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Badugu Rao Bahadur
Assistant Professor, Department of Obstetrics and Gynaecology, NRI Medical College and General Hospital, Chinakakani, Mangalagiri, Guntur, Andhra Pradesh, India

Prabha Devi Kodey
Professor and Head, Department of Obstetrics and Gynaecology, NRI Medical College and General Hospital, Chinakakani, Mangalagiri, Guntur, Andhra Pradesh, India

Amrutha Mula
Resident, Department of Obstetrics and Gynaecology, NRI Medical College and General Hospital, Chinakakani, Mangalagiri, Guntur, Andhra Pradesh, India

Correspondence
Badugu Rao Bahadur
Assistant Professor, Department of Obstetrics and Gynaecology, NRI Medical College and General Hospital, Chinakakani, Mangalagiri, Guntur, Andhra Pradesh, India

Maternal and fetal outcome in HELLP syndrome

Badugu Rao Bahadur, Prabha Devi Kodey and Amrutha Mula

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Abstract
Background: HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome is a severe complication of pregnancy with high risk for both mother and fetus and it complicated 0.2–0.6 % of all pregnancies. This present study was designed to understand maternal and fetal outcome in HELLP syndrome complicating pregnancy.
Methods: Study was conducted over a period of 24 months. Antenatal women above 20 weeks gestation, who fulfilled the criteria for HELLP syndrome, were included in the study. Detailed histories, clinical examination, blood pressure measurement, obstetric examination, blood investigation were done. Maternal and fetal complications were noted and subjected to statistical analysis.
Results (n=40): Incidence of HELLP syndrome was 0.7% of all deliveries and 22.4% of preeclampsia & eclampsia cases. Mean gestational age was 32.5 weeks. Common maternal complication was acute renal damage seen in 30% cases. Perinatal mortality was 42.5%.
Conclusion: HELLP Syndrome is a life threatening complication, associated with maternal and fetal risk. It requires multidisciplinary approach and tertiary hospital care.

Keywords: HELLP syndrome, eclampsia, platelets

Introduction
HELLP syndrome comprises a triad of hemolysis, elevated liver enzymes and low platelet count in a woman with preeclampsia and eclampsia [1]. The term Help syndrome was coined by Weinstein in 1982 [2]. HELLP syndrome is a severe complication of preeclampsia and eclampsia with high risk for both mother and fetus.
HELLP syndrome in general complicates 0.2–0.6 % of all pregnancies but its incidence is increased to 4-12% in severe preeclampsia [3]. 70% of HELLP syndrome develops in antepartum period and the rest in postpartum period [4]. 15% of HELLP syndrome patients present with mild hypertension or without significant proteinuria [5]. HELLP syndrome is associated with poor maternal and fetal outcome [6]. The reported maternal mortality of the HELLP syndrome ranges from 0% to 24% [5]. 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 [7, 8].
This present study was designed to understand maternal and fetal outcome in HELLP syndrome.

Methods
This is a prospective study conducted in the Department of Obstetrics & Gynaecology, NRI Medical College and General Hospital, Chinakakani, Andhra Pradesh from October 2015 to September 2017. All antenatal women above 20 weeks gestation, who fulfilled the criteria for HELLP syndrome, were included in the study after taking informed consent. Approval was taken from institutional ethical committee.

Inclusion Criteria
Pregnant women above 20 weeks of gestational age with preeclampsia and eclampsia with one or more of the following:
- Haemolysis detected either by peripheral smear or elevated indirect bilirubin or elevated LDH levels.
- Elevated liver enzymes.
- Decreased platelet count less than 100,000/ mm^3.

Exclusion Criteria

- Known Hepatic disease.
- Pre-existing Haemolytic anaemia.
- Known Platelet disorders.
- Chronic renal diseases.
- Multiple gestations.
- Placenta praevia.
- Acute fatty liver of pregnancy.

All cases that fulfilled inclusion criteria were included, detailed history, thorough clinical examination, blood pressure measurement, obstetric examination, blood investigations were done (Table 1). Maternal and fetal complications were noted. Data was collected and subjected to statistical analysis and inference was drawn.

Table 1: Investigations done

Complete blood picture with platelet count
Complete urine examination
Peripheral blood smear
Bleeding time
Clotting time.
Liver function tests
• Total bilirubin
• Direct bilirubin
• Indirect bilirubin
• LDH
• AST
• ALT
Renal function test
Coagulation profile
Fundoscopy
Obstetric ultrasonography, foetal doppler study, Non stress test

Results

Duration of study period - 2 years
Total no of deliveries during study period - 5,564
Total no of preeclampsia cases - 123 (2.21%)
Total no of eclampsia cases - 55 (0.98%)
Total no of HELLP syndrome cases - 40

Incidence of HELLP syndrome was 0.7% of all deliveries and 22.5% of preeclampsia and eclampsia cases. 29 cases (23.57%) from 123 preeclampsia and 11 cases (20%) from 55 eclampsia cases developed HELLP syndrome.

