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Clinical Study on Hellp Syndrome- Maternal and Perinatal Outcome

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Abstract: *The HELLP syndrome is a serious complication in pregnancy characterized by haemolysis, elevated liver enzymes and low platelet count occurring in 0.5 to 0.9% of all pregnancies and in 10–20% of cases with severe preeclampsia. Aim: The objective of the present prospective study is on incidence, diagnosis, and its variable presentations of HELLP syndrome in preeclampsia, eclampsia to analyze the severity and complications, as it is associated with maternal, perinatal morbidity and mortality. HELLP syndrome is difficult to diagnose when it presents with atypical clinical features like high blood pressure and no protienuria, flu like symptoms, malaise, fever, nausea, vomiting, epigastric pain. Methods: In the prospective study of 414 admitted cases with more than 24 weeks of gestation, 324 were preeclampsia while 90 were eclampsia. The selected cases were analyzed clinically with relevant history, clinical data and detailed laboratory investigations the classification is made for better analyses of complications and outcome in HELLP syndrome. RESULTS: Under further clinical diagnosis of 324 cases of preeclampsia, 116 cases (35%) were of HELLP Syndrome and out of 90 cases of eclampsia, 17(18%) cases were HELLP Syndrome. Majority of the cases belonged to 19-28 years age group and were mostly from lower socio-economic conditions. The present study shows 4.5% maternal mortality and perinatal mortality as 35.33%. Conclusion: The diagnosis of HELLP Syndrome has been made as a severe variant and complication of severe preeclampsia and eclampsia. It needs early diagnosis, timely intervention to arrest further progress and complications like multi organ dysfunction, renal failure, DIC, abruption etc and to improve perinatal outcome.*

Keyword: *HELLP Syndrome, perinatal mortality and maternal morbidity*

I. Introduction

HELLP syndrome is a life-threatening pregnancy complication usually considered to be a severe and variant form of preeclampsia, ecclampsia or its complication. This is characterized by vasospasm and endothelial dysfunction, fibrin deposition and varied degree of hepatic ischemic damage, micro angiopathic hemolytic anemia and thrombocytopenia. The HELLP syndrome occurs in about 0.5 to 0.9% of all pregnancies and in 10 to 20% of cases with severe preeclampsia. In about 70% of the cases, the HELLP syndrome develops before delivery with a peak frequency between the 27th and 37th gestational weeks; 10% occur before the 27th week, and 20% beyond the 37th gestational week [6]. In the post-partum period the HELLP syndrome usually develops within the first 48 hours after delivery.

The onset of HELLP syndrome is rapid and variable. Because of the variable atypical clinical presentation, the diagnosis of HELLP syndrome is generally delayed for 5-7 days. Many women with this syndrome are initially misdiagnosed with other disorders, such as viral fevers, cholecystitis, esophagitis, gastritis, hepatitis or idiopathic thrombocytopenia. This syndrome is common during the third trimester (69%) and post partum (31%).Typical clinical symptoms are abdominal pain in the right upper quadrant or epigastric pain, nausea and vomiting. The upper abdominal pain may be intermittent, colicy type with malaise some days before presentation. 30–60% of women have headache while 20% with visual disturbances. However, women with a HELLP syndrome might also have non-specific symptoms or subtle signs of preeclampsia or viral syndrome-like symptoms.

HELLP syndrome was named by Dr. Louis Weinstein(1) in 1982 based on its clinical features **H** (hemolysis,) is microangiopathic hemolytic anemia, **EL** (elevated liver enzymes),**LP** (low platelet count). It is considered to be a progressive and severe form of preeciamsia and eclampsia. In Tennessee Classification system, Sibai has proposed a criterion for true or complete HELLP syndrome.

The triad signs of haemolysis, elevated liver enzymes and thrombocytopenia proposed by Sibai et al.(2) Haemolysis, one of the major characteristics of the disorder, is due to a microangiopathic haemolytic anemia which is diagnosed by the presence of fragmented (schizocytes) or contracted red cells with spicula (Burr cells)

in the peripheral blood smear the and increased reticulocyte counts, increased serum lactate dehydrogenase level (LDH,>600U/L), decreased haemoglobin concentrations. Low haptoglobin concentration (< 1 g/L – < 0.4) is a more specific indicator of hemolysis and the presence of unconjugated bilirubin(>1.2mg/100ml). 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 asparate aminotransferase (AST) and alanine aminotransferase (ALAT) levels are mostly due to liver injury. Decreased PLT count in the HELLP syndrome is due to their increased consumption; Platelets are activated, and adhere to damaged vascular endothelial cells.

