Original Research Paper Obstetrics and Gynaecology

# Predicting Feto-Maternal Outcome in Hellp Syndrome Complicating Pregnancy


| | |
|---|---|
| **Dr. S. Usha Rani MD** | DGO, Professor, Institute of Obstetrics and Gynaecology. Madras Medical College |
| **Dr. S. Vanitha** | MD, Assistant Professor ., Institute of Obstetrics and Gynaecology.Madras Medical College |
| **Dr. V. Rekha MS** | Assistant Professor,Institute of Obstetrics and Gynaecology. Madras Medical College |



**ABSTRACT**

**AIM –** To study the maternal and fetal outcome in HELLP syndrome and the clinical profile and parameters associated with it. To study factors that might help in predicting feto-maternal outcomes in HELLP syndrome.

**Material and methods –** A retrospective analysis of the medical records was performed of patients with HELLP syndrome managed at a tertiary Obstetric unit, Chennai between june 2013 and may 2015, who were admitted and had documented evidence of hemolysis, elevated liver enzymes and low platelet count. Maternal and neonatal complications were recorded and analyzed.**Results –** The incidence of HELLP syndrome in our study was 0.31%. Maternal death was reported in 32.5%. The most common maternal complication was DIC (41.8%). Eclampsia was present in 33%, abruptio placentae in 16.2%, pulmonary edema in 17.45% and PRES in 4.65%. 7% had acute renal failure and 75% had cesarean section. Bilirubin value more than 2.2 is associated with higher incidence of maternal death and intrauterine fetal death. LDH value more 2320 was significantly associated with IUD and Low birth weight.


**KEYWORDS** HELLP, predictors in HELLP, Outcomes in HELLP., Preeclampsia/Eclampsia

**Intoduction –**

Preeclampsia is a complication of pregnancy traditionally characterized by the triad of elevated blood pressure, proteinuria, and generalized edema. Weinstein[1] coined the term "HELLP syndrome" to describe a special group of preeclamptic pregnant women with evidence of hemolysis ("H"), elevated liver enzymes ("EL"), and low platelet ("LP") count. Maternal and perinatal morbidity and mortality are increased in these patients and their progeny. [2]

Haemolysis, one of the major characteristics of the disorder, is due to a microangiopathic haemolytic anaemia (MAHA). Red cell fragmentation caused by high-velocity passage through damaged endothelium appears to represent the extent of small vessel involvement with intima damage, endothelial dysfunction and fibrin deposition. Presence of fragmented (schizocytes) or contracted red cells with spicula (Burr cells) in the peripheral blood smear reflects the haemolytic process and strongly suggests the development of MAHA [3, 4]. Destruction of red blood cells by haemolysis causes increased serum lactate dehydrogenase (LDH) levels and decreased haemoglobin concentrations [5, 6]. Haemoglobinaemia or haemoglobinuria is macroscopically recognizable in about 10% of the women [7]. Liberated haemoglobin is converted to unconjugated bilirubin in the spleen or may be bound in the plasma by haptoglobin. The haemoglobin-haptoglobin complex is cleared quickly by the liver, leading to low or undetetable haptoglobin levels in the blood, even with moderate haemolysis [5, 6]. Low haptoglobin concentration (< 1 g/L – < 0.4 g/L) can be used to diagnose haemolysis [6, 7, 8, 9] and is the preferred marker of haemolysis [10]. Thus, the diagnosis of haemolysis is supported by high LDH concentration and the presence of unconjugated bilirubin, but the demonstration of low or undetectable haptoglobin concentration is a more specific indicator.

Elevation of liver enzymes may reflect the haemolytic process as well as liver involvement. Haemolysis contributes substantially to the elevated levels of LDH, whereas enhanced aspartate aminotransferase (AST) and alanine aminotransferase (ALAT) levels are mostly due to liver injury. Plasma glutathione S-transferase-a1 (α-GST or GST-a1) may provide a more sensitive indicator for acute liver damage than AST and ALAT, and allow earlier recognition [11]. However, measurement of α-GST is not widely available, and has not yet found its place in the routine diagnostic procedure [12].