According to Tennessee classification, 23 (57.5%, partial HELLP, 17 (42.5%) had complete HELLP syndrome and according to Mississippi classification 22 (55%), 11(27.5%), 7(17.5%) cases developed class III, Class II and Class I HELLP syndrome respectively. 25 (62.5%) cases were in the age group of 20 to 25 years, with mean age of 23.8 years. All 40 cases presented with edema. 13 cases had nausea, vomiting and epigastric pain 1 cases had headache.

14 (35%) of partial HELLP, 12 (30%) of complete HELLP, 12 (30%) of class III, 9 (22.5%) of class II, 5 (12.5%) of class I had systolic blood pressure in range of 141 to 160 mmHg. Only 1 case had systolic blood pressure of more than 180 mm of Hg. Mean Systolic Blood Pressure was 155.25 mm of Hg. 16 (40%) of partial HELLP, 15 (37.5%) of complete HELLP, 16 (40%) class III, 10 (25%) had class II, 5(12.5%) of class I had diastolic blood pressure in range 90 to 110 mm of Hg. Mean diastolic blood pressure was 103.25 mm of Hg.

Most of the cases (n= 27) (67.5 %) were referred from outside in view of HELLP syndrome for further management and13 cases (32.5%) were from our hospital follow-up.

In 15 cases (37.5%), HELLP syndrome was diagnosed between 28 to 34 weeks of gestation, followed by 11cases (27.5%) at term gestation, with mean gestational age of 32.5 weeks gestation. No case of HELLP syndrome was reported in postpartum period.

20(50%) cases had Lactate dehydrogenase (LDH) levels of more than 1,000 U/L. 12 (30%) cases were in the range of 601-800 U/L. Mean LDH levels was 1,188.28 U/L with a maximum level of 2,766 U/L.

15 (37.5%) cases showed alanine transaminase (ALT) value in the range of 40 to 60 U/L,14(35%) cases had ALT more than 100 U/L. Maximum level was 390 U/L, with complete HELLP syndrome. Mean ALT value was 110 U/L. 17(42.5%) cases showed aspartate transaminase (AST) value more than 100 U/L, of which 11(64.7%) had complete HELLP syndrome, 6(35.29%) had class I HELLP syndrome. Maximum level AST was 689 U/L. 16(40%) cases had platelets in the range of 50,000 to 1,00,000/mm^3, 6(15%) cases had platelets less than 50,000/mm^3. 11(27.5%) had platelets between 1,00,001 to 1,50,000/mm^3. Mean platelet value was 1,12,425 / mm^3. 20 (50%) cases had vaginal delivery and 20 (50%) were terminated by caesarean section. Of the vaginal deliveries 7(35%) were preterm deliveries. Induction was done in 22 (55%) cases. Out of these 22 cases, 11 (50%) cases had failed induction and underwent cesarean section. 9(22.5%) patients needed blood products.

12 (30%) cases developed acute renal damage of which 8 cases developed complete HELLP syndrome. 10 (25%) had jaundice, 9 (22.5%) had disseminated intravascular coagulation (DIC), retinopathy seen in 8 (20%) cases, 3 (7.5%) patients had PPH. 2 (5%) cases each had cardiac failure, pulmonary edema & sepsis. 1(2.5%) cases each had MODS, Posterior Reversible Encephalopathy Syndrome (PRES), abruptio placenta. Intensive care unit (ICU) admission was required in 5 cases. No maternal mortality was seen (Table 2).

Table 2: Distribution according to maternal complications

Complication	Partial HELLP	Complete HELLP	Class I	Class II	Class III
Renal damage	4 (10%)	8 (20%)	6 (15%)	2 (5%)	4 (10%)
Jaundice	1 (2.5%)	9 (22.5%)	4 (10%)	5(12.5%)	1 (2.5%)
Disseminated intravascular coagulation	3 (7.5%)	6 (15%)	4 (10%)	2 (5%)	3 (7.5%)
Retinopathy	3 (7.5%)	5 (12.5%)	3 (7.5%)	3 (7.5%)	2 (5%)
Intensive care unit admission	1 (2.5%)	4 (10%)	3 (7.5%)	2 (5%)	0 (0%)
Postpartum haemorrhage	1 (2.5%)	2 (5%)	2 (5%)	0 (0%)	1(2.5%)
Cardiac failure	0 (0%)	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)
Pulmonary edema	0 (0%)	2 (5%)	2 (5%)	0 (0%)	0 (0%)
Sepsis	0 (0%)	2 (5%)	2 (5%)	0 (0%)	0 (0%)
Abruptio placenta	0 (0%)	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)
PRES	0 (0%)	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)

