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Clinical study of HELLP syndrome in tertiary care Hospital

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Abstract

Introduction: Every woman's wish is to end her pregnancy with a healthy baby and a healthy mother. Unfortunately, some women develop pregnancy induced hypertension sometimes ending in its dreaded complications. PIH is one among the leading causes of maternal and perinatal morbidity and mortality. It has higher prevalence in nulliparous and is present as a maternal syndrome, characterized by arterial hypertension generally with Proteinuria, and a foetal syndrome, with foetal growth restriction and amniotic fluid reduction. It may have several systemic manifestations, variable degrees of severity and either an early onset with maternal and foetal morbidity, or a late onset, near term, with less severity and reduced foetal compromise. Preeclampsia is characterized by hypertension (systolic and diastolic blood pressure of ≥ 140 and 90 mm Hg, respectively, on two occasions, at least 6 hours apart) and Proteinuria (protein excretion of ≥ 300 mg in a 24 h urine collection, or a dipstick of ≥ 1+), developing after 20 weeks of gestation in previously normotensive women. The analysis of the physio-pathological process shows that its origins are related to an immunological process associated with a defective and insufficient placentation.Although the placental origins of the disease are largely accepted maternal or foetal predisposing factors are also considered when an early onset or a high severity are present.

Aim and Objectives: To study the maternal outcome and perinatal outcome in pregnancy complicated with HELLP syndrome.

Materials and Methods: An observational study identified 50 cases of HELLP syndrome from a total of 7352 deliveries over a 22 months period.

Results: The mean maternal age was 26.73 years with HELLP syndrome diagnosed. There were 29 cases of partial HELLP syndrome & 21 cases of complete HELLP syndrome. The average platelet was 53000 with elevated liver enzymes in all cases.23 (46%) were posted for Caesarean section and 27(54%) delivered by vaginal route. There were 4 maternal deaths, 13 stillbirth and 7 neonatal deaths.

Conclusion: HELLP syndrome is an obstetric complication. Early diagnosis and treatment is main stay of management. Use of corticosteroids improves in lab parameters, better maternal and perinatal outcome.

Keywords: HELLP syndrome, pregnancy, PIH, nulliparous

Introduction

The syndrome characterized by micro-angiophatic hemolysis, liver enzymes elevation and thrombocytopenia (HELLP syndrome) was individualized in 1982 by Weinstein and is considered a severe form of preeclampsia, occurring in 0.5% to 0.9% of all pregnancies and complicating 10% to 20% of severe preeclampsia cases. It may have a sudden aggravation and even though some clinical aspects may be similar to preeclampsia, in HELLP syndrome the blood pressure can be normal, the proteinuria is not always present and there is more expression of inflammation markers.

Additional characteristics of HELLP syndrome include higher platelet and coagulation activation, with thrombocytopenia, coagulation disorders and disseminated intravascular coagulation (DIC).

Hemolysis is the main finding of this syndrome and can be documented by an elevation of serum lactic dehydrogenase (LDH), anemia with presence of schistocytes in peripheral smear and low haptoglobin concentration. The elevation of both aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are mainly due to a hepatic lesion. Low platelet count is a result of a higher consumption: activated platelets adhere to endothelial cells with a reduced life-span. Perinatal morbidity and mortality are greater in HELLP syndrome and are related to gestational age of the onset of the clinical situation. Excluding cases with no doubts

in the classification of HELLP syndrome, when there is an hepatic involvement and coagulation disorders, sometimes the distinction with severe preeclampsia is difficult.

Aims and objectives

To study the maternal outcome and perinatal outcome in pregnancy complicated with HELLP syndrome.

Study Design: Clinical study

Study period: (JUN2015 –JUNE 2017)

Sample Size: 50 HELLP cases

Study Population: All cases which had been diagnosed as HELLP Syndrome from JUNE 2015 to JUNE 2017

Inclusion criteria:

- Blood pressure =/> 160/110
- Platelet Count =/< 1,50,000 / mm3
- Gestational age >20 weeks

Exclusion criteria:

- Gestational age < 20 weeks.

Induction of labour will be done after informed consent. Platelet count was monitored every 12th hourly and LDH, and Liver enzymes monitored every 24th hourly.