Thrombocytopenia (platelets (PLTs) < $150 \cdot 10^9$/L) in pregnancy may be caused by gestational thrombocytopenia (GT) (59%), immune thrombocytopenic purpura (ITP) (11%), preeclampsia (10%), and the HELLP syndrome (12%)[29]. PLTs < $100 \cdot 10^9$/L are relatively rare in preeclampsia and gestational thrombocytopenia, frequent in ITP and obligatory in the HELLP syndrome (according to the Sibai definition). Decreased PLT count in the HELLP syndrome is due to their increased consumption. Platelets are activated, and adhere to damaged vascular endothelial cells, resulting in increased platelet turnover with shorter lifespan [13, 14].

**The main diagnostic criteria for HELLP are Mississippi classification**

| | Class 1 (Severe) | Class 2 (Moderate) | Class 3 (Mild) |
|---|---|---|---|
| Platelets | ≤50,000/μL | 50,000 – 1,00,000/μL | 1,00,000 -1,50,000/μL |
| AST or ALT | ≥70 IU/L | ≥70 IU/L | ≥40 IU/L |
| LDH | ≥600 IU/L | ≥600 IU/L | ≥600 IU/L |

In The Mississippi-Triple Class System, a further classification of the disorder is based on the nadir PLT count any time during the course of the disease [15]. Class 1 and class 2 are associated with hemolysis (LDH > 600 U/L) and elevated AST (≥ 70 U/L) concentration, while class 3 requires only LDH > 600 U/L and AST ≥ 40 U/L in addition to the specific platelet count [15, 16, 17]. Class 3 HELLP syndrome is considered as a clinical signifi-

cant transition stage or a phase of the HELLP syndrome which has the ability of progression [17].

**Tennessee Classification**

| | |
|---|---|
| Complete HELLP | Platelet count of 1,00,000/µL or Less<br>AST or ALT levels of 70 IU/L<br>LDH ≥600 IU/L |
| Partial HELLP<br>Severe Preeclampsia with one of the features | ELLP – Elevated liver enzymes, Low platelets. No Hemolysis.<br>EL – Elevated liver enzymes. No thrombocytopenia, No hemolysis.<br>LP – Low platelets. No Hemolysis, Normal liver enzymes.<br>HEL – Hemolysis, Liver dysfunction, No thrombocytopenia. |

**Materials and Methods**

A retrospective analysis of the medical records was performed of patients with HELLP syndrome managed at a tertiary Obstetric unit, Chennai between june 2013 and may 2015, who were admitted and had documented evidence of hemolysis, elevated liver enzymes and low platelet count. Maternal and neonatal complications were recorded and analyzed.

Maternal outcomes analyzed included eclampsia, abruptio placentae, disseminated intravascular coagulopathy (DIC), acute renal failure, pulmonary edema, cesarean delivery and maternal death. Risk factors included maternal age, parity, gestational age at diagnosis, mean arterial blood pressure, blood platelet count serum bilirubin levels and peak serum levels of aspartate aminotransferase. Fetal outcomes analyzed were gestational age, apgar score, birth weight and the incidence of IUD, still birth and neonatal death.

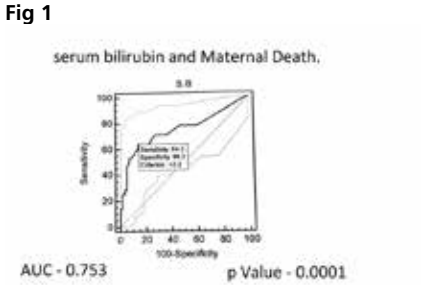
**Results –**

HELLP syndrome occurred in 86 patients among 27064 deliveries during the study period between june 2013 and may 2015. The incidence of HELLP syndrome is 0.31%. Maternal mortality occurred in 28(34%) patients.