Multi organ dysfunction	0 (0%)	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)
Maternal death	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

23 cases had preterm deliveries. 19 neonates required Neonatal ICU (NICU) admission. Low Apgar score noted in 7 cases. Perinatal mortality in our study was 42.5% (17 cases) (Table 3).

Table 3: Distribution according to perinatal complications

Complication	Partial HELLP	Complete HELLP	Class I	Class II	Class III
Pre term	14 (35%)	9 (22.5%)	2 (5%)	7 (17.5%)	14 (35%)
NICU admissions	10 (25%)	9 (22.5%)	3 (7.5%)	6 (15%)	10 (25%)
Oligohydramnios	11(27.5%)	5 (12.5%)	1 (2.5%)	3 (7.5%)	12 (30%)
Fetal growth restriction	7 (17.5%)	8 (20%)	3 (7.5%)	4 (10%)	8 (20%)
Low birth weight	8 (20%)	6 (15%)	3 (7.5%)	4 (10%)	7 (17.5%)
Respiratory distress syndrome	7 (17.5%)	7 (17.5%)	2 (5%)	5 (12.5%)	7 (17.5%)
Still born	4 (10%)	4 (10%)	3 (7.5%)	1 (2.5%)	4 (10%)
Intra uterine death	3 (7.5%)	4 (10%)	2 (5%)	2 (5%)	3 (7.5%)
Low APGAR	4 (10%)	3 (7.5%)	1 (2.5%)	1 (2.5%)	5 (12.5%)
Convulsions	2 (5%)	3 (7.5%)	2 (5%)	1 (2.5%)	2 (5%)
Sepsis	1 (2.5%)	3 (7.5%)	1 (2.5%)	1 (2.5%)	2 (5%)
Meconium aspiration syndrome	1 (2.5%)	0 (0%)	0 (0%)	0 (0%)	1 (2.5%)
Neonatal death	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)	2 (5%)

Discussion

Incidence of HELLP syndrome was 0.7% among all deliveries which is higher as compared to Campos A *et al.* [9] (0.2%) and 22.8% (40/178) among preeclampsia and eclampsia which was similar to Campos A *et al.* [9] (28%). Sowjanya *et al.* [10] Ara S *et al.* [11] Lakshmi N *et al.* [12] showed incidence of 30.23%, 6.5% and 13.18% respectively. Early identification of risk factors in pregnancy and timely intervention gives better maternal and perinatal outcome.

Out of the 123 cases of preeclampsia, 29 (23.57%) developed HELLP syndrome and from 55 eclampsia cases, 11 (20%) developed HELLP syndrome. In a study conducted by Lakshmi N *et al.* [12] 13.18% cases of Preeclampsia, 27.27% cases of eclampsia developed HELLP Syndrome. 62.5% cases were in range 20 to 25 years, with mean age of 23.8 years which is comparable to Lakshmi N *et al.* [12] where 60% cases were in the age group of 21-25 years. Murray D *et al.* [13] Vallejo Maroto *et al.* [14] Campos A *et al.* [9] showed mean age of 29.8 years, 30.06 years, 31.3 years respectively. In our study there was equal distribution between primigravida 20 (50%) and multigravida 20 (50%). Vallejo Maroto I *et al.* [14] showed 57.4% cases were primigravida & 42.6% cases were multigravida. Campos A *et al.* [9] showed 68% cases were primigravida and 31% were multigravida.

Most commonly observed sign was edema seen in all 40 cases. 5 (12.5%) cases had grade IV edema. Nausea & vomiting and epigastric pain was seen in 13 (32.5%) cases each. Sowjanya *et al.* [10] showed nausea and vomiting as common symptom, followed by headache.

Mean systolic blood pressure was 155.25 mmHg and mean diastolic blood pressure was 103.25 mmHg. Celik C *et al.* [15] observed mean systolic blood pressure of 161.6 mmHg and mean diastolic blood pressure of 98.5 mmHg.

27 cases (67.5 %) were referred from other hospitals in view of HELLP syndrome for further management. In Lakshmi N *et al.* [12] study 80% of the cases were referred.