II. Materials And Methods

This is a prospective study of 133 cases of HELLP syndrome admitted in SVMC, GMH, Tirupathi for a period of 9 months from Jan 2014 to September, 2014**.**

Inclusion Criteria:

1) Women with severe preelampsia, eclapmsia with abnormal lab findings.
2) Women with severe hypertension >24 weeks of gestation.

Exclusion Criteria:

1) Women with less than 24 weeks of pregnancy
2) Women with other abnormalities like viral hepatitis, gastro enteritis, cholecystis, and pancreatitis
3) Women with other differential diagnosis of HELLP

The selected cases were analyzed clinically with relevant history, clinical data and detailed laboratory investigations including complete haemogram, peripheral blood smear ,complete liver function, coagulation profile and renal function tests have been prospectively recorded among the cases admitted in GMH, SVMC, Tirupati and the classification is made for better analyses of complications and outcome in HELLP syndrome

Two classification systems are used for diagnosis and analysis of HELLP syndrome. The first is based on the number of abnormalities that are present. In this system, patients are classified as: Partial HELLP syndrome (one or two abnormalities) or Complete HELLP syndrome (all three abnormalities).Alternatively, HELLP syndrome can be classified on the basis of platelet count by Nadir: Class I-less than 50,000 per mm^3 (50 × 10^9 per L); Class II- 50,000 to less than 100,000 per mm^3 (50 to 100 × 10^9 per L), Class III-100,000 to 150,000 per mm^3 (100 to 150 × 10^9 per L).

Tennessee classification based on the number of abnormalities that are present. In this system, patients are classified as having partial HELLP syndrome (one or two abnormalities) or complete HELLP syndrome (all three abnormalities).	**Mississippi classification classified on the basis of "platelet count nadir"**
Complete HELLP Platelets ≤ 1,00,000/L, AST ≥ 70 IU/L LDH ≥ 600 U/L	*Class I :* Platelets ≤ $50 \cdot 10^9$/L AST or ALT ≥ 70 IU/L LDH ≥ 600 U/L
Partial HELLP Presence of only 1or 2 factors of triad.	*Class II:* Platelets 50,000 to 1,00,000 /Miro L AST or ALT ≥ 70 IU/L LDH ≥ 600 U/L
	Class III: Platelets ≤ 1,00,000 -1,50,000/Micro L AST or ALT ≥ 40 IU/L LDH ≥ 600 IU/L

III. Observations And Results

In the present study, 324 admitted cases of preeclampsia and 90 cases eclampsia, a total of 414 cases were analyzed prospectively and 133 cases were diagnosed as HELLP syndrome, of which 116 cases from preeclampsia and 17 from eclampsia. Out of 133 cases, 63 cases were unbooked and belonged to lower socioeconomic status and referred from PHC, CHC and other private nursing homes. Majority of cases belonged to 19–28 years age group. 62(46.6%) cases were primi, 71 cases (53.4%) were multi.

Table 1: No. Of Cases According To the Classification

		HELLP	%	Complete	%	Partial	%
Severe Preeclampsia	324	116	35.5	30	25.8	86	74.2
Eclampsia	90	17	18.8	6	35.3	11	64.7
Total	414	133	32.1	36	27.1	97	72.9

In total 133 cases, 97 cases (72.9%) were partial HELLP and 36 cases (27.1%) were complete HELLP syndrome. The incidence of HELLP syndrome in the present study is 32.1% in severe preeclampsia-Eclampsia.

Table 2: Cases according to the time of onset & Type of HELLP syndrome

Type	No. cases	Complete (%) Type-1	Partial (%) Total	Type -2	Type-3
Antepartum	112 (84.21%)	27 (24.10%)	85 (75.90%)	33	52
Postpartum	21 (15.79%)	9 (42.85%)	12 (57.15%)	5	7
Total	133	36 (27.1%)	97 (72.9%)	38	59

In the present study, 112 cases (84.21%) belonged to antepartum and 21 cases (15.79%) were postpartum HELLP syndrome, in which 36 cases (27.1%) complete and 97 (72.9%) were partial HELLP.

