Bleeding	5	9.8
Pulmonary edema	4	7.8
Jaundice	3	5.9

As per Mississippi triple-class system 70.59% patients had partial HELLP, 29.41% had complete HELLP. 3.92%, 9.8 % and 15.69 % patients had HELLP class I, II and III respectively. Placental abruption (35.29 %) was most common complication noted, followed by postpartum hemorrhage (29.41 %), acute kidney injury (13.73 %), pulmonary oedema (7.84 %), DIC (7.84 %), multiorgan dysfunction (7.84 %) and eclampsia (3.92 %). Maternal death was noted in 2 (3.92 %) patients.

Table 4: Maternal complications

Maternal complications	Partial HELLP	HELLP			Total
		Class 1	Class 2	Class 3	
Total cases of HELLP syndrome	36 (70.59 %)	2 (3.92 %)	5 (9.8 %)	8 (15.69 %)	51
Placental abruption	9 (17.6 %)	1 (1.96 %)	3 (5.88 %)	5 (9.8 %)	18 (35.29 %)
Postpartum hemorrhage	7 (13.73 %)	1 (1.96 %)	3 (5.88 %)	4 (7.84 %)	15 (29.41 %)
Acute kidney injury	2 (3.92 %)	1 (1.96 %)	1 (1.96 %)	3 (5.88 %)	7 (13.73 %)

Pulmonary oedema	2 (3.92 %)	1 (1.96 %)	1 (1.96 %)		4 (7.84 %)
DIC	2 (3.92 %)	1 (1.96 %)	1 (1.96 %)		4 (7.84 %)
Multiorgan dysfunction	1 (1.96 %)	1 (1.96 %)	2 (3.92 %)		4 (7.84 %)
Eclampsia	1 (1.96 %)			1 (1.96 %)	2 (3.92 %)
Death		1 (1.96 %)	1 (1.96 %)		2 (3.92 %)

In present study, most babies had 1.5-2.4 kgs (47.1 %) birth weight. APGAR ≤ 7 at 1 min was noted in 37.3 % neonates while APGAR ≤ 7 at 5 min was noted in 21.6 neonates. 15 neonates (29.4 %) required neonatal resuscitation. Common neonatal high-risk factors were prematurity (74.5 %), IUGR (35.3 %), Respiratory distress (60.8 %), Neonatal jaundice (11.8 %). During early neonatal period 29 neonates (56.9 %) required admission to NICU. Total neonatal deaths were 22 (43.1 %), 9 were intrauterine deaths (17.6 %) and 13 were early neonatal death (25.5 %).

Table 5: Perinatal outcome

Outcome measure	No. of patients	Percentage
Birth weight (kg)		
< 1.5	9	17.6
1.5-2.4	24	47.1
2.5-3.4	16	31.4
3.5-4.4	2	3.9
APGAR score		
APGAR ≤ 7 at 1 min	19	37.3
APGAR ≤ 7 at 5 min	11	21.6
Required neonatal resuscitation	15	29.4
Prematurity	38	74.5
IUGR	18	35.3
Respiratory distress	31	60.8
IUD	9	17.6
Hyperbilirubinemia (Neonatal jaundice)	6	11.8
Admission to NICU	29	56.9
Early neonatal death	13	25.5
total neonatal deaths	22	43.1