All 40 cases developed HELLP syndrome in antenatal period, with mean gestational age of 32.5 weeks. This was comparable to Celik C *et al.* [15] and Turki Gasem *et al.* [16] study with 32.6 weeks, 32.4 weeks of gestation respectively. 37.5% of cases were between 28 to 34 weeks of gestation. In Lakshmi N *et al.* [12] study most of the cases were between 32 to 36 weeks of gestation. Romero Arauz JF *et al.* [17] study noted 66% cases were between 28 to 36 weeks of gestation, 25% at term gestation and 9% were less than 27 weeks gestation.

In 50% cases LDH levels was more than 1000 U/L, 30% (n=12) were in the range of 601 to 800 U/L, with mean LDH level of 1188.28 U/L. Lakshmi N *et al.* [12] 75% of cases had LDH level more than 1000 U/L. In Sowjanya *et al.* [10] study 75% of cases had LDH level more than 1400 U/L. 15 (37.5%) cases showed serum ALT value more than 100 U/L. More complications were seen in cases with ALT value more than 100 U/L, comparable with Lakshmi N *et al.* [12] and Sowjanya *et al.* [10] study where more complications were seen with serum ALT value more than 140 & 100U/I respectively.

42.5% (n=17) of cases had AST level more than 100 U/L. 80% of cases who had AST level more than 140 U/L had severe complications, similar to study by Lakshmi N *et al.* [12] were 75% of cases who had AST value more than 140 U/L had severe complications and in Sowjanya *et al.* [10] study 75% of cases with AST value more than 100 U/L showed severe complications.

40% (n=16) of cases had platelets in range of 50,000 to 1,00,000 /mm^3, 27.5% (n=11) had platelets between 1,00,000 - 1,50,000/mm^3 and 15% (n=6) of cases had platelets less than 50,000/mm^3. 17.5% (n=7) had more than 1,50,000/mm^3. Mean platelet value was 1,12,425 / mm^3. Sowjanya *et al.* [10] study showed, 57% of cases had platelets in range 50,000 to 1,00,000/mm^3 & 23% had less than 50,000/mm^3.

In Lakshmi N *et al.* [12] study, 40% cases had platelets between 1,00,000 to 1,50,000/mm^3, 40% cases between 50,000 to 1,00,000/mm^3 and 20% cases had platelets less than 50,000/mm^3.

In our study 50% (n=20) of cases had vaginal delivery & 50% (n=20) cases underwent cesarean section. Celik C *et al.* [15] Sowjanya *et al.* [10] showed 36%, 71.5% had vaginal delivery and 64%, 28.5% underwent cesarean section respectively. Ben Letaite D *et al.* [18] showed 6% vaginal delivery and 94% cesarean section.

30% (n= 12) of cases had acute renal damage as a complication of HELLP syndrome. No case required dialysis. Acute renal damage was most common maternal complication noted. Lakshmi N *et al.* [12] noted 33% and Celik C *et al.* [15] noted 36% of cases had acute renal damage. Sowjanya *et al.* [10] showed 4% cases with acute renal damage.

In present study 25% (n=10) cases had elevated bilirubin levels. Out of these 90% (n=90) had complete HELLP syndrome. Maximum bilirubin level was 17.8 mg/dl with severe anemia

(Hemoglobin 7.4gm %) and was treated with fresh frozen plasma (FFP), platelet transfusion and packed cells. 22.5% (n=9) of cases developed DIC. Out of these 66.6% (n=6) had complete HELLP syndrome. All these 6 cases required transfusion of blood products. Sadaf N *et al*. [19] Lakshmi *et al*. [12] Soujanya *et al*. [10] had 15%, 33%, 4.5% cases with DIC.

In this study 20% (n=8) of cases had hypertensive retinopathy, out of these 50% (n=4) of cases had grade II hypertensive retinopathy, 50% (n=4) of cases had grade I hypertensive retinopathy. In a study conducted by Lakshmi N *et al*. [12] 6.6% cases had retinal detachment, in our study no case of retinal detachment was reported.

In our study 12.5% (n=5) of cases required ICU admission due to various reasons like coagulopathy, pulmonary edema, cardiac failure, MODS, PRESS etc. 7.5% (n=3) of cases developed PPH. Lakshmi N *et al*. [12] Sowjanya *et al*. [10] had 6.2%, 12.03% cases with PPH. 5% (n=2) of cases developed pulmonary edema, both cases had complete HELLP syndrome. Both admitted in ICU, and developed cardiac failure. In a similar study conducted by Sadaf N *et al*. [19], Lakshmi N *et al*. [12] Ben Letaifa D *et al*. [18] 5%, 6%, 6.25% of cases developed pulmonary edema respectively.