Table 3: Cases Grouped According To The Missisipi Classification

Type	Total (%)	Ante partum (%)	Post partum (%)
Type -1	36 (27.1%)	27 (24.10%)	9
Type -2	38 (28.57%)	33 (29.4%)	5
Type -3	59 (44.36%)	52 (46.43%)	7
Total:	133	112	21

In the present study, maximum no. of cases (59) belonged to type-3 (44.36%), 38 cases (28.57%) type-2, i.e. (partial 97(72.9%)) and 36 cases (27.1%) belonged to type-1 which is severe form of HELLP syndrome.

Table 4: According to clinical features

Clinical features	Complete (%) Type -1	Partial (%) Type-2	Type-3
Headache, visual disturbances	19	40	
Nausea, vomiting, epigastric pain	28	15	
Fever, malaise, body pains	14	12	
Dizziness	32	25	
Oliguria	9	6	
Nonspecific	12	28	
Signs of preeclampsia	18	40	

The most commonly observed feature is Dizziness which was observed more in Type-1 and Type-2 HELLP syndrome. 28 cases have nausea and epigastric pain in type-1 (Complete) HELLP syndrome, headache and visual symptoms more in type-2 (partial), next fever and malaise observed in 14 cases in complete HELLP and 12 cases of partial HELLP. 12 cases of complete HELLP have non-specific features.

Table 5: Number Of Cases According To The Lab Findings

According to the investigations, laboratory thresholds that indicate more than 75% risk of serious maternal morbidity are LDH concentrations>1400U/L, AST>150U/L, ALT>100U/L and uric acid concentrations > 7.8mg/100ml.

AST > 40	ALT >70 IU	LDH >600IU/L	Bilirubin >1.2 mg	Platelet count<50,000	Platelet count 50,000 - 1,00,000	Platelet count < 1 lakh – 1.5 lakhs
60	53	28	44	31	76	26

Table 6: Cases According To Gestational Age

Gestational age	No. cases	Type-1	Type-2	Type-3
28 – 32 wks	26	8	11	7
32 – 36 wks	48	12	12	24
> 36 wks	38	16	10	12
Total	112	36	33	43

Maximum number (48) of cases observed during 32 – 36 wks gestation in which 12 cases were complete (type1) HELLP and 12 were type 2, 24 in type 3 (36 cases were partial HELLP). In 38 cases reported >36 wks, 16 cases were in type1, 10 cases in type 2, 12 were in type 3.

Table 7: According To The Biochemical Features

Biochemical tests	Complete Type-1	Partial Type-2	Type-3
Haemolysis Abnormal peripheral smear LDH	28	16	12
Haemolysis and Elevated liver enzymes	12	16	2
Elevated liver enzymes	32	28	20
Low platelet count	26	16	06
Low platelet and increased liver enzymes	15	14	5

In type-1 28 cases have abnormal peripheral smear, elevated liver enzymes in 32 cases and low platelet count in 26 cases. Whereas in type-2, low platelet count is observed in 16 cases, elevated enzymes in 28 cases and Haemolysis in 16 cases. In type-3, elevated liver enzymes found in 20 cases. Low platelet count was observed more in type1. The most common lab finding was elevated liver enzymes followed by haemolysis and low platelet count.

Table 8: Mode of Delivery

Mode of delivery	No. cases	Complete (%)	Partial (%)
Vaginal delivery	95(71.5%)	28(29.5%)	67(70.5%)
Caesarean delivery	38(28.5%)	8(21.5%)	30(79%)
Total	133	36	97

95 cases (71.5%) were delivered vaginally among which 28 cases (29.5%) were complete, while 67 cases (70.5%) were partial HELLP syndrome and 38 (28.57 %) cases were delivered by caesarean section out of which 8 cases(21.5%) were complete and 30cases (79%) were in partial HELLP Syndrome.