Results

Table 1: Distribution of study subjects based on the Tennessee classification of HELLP syndrome

HELLP Syndrome	No. of patients (%) N=50
Partial HELLP syndrome	29(58%)
Complete HELLP syndrome	21(42%)

In our study, 58% of cases were partial HELLP and 42% cases were complete HELLP syndrome.

Table 2: Distribution of study subjects based on the age groups

Age (yrs)	Partial help N(29)	Complete help N(21)	Total N(50)
18-20	2	1	3(6%)
21-25	17	16	33(66%)
26-30	9	3	12(24%)
31-35	1	1	2(4%)

The mean age of the study subjects was 26.34 ± 4.92 years. Majority of HELLP cases were in the age group of 20 to 30 years, followed by 30 to 40 years and less than 20 years.

Table 3: Distribution of study subjects based on the gestational age

Gestational age	Partial help(29)	Complete help N(21)	TotalN(50)
<28 Weeks	0	0	0(0%)
28-34 Weeks	12	10	22(44%)
35-37 Weeks	13	5	18(36%)
>37 Weeks	3	5	8(16%)
Postpartum	1	1	2(4%)

- Majority of our patients presented between 29 to 34 weeks of gestation 22(44%).
- The mean gestational age was 33.75.
- There is statistical significance of gestational age among different classes (p=0.000).

The mean gestational weeks were 33.75 ± 3.06 weeks. Majority of the HELLP cases were in the range of 28 to 34 weeks of gestation, followed by 34 to 37 weeks of gestation and more than 37 weeks of gestation.

Table 4: Distribution of the study subjects based on the parity

Parities	Partial hellp N (29)	Complete hellp N(21)	Total N(50)
Primigravida	11	6	17(34%)
Graviga 2	9	5	14(28%)
Gravida 3 and above	8	9	17(34%)
Postpartum	1	1	2(4%)

Although Primigravidae are more in our study (17), Gravida 3 and above patients were also in significant number. In complete HELLP Syndrome majority were Gravida 3 and above when compared to partial HELLP Syndrome where Primigravida were more

In our study, 34 % were Primi Gravida, 28% were Gravida 2, 34% were Gravida 3 and above, and 4% cases were post partum.

Table 5: Distribution of study subjects based on the clinical features

Complaints	Partial hellp N(29)	Complete hellp N(21)	Total N(50)
Malaise	21	20	41(82%)
Epigastripain	8	8	16(32%)
Headache	6	6	20(40%)
Blurring of vision	5	6	11(22%)
Edema	23	11	34(68%)
Convulsion	6	8	14(28%)
Vomiting	4	10	14(28%)
Hematuria	0	3	3(6%)

*significant values

In our study, over all malaise was the most common complaint reported, followed by pedal edema and Epigastric pain. The proportion of pedal edema was significantly higher in partial HELLP cases when compared with complete HELLP cases. ($p<0.05$) Further, proportion of vomiting as a complaint was significantly higher in case of complete HELLP when compared to partial HELLP ($p<0.05$).

Table 6: Distribution of study subjects based on the Proteinuria findings

Proteinuria	Partia help N(29)	Complete help N(21)	Total(%)N(50)
1+	6	2	8(16%)
2+	9	5	14(28%)
3+	7	5	12(24%)
4+	7	9	16(32%)

- Majority of the patients presented with proteinuria of 3+ and 4+.
- 4+ proteinuria was present in 32% of cases.
- There is a statistical significance of proteinuria among different classes ($p <0.002$).

Table 7: Distribution of study subjects based on platelet counts

Platelets	Partial hellpN(29)	Complete hellpN(21)	Total(%) N(50)
<50000	8	11	19(38%)
50000-1lakh	7	8	15(30%)
1-1.5lakh	14	2	16(32%)

*significant values

Majority of the patients who had complete HELLP syndrome had platelet counts less than 1 lakh and this was significantly higher when compared to partial HELLP cases. There was a significant association between the platelet counts and classification of HELLP syndrome.