In this study 2.5% (n=1) of cases had abruptio placenta. Study by Lakshmi N *et al*. [12] had 6% and Sowjanya *et al*. [10] had 8% of cases with abruptio placenta.

2.5% (n=10) of cases developed PRES as CNS abnormality and required ICU admission. In comparison with Lakshmi N *et al*. [12] Sowjanya *et al*. [10] study showed 6%, & 9, 77% cases with CNS abnormality. This may be due to early intervention and thus preventing the progression of disease. 2.5% (n=1) of cases developed MODS. 2 (5%) cases had sepsis and one case developed MODS requiring ICU. In Lakshmi N *et al*. [12] study incidence of MODS was 3%.

No maternal death was reported in our study. Turki Gasem *et al*. [16] Murray D *et al*. [13] also had no maternal death. This was may be due to early intervention.

In present study 22.5% (n=9) of cases required transfusion of blood products, comparable to Haddad B *et al*. [20] study in which 22% cases required blood transfusion.

57.5% (n=23) had preterm deliveries with HELLP syndrome. This was comparable to Sadaf N *et al*. [19] study, where incidence was 50%. This may be due early termination of pregnancy to prevent maternal morbidity and mortality. Lakshmi *et al*. [12] Sowjanya *et al*. [10] 86.7% & 84.06% had preterm deliveries with HELLP syndrome.

47.5% (n=19) of neonates needed NICU admission for birth asphyxia, respiratory distress syndrome, meconium aspiration syndrome, low birth weight, preterm etc. out of these one infant died on day 5 of life due to sepsis and respiratory distress syndrome. In a similar study conducted by Lakshmi N *et al*. [12] Sowjanya *et al*. [10] Murray D *et al*. [13] 40%, 12.03%, 10% of neonates were admitted in NICU.

Oligohydramnios was seen in 40% (n=16) of cases. This was Comparable with Lakshmi N *et al*. [12] study in which 40% of cases had oligohydramnios. 37.5% (n=15) of cases had fetal growth restriction (FGR). This was comparable with Sadaf N *et al*. [19] study where 45% of cases had FGR. 35% (n=14) of neonates had low birth weight, in comparison to Celik C *et al*. [15] study, where 30% neonates had low birth weight. This may be due to higher incidence of preterm deliveries and fetal growth restriction.

35% (n=14) of neonates developed respiratory distress syndrome, in a similar study by Murray D *et al*. [13] Sowjanya *et al*. [10] 40%, 10.5% neonates developed respiratory distress syndrome. 8 (20%) cases were babies born were stillborn. Lakshmi N *et al*. [12] Sowjanya *et al*. [10] study showed 13.3%, 9.02% had stillborn babies. 17.5% (n=7) of cases had intra uterine death (IUD). Sowjanya *et al*. [10] Lakshmi N *et al*. [12] Aslam H *et al*. [21] study showed IUD in 5.26%, 13.3% & 6.9% respectively. 18% (n=7) of cases had babies with low APGAR scores at birth, which was comparatively lower than Lakshmi N *et al*. [12] study (26.6%), higher than Sowjanya *et al*. [10] study (9.02%). 12.5% (n=5) of neonates developed convulsions which may be due to birth asphyxia, low birth weight and fetal growth restriction. 10% (n=4) neonates developed sepsis, out of this 1 neonate died due to sepsis. Our study 1(2.5%) neonate developed meconium aspiration syndrome. Study conducted by Sowjanya *et al*. [10] Lakshmi N *et al*. [12] also showed this complication in 2.25%, 33.3% cases respectively.

Over all perinatal mortality in our study was 40% (n=16), similar to Lakshmi N *et al*. [12] 46.6%, Ben Letaifa D *et al*. [18] 37.5%. Sowjanya *et al*. [10] Sadaf N *et al*. [19] noted perinatal mortality of 35.3% & 57.5% respectively.

Conclusion

Regular antenatal checkup plays a major role in early diagnosis and classification of HELLP Syndrome. Availability of better transport facilities and prompt referral is essential. HELLP Syndrome must be treated in a tertiary care hospital as it is one of the dreadful obstetric complication which needs multidisciplinary team approach and availability of lifesaving facilities like mechanical ventilator, dialysis equipment, blood products, and neonatal care facilities.

For this reason, obstetrician at any level should be attentive, alert and need to improve quality care and make efforts for early identification and provide skilled care till the case is shifted to tertiary level hospital.

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