In this present study expectant management has been adapted in cases prior to 34 weeks of gestation and in less severe disease, 95 cases (71.5%) were delivered vaginally in HELLP syndrome and caesarean section rate (28%).

Table 9: Maternal Complications In HELLP Syndrome

Complication	No. cases	Type-1	Type-2	Type-3
Cardio vascular disturbance	8	4	2	2
Heart failure	5	3	1	11
Severe anemia	23	6	5	12
DIC	6	4	2	-
Abruption	11	6	3	2
PPH	16	6	8	2
Renal complication Oliguria	9	4	3	2
Renal Failure	5	4	2	
Pulmonary edema	2	2	-	-
CNS complications: Encephalopathy Cerebral Haemorrhage	 10 3	 6 2	 4 1	 - -
Eclampsia	17	6	7	4
Multi organ failure	4	3	1	-

In 133 cases of HELLP syndrome 23 cases have severe anemia (Hb <6 g%), 11 cases developed placental abruption, 16 cases were complicated with PPH, 10 cases with Encephalopathy, 2 cases developed Cerebral Haemorrhage in complete HELLP syndrome and 1 case in partial HELLP Syndrome. 9 cases developed Renal Complications (4 with acute renal failure in type-1 and 2 cases with moderate renal dysfunction in type-2 and 2cases in type-3). Nearly 4 cases developed multi organ failure (3 in complete HELLP, 1 in type-2 HELLP). 2 cases died of Cerebral Haemorrhage and Pulmonary edema, 1 case died of Heart failure, 2 cases died with renal failure and multi organ dysfunction. The total maternal deaths reported in this present study were (6)4.5%

Table 10: Perinatal Outcome

Complication	Type-1	Partial		Total
		Type-2	Type-3	
Preterm	10	16	5	32
IUGR	6	9	6	21
Birth asphyxia	14	8	4	26
Still birth	12	7	6	25
MAS	3	8	3	14
Low APGAR	12	9	6	27
NICU Admissions	16	14	8	56
IUD	7	8	3	18

In the study preterm babies were 32(24.06%), 10 from complete HELLP group and 22 were in partial HELLP syndrome, the babies born with birth asphyxia were 26. Low APGAR babies were 27, still births were 25 - more in complete HELLP (12 babies). The number of IUD were 18, the overall perinatal deaths were 47(35.33%). It is comparatively less in the study of R.Shaheen Ara etal had 44.5%. Birth asphyxia and prematurity were the commonest causes of death. 12 early neonatal deaths were reported.

IV. Discussion

HELLP syndrome in preeclampsia – eclampsia contribute to many life threatening complications as the pathophysiologic mechanism remains obscure. Sibai defined criteria for diagnosis which have been used in this study to define women with HELLP Syndrome.The incidence of Hellpsyndrome in the present prospective study to be 30.23%.ie 133/440 cases.Which is comparatively higher than 6.5% in the study of r.Shaheen Ara et al,due to better availability of lab facilities and better interpretation of Sibai's diagnostic criteria. Early identification of risk factors in Pregnancy and timely intervention gives better maternal and perinatal outcome.
In the study of 133 cases of HELLP syndrome, 116 from preeclampsia and 17 manifested from Eclampsia were analyzed.In 133 cases and70(52.64%)were booked comparable to 38.23%of booked cases of r.Shaheen Ara et al Sibai BM (21%), Imir GM et al (32.8%)and63(47.36%)were unbooked in the study.46.62%(62)cases were belonged to primipara and71(53.4%)were belonged to multiparous.

In the present study 112(84.21%)cases were in ante partum which was comparatively higher than 75%0f r.Shaheen Ara et al,and majority of them were in 32 to 36 weeks of gestation (48/112) comparable to Vigil P de Gracia 40%. In the present study the postpartum HELLP Syndrome were 21/133 (15.8%) comparable to25%of r.Shaheen Ara et al, 22% of Hadded et al . The partial HELLP syndrome can progress to Complete or True HELLP syndrome which is associated with serious maternal morbidity. In the present study the true HELLP syndrome cases (type-1) were 36 (27.1%). In these cases studied, preference for vaginal deliveries increased 95/133(71.5%) expecting less complications compared to caesarean delivery, 38/133 (28.5%).