Incidence of HELLP was high between the age group of 20 – 25 about 44% (38). Total number of maternal deaths were 28, 50% (14) were in the age group of 20 -25 years. Two thirds of the patients were in antenatal period and one third was in post-partum period. Highest incidence of 37% (32) occurred during the gestational period of of 32 – 37 weeks. (table1)

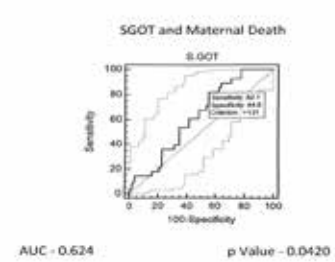
| | No of patients |
|---|---|
| Gestational Age | |
| <28 weeks | 7 |
| 28 – 32 weeks | 7 |
| 32 – 37weeks | 32 |
| >37 weeks | 15 |
| Post-partum | 25 |
| Table 1 | |

**Fig 1**



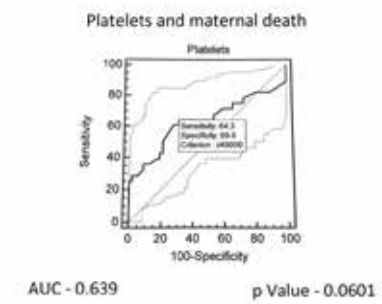

The Fig 1 ROC shows that significant association was found between serum bilirubin values (>2.2) and maternal death.

**Fig 2**




The figure 2 ROC shows that that significant association was found between SGOT values (>130) and maternal death.

**Fig 3**




No significant association was found between the value of platelets and maternal death.

29 patients (33%) had a LDH value of more than 5000IU/L at clinical presentation.

No significant association was between SGPT and maternal death.

On comparison with the mode of delivery caesarean section was performed in 75% (64) of the case and rest 25% (22) had vaginal delivery.

**Table 2**

| Maternal Complications | No | Percentage % |
|---|---|---|
| Antepartum Eclampsia | 15 | 17.4 |
| Post-partum Eclampsia | 6 | 16.2 |
| DIVC | 36 | 41.8 |
| Placental Abruption | 14 | 16.2 |
| Pulmonary edema | 15 | 17.5 |
| PRES | 4 | 4.7 |
| Renal Failure | 6 | 7.0 |
| Others | 8 | 9.3 |

The most common maternal complication was DIC (41.8%). Eclampsia was present in 33.6%, abruptio placentae in 16.2%, pulmonary edema in 17.45% and PRES in 4.65%. 7% had acute renal failure (Table 2) and 75% had cesarean section.

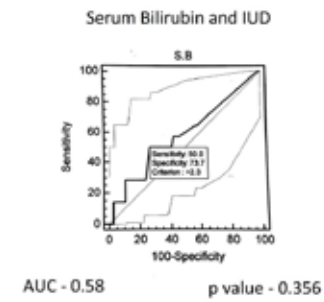
**Neonatal Outcome**

**Table 3**

| Outcome | No | Percentage % |
|---|---|---|
| Low birth Weight | 62 | 72 |
| Apgar at 5 mins (<7) | 28 | 32.6 |
| IUFD | 14 | 16.2 |
| IUGR | 25 | 29 |
| Still Born | 15 | 17.4 |
| Neonatal death | 5 | 5.8 |

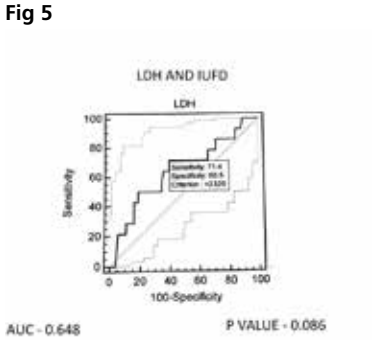
Neonatal morbidity is high in HELLP syndrome. Incidence of IUD -14(16.2%), Still Born -15 (17.4%) is high when compared with general population. Low apgar babies were 28 (32.6%), IUGR babies were 25 (29%) and Neonatal death- 5 (5.8%). The low birth weight was 62 (72%) was high because of the increase in preterm deliveries as the decision is taken to terminate the pregnancy as soon as HELLP is diagnosed in order to prevent its worsening.