DISCUSSION

Hypertensive disorders are among the most common medical disorders during pregnancy and continue to be the major cause of maternal and perinatal morbidity and mortality. HELLP syndrome is often associated with preeclampsia, as up to 20% of women with severe preeclampsia develop HELLP syndrome.[9] The clinical presentation of hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is one of the more severe forms of preeclampsia because it has been associated with increased rates of maternal morbidity and mortality.[10] HELLP syndrome is characterized by thrombocytopenia and microangiopathic hemolytic anemia leading to end-organ injury and is considered to be the classic thrombotic microangiopathy (TMA) of pregnancy. In HELLP syndrome, the main presenting symptoms are right upper quadrant pain and generalized malaise in up to 90% of cases and nausea and vomiting in 50% of cases.[11] The clinical course of HELLP syndrome often is characterized by progressive and sometimes sudden deterioration in maternal and fetal condition and women with HELLP syndrome should be delivered regardless of their gestational age.[11] Shelat PM *et al.*,[12] noted that HELLP syndrome was more common in younger age group (45%) and in primigravida (52.5%). Most of the patients presented at >36 weeks of gestation (40%) and most of the patients delivered by caesarean section (67.5%). Maternal complications were acute renal failure (27.5%), DIC (22.5%), maternal mortality (7.5%). Neonatal complications associated were intrauterine death (27.5%), prematurity (25%) and intrauterine growth retardation (15%). Similar findings were noted in present study. In study by Rakshit A *et al.*,[13] prevalence of HELLP syndrome and partial HELLP syndrome were found to be 7.3% and 5.3% respectively in preeclampsia. The systolic blood pressure, gestational age at admission and during delivery, hematological and biochemical variables, rate of spontaneous vaginal delivery and type of anaesthesia were significantly different in HELLP syndrome and partial HELLP syndrome than in the preeclampsia group. There were statistically significant difference in perinatal outcome like birth weight, intrauterine death, neonatal death, and admission in NICU. They concluded that termination of pregnancy is the definitive treatment for HELLP syndrome and it should be treated only in a tertiary care center, as it needs a multidisciplinary team approach work by the obstetrician, paediatrician, physician, transfusion medicine specialist, anaesthesiologist etc. Chidanandaiah SK *et al.*,[14] noted, incidence of HELLP syndrome during 1 year period as 1.14% of total deliveries

and 3.82% of pregnancy induced hypertension (PIH). Majority (50%) patients belong to age group of 21-25 years, mean age was 22.5 years, most of them were primigravida (55%) and majority (52.5%) was in 36-40 weeks gestation and mean gestational age was 33.6 weeks. Headache (56.25%) was the most common imminent symptom. Most of symptoms were nonspecific like malaise (50%), edema (45%), vomiting (20%) and epigastric pain (7.5%). Out of 80 patients of HELLP syndrome 19 delivered by LSCS and 61 delivered vaginally. Ascites (26.25%), PPH (25%) and placental abruption (22.5%) were the most common maternal complications in HELLP syndrome followed by acute renal failure (18.75%), pulmonary edema (12.5%), DIC (6.25%) and cerebrovascular accidents (6.25%). Maternal mortality was 11.25% and perinatal mortality was 41.25%. In a retrospective study, Divya MB *et al.*,[15] analyzed fetomaternal outcome in women diagnosed with HELLP syndrome over 2 year study period. Among 7,566 deliveries, 63 women (0.83%) had HELLP syndrome. Mean age was 29.5 years. 47.6% (n=30) women developed HELLP syndrome at gestational age less than 34 weeks. Maternal complications were abruption (27.78%), acute kidney injury (16.67%), DIC (16.67%), sepsis (11.11%) and postpartum hemorrhage (11.11%). In this study, HELLP syndrome led to one maternal death (1.58%). The perinatal mortality was 25.75%. Novotny S *et al.*, recently reported an association between PR-AKI and obstetric complications, indicating that 24% and 22% of women with PRAKI complicated with HELLP syndrome had placental abruption and obstetric hemorrhage, respectively compared to the 13 and 11% of HELLP patients without PR-AKI. Early detection, prompt referral, better transport facility, appropriate and timely intervention, availability of life saving facilities like mechanical ventilators, dialysis equipment and blood products like FFP, Platelets, Packed cell transfusion at tertiary care centers will significantly reduce the maternal and fetal morbidity and mortality.

CONCLUSION

HELLP syndrome is associated with poor outcome for the mother and fetus. Timely diagnosis and management of HELLP syndrome by induction and delivery by vaginal route or by cesarean section is beneficial and prevents complications in mother and fetus.

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