Depending on the clinical and laboratory findings the HELLP Syndrome is classified into- complete or partial. Women with complete HELLP syndrome are at higher risk for complications, than women with the partial syndrome. Consequently, patients with complete syndrome should be considered for delivery within 48 hours as it needs active intervention and immediate delivery, irrespective of gestational age, whereas those with partial HELLP syndrome with gestation between 34-36 weeks are treated with conservative management for >48hrs.Alternatively, HELLP syndrome can be classified on the basis of platelet count by Nadir: Class I-less than 50,000 per mm^3 (50×10^9 per L); Class II- 50,000 to less than 100,000 per mm^3 (50 to 100×10^9 per L),Class III-100,000 to 150,000 per mm^3 (100 to 150×10^9 per L). Patients with class I HELLP syndrome are at higher risk for maternal morbidity and mortality than patients with class 2 or 3 HELLP syndrome.[5] The most common complications are Hamatalogical, Renal, Coagulation abnormalities, cerebral, etc.

It is considered to be a variant or severe form of preeclamsia – eclampsia, its outcome depends on its severity, timely intervention, availability of tertiary care facilities like dialysis, ventilator supporting equipments and availability of blood products. In this study, 14 cases needed intensive care treatment, of which 6 cases were treated with dialysis among which 4 cases survived. 5 cases needed with ventilatory support while 3 survived (13.53%). 18 cases were treated with FFP, platelet transfusion and other blood products. In this present study the maternal mortality was 4.5% (6 deaths) because of late referral of cases in bad condition. This is comparable to Vigil P de Gracia (2.3%), Sibai BM et al (1.8%), Isler CM et al (7.8%). The perinatal deaths were 47 (35.33%) was comparable to Gui et al 42 but higher than Sibai BM 33.3%, Magann EF et al 23.2%, Wiley visser 14.1%.The main cause of perinatal deaths in this study was mainly prematurity(24.06%) was compared to49.62% of r.Shaheen Ara,followed by birth asphyxia and low apgar.The stillbirth rate in the present study was 25(18.79%),expectant management,appropriate intervention,sncu facilities will improve the perinatal outcome.

Partial HELLP syndrome can progress to complete HELLP. Audibert et al suggest that complications with partial HELLP syndrome are not as severe as in complete HELLP syndrome with severe preeclampsia - eclampsia, which has serious maternal morbidity. In this present study expectant management has been adapted in cases of partial HELLP syndrome with 32-36 weeks of gestation with continuous monitoring, timely active intervention & immediate delivery. Active management is adapted in type 1 or complete HELLP syndrome, basing on the severity.In the present study majority of 48 (36.o9%) cases of Hellpsyndrome were in32-36 weeks of gestation and 38 (28.57%) were >36 wks of gestation comparable toVigil p de Gracia of 40%.Pregnancy is terminated,with irrespective of gestation as delivery being definitive treatment to prevent further complications. Caesarean section in the present study is 28.5 % where early termination was indicated which is comparatively lesser than71% ofVigil p de gracia,40% ofShafika Banoo,63% ofHadded et al.

V. Conclusion

Early detection and classification of HELLP Syndrome and avoiding miss diagnosis and delayed treatment helps in providing better management.Early registration and regular ante natal care has play a major role in early diagnosis and to reduce complications like Hellpsyndrome. Early detection, prompt referral, better transport facility,appropriate intervention, availability of life saving facilities like mechanical ventilators, dialysis equipment and blood products like FFP, PRP, Packed cell transfusion at tertiary care centers will significantly reduce the maternal and fetal morbidity. HELLP syndrome should be treated at tertiary care centers. The obstetricians at any level should be attentive, alert and need to improve quality care and make efforts for early identification even at its atypical presentation of HELLP Syndrome cases and provide skilled management techniques. Doctors should promote early and regular antenatal care at community health centers and ensure availability of new born care equipment that will provide better maternal and perinatal outcome. The global mortality rate of HELLP syndrome has been reported to be as high as 25%. That's why it's critical for expecting mothers to be aware of the condition and its symptoms so they can receive early diagnosis and treatment.Doctors should enhance their skills in antenatal care to intensify to identify the high risk factors at primary and tertiary care centers.

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