**FIG 4**




The fig 4 ROC curve shows that the serum bilirubin level of above 2.3 mg/dl there is significant association with the occurrence of IUD.

**Fig 5**




The Fig 5 ROC curve shows that the serumLDH level of above 2320 mg/dl there is significant association with the occurrence of IUD.

There was no significant association found between SGOT, SGPT and Platelet values with IUFD.

**Discussion**

HELLP syndrome occurred in 86 patients among 27064 deliveries during the study period between june 2013 and may 2015. The incidence of HELLP syndrome is 0.31%. Similar incidence was reported by Werner Rath et al [18].

Maternal mortality was 34% in our study; similarly mortality rate was reported by Gulseren Yucesoy et al of 40% [19]. In our study we found that there is significant correlation between serum bilirubin, serum SGOT and maternal death. An initial presentation with a serum bilirubin value of more than >2.2mg/dl is increasingly associated with maternal death. In our study 19 patients had bilirubin value more than 2.2mg/dl and only 5 patients recovered finally. Patients with a higher value of bilirubin had a rapid course towards death. Similarly a serum SGOT value of more than 120 mg/dl was associated with higher maternal death. LDH value of more than 5000IU/L was seen in 29 (33%) of the patients. These can be a result of significant hemolysis at initial presentation.

No significant association was found between maternal mortality and platelet values. This is unlike the reporting of Gulseren Yucesoy et al [19] who found had previously found a significant relation between low platelet values and maternal death.

The most common maternal complication was DIC (41.8%). Eclampsia was present in 33.4%, abruptio placentae in 16.2%, pulmonary edema in 17.45% and PRES in 4.65% 7% had acute renal failure (Table 2).

The caesarean section rate was high (75%) because most of the presentation of HELLP syndrome was at between gestational period of 32 – 37 weeks and with unfavorable cervix. And the decision to immediately terminate the pregnancy resulted in a higher caesarean section rate.

Neonatal morbidity is high in HELLP syndrome. Incidence of IUD -14(16.2%), Still Born -15 (17.4%) is high when compared with general population. The low birth weight was 62 (72%) was high because of the increase in preterm deliveries as the decision is taken to terminate the pregnancy as soon as HELLP is diagnosed in order to prevent its worsening.

The Serum bilirubin value more than 2.3 mg/dl and the serum LDH level of above 2320 mg/dl there is significant association with the occurrence of IUD. Initial presentation with these values should warrant a more careful and intensive intrauterine fetal surveillance.

There were a few limitations in our study, follow up of the mother and neonate was not done to know the long term morbidity associated with HELLP syndrome. In addition the requirement of blood products needed in management was not studied.

**Conclusion**

There is significant maternal and fetal morbidity associated with HELLP syndrome. Intensive monitoring can help in prevent the mortality associated with HELLP syndrome. There is significant correlation between serum bilirubin (>2.2mg/dl), serum SGOT (>120mg/dl) and serum LDH values and maternal death. The Serum bilirubin (>2.3 mg/dl) and the serum LDH level (>2320 mg/dl) there is significant association with the occurrence of IUD.

**Reference -**

1. Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. AM j OSSTET GVNECOL 1982; 142:159-67.
2. Sibai BM, Taslimi MM, El-Nazer A, et al. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelet count in severe preeclampsia-eclampsia. AM j OSSTET GVNECOL 1986; 155: 501-9.
3 Magann EF, Martin JN: Twelve steps to optimal management of HELLP syndrome. Clin Obstet Gynecol. 1999, 42: 532-550. 10.1097/00003081-199909000-00009.
4 Baxter JK, Weinstein L: HELLP syndrome: the state of the art. Obstet Gynecol Surv. 2004, 59: 838-845. 10.1097/01.ogx.0000146948.19308.c5.
5 Marchand A, Galen RS, Van LF: The predictive value of serum haptoglobin in hemolytic disease. JAMA. 1980, 243: 1909-1911. 10.1001/jama.243.19.1909.
6 Wilke G, Rath W, Schutz E, Armstrong VW, Kuhn W: Haptoglobin as a sensitive marker of hemolysis in HELLP-syndrome. Int J Gynaecol Obstet. 1992, 39: 29-34. 10.1016/0020-7292(92)90776-F.
7 Rath W, Faridi A, Dudenhausen JW: HELLP syndrome. J Perinat Med. 2000, 28: 249-260. 10.1515/JPM.2000.033.
8 Deruelle P, Coudoux E, Ego A, Houfflin-Debarge V, Codaccioni X, Subtil D: Risk factors for post-partum complications occurring after preeclampsia and HELLP syndrome. A study in 453 consecutive pregnancies. Eur J Obstet Gynecol Reprod Biol. 2006, 125: 59-65. 10.1016/j.ejogrb.2005.07.011.
9 Poldre PA: Haptoglobin helps diagnose the HELLP syndrome. Am J Obstet Gynecol. 1987, 157: 1267-
10 van Runnard Heimel PJ, Franx A, Schobben AF, Huisjes AJ, Derks JB, Bruinse HW: Corticosteroids, pregnancy, and HELLP syndrome: a review. Obstet Gynecol Surv. 2005, 60: 57-70. 10.1097/01.ogx.0000150346.42901.07.
11 Knapen MF, Mulder TP, Bisseling JG, Penders RH, Peters WH, Steegers EA: Plasma glutathione S-transferase alpha 1-1: a more sensitive marker for hepatocellular damage than serum alanine aminotransferase in hypertensive disorders of pregnancy. Am J Obstet Gynecol. 1998, 178: 161-165. 10.1016/S0002-9378(98)70645-3.
12 Parnas M, Sheiner E, Shoham-Vardi I, Burstein E, Yermiahu T, Levi I, Holcberg G, Yerushalmi R: Moderate to severe thrombocytopenia during preg-

nancy. Eur J Obstet Gynecol Reprod Biol. 2006, 128: 163-168. 10.1016/j.ejogrb.2005.12.031.

13 Redman CW, Bonnar J, Beilin L: Early platelet consumption in pre-eclampsia. Br Med J. 1978, 1: 467-469.

14 Stubbs TM, Lazarchick J, Van Dorsten JP, Cox J, Loadholt CB: Evidence of accelerated platelet production and consumption in nonthrombocytopenic preeclampsia. Am J Obstet Gynecol. 1986, 155: 263-265.

15 Martin JN, Rose CH, Briery CM: Understanding and managing HELLP syndrome: the integral role of aggressive glucocorticoids for mother and child. Am J Obstet Gynecol. 2006, 195: 914-934. 10.1016/j.ajog.2005.08.044.

16 Martin JN, Blake PG, Perry KG, McCaul JF, Hess LW, Martin RW: The natural history of HELLP syndrome: patterns of disease progression and regression. Am J Obstet Gynecol. 1991, 164: 1500-1509.

17 Martin JN, Rinehart BK, May WL, Magann EF, Terrone DA, Blake PG: The spectrum of severe preeclampsia: comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification. Am J Obstet Gynecol. 1999, 180: 1373-1384. 10.1016/S0002-9378(99)70022-0.

18 Werner Rath, Andree Faridi, Joachim W. Dudenhausen: HELLP Syndrome: Journal of Perinatal Medicine. Volume 28, Issue 4, Pages 249–260, ISSN (Print) 0300-5577, DOI: 10.1515/JPM.2000.033, June 2005.

19 Gulseren Yucesoy, Yigit Cakiroglu,Harika Bodur, Sebiha Ozkan, Temel Tan: An analysis of HELLP syndrome cases: does platelet count predict adverse maternal and fetal outcomes in women with HELLP syndrome?