Table 8: Distribution of study subjects based on ALT levels

Alt (iu/lt)	Partial help N(29)	Complete help N(21)	Total(%) N(50)
<70	12	0	12(24%)
71-100	7	9	16(32%)
101-150	4	2	6(12%)
151-200	1	1	2(4%)
>200	5	9	14(28%)

The ALT levels were in range of <70IU/L in majority of complete HELLP cases and few cases were in the range of 70 to 150 IU/L. Among the partial HELLP cases, levels less than 70IU/L were in majority followed by range of 100 to 150IU/L and few cases in 70 to 100 IU/L range and few in 150 to 200 IU/L range. We did not find significant association between the ALT levels and type of HELLP syndrome.

Table 9: Distribution of study subjects based on AST levels

Ast(iu/lt)	Partial hellpN(29)	Complete hellpN(21)	Total (%) N(50)
<70	17	11	28(56%)
71-100	2	2	4(8%)
101-150	4	1	5(10%)
151-200	1	0	1(2%)
>200	5	7	12(24%)

*Significant levels

The majority of complete cases had more 200 IU/L of AST levels, followed by 70 to 100 IU/L and 100 to 150 IU/L range. Among the partial cases, less than 70 IU/L range had majority of cases. The AST levels were significantly higher in case of complete HELLP when compared to partial HELLP. ($p<0.05$)

Table 10: Distribution of study subjects based on LDH levels

Ldh (iu/l)	Partial help N(29)	Complete help N(21)	Total(%)N(50)
<600	1	0	1(2%)
600-1000	11	9	20(40%)
1001-1500	8	4	12(24%)
1501-2000	0	5	5(10%)
2001-3000	5	2	7(14%)
>3000	4	1	5(10%)

Majority of complete cases were in the LDH range of 600 to 1000 IU/L followed by 1500 to 2000 IU/L and 1000 to 1500 IU/L. Among the partial HELLP cases, majority of them were in the range of 600 to 1000 IU/L followed by 1000 to 1500 IU/L and 2000 to 3000 IU/L. We did not find significant association between the LDH levels and the type of HELLP syndrome. ($p >0.05$)

Table 11

	N	Min	Max	Mean	Std Deviation	P value
Platelets	50	10000	150000	70908.86	35630.47	0.0022
Ast	50	10	752	141.87	168.81	0.1900
Alt	50	8	627	187.51	186.37	0.0240
Ldh	50	386	3180	1528.32	979.03	0.0879

- Minimum platelet count was 10000 with a mean platelet count of 70908.86.P value is 0.0022
- Maximum AST value was 752 IU/L with a mean value of 141.87.P value is 0.1900
- Maximum ALT value was 627 IU/L with a mean value of 186.37.P value is 0.0240
- Minimum LDH value was 386 IU/L and maximum was 3180 IU/L with a
- Mean value of 979.03. P value is 0.0879

Table 12: Distribution of study subjects based on the laboratory parameters before and after 24 hours giving corticosteroids

Laboratoy parameters	Before		After		P value*
	Mean	SD	Mean	SD	
Platelets	73500	41029.73	91301.20	38644.12	0.0278*
LDH	1551.88	1066.66	1161.68	632.10	0.0288*
AST	176.80	193.93	98.16	74.81	0.0094*
ALT	136.48	168.15	97.6	121.46	0.1884

*unpaired t test applied

After administration of corticosteroids to the patients, the platelet counts increased significantly, the LDH and AST levels decreased significantly, ALT levels also decreased but did not attain the level of statistical significance.

Table 13: Distribution of study subjects based on the type of delivery

Mode of delivery	No. of Patients n=50	
	Partial hellp(29)	Complete hellp(21)
Caesarean section	11(22%)	12(24%)
Vaginal delivery	18(36%)	9(18%)

54% of cases had vaginal delivery. Caesarean section was done in 46%), mainly for Obstetric indications. Both postpartum were vaginal delivery, and referred to our hospital. In our study, majority of the cases delivered by normal vaginal delivery.

Table 14: Distribution of study subjects based on the indication for C section (n=23)

Indication	No. of Cases
Iugr	15
Failed induction	3
Fetal distress	8
Severe pih	8
Previous lscs	7
Oligohydramnios	11
Cpd	3
Eclampsia	15

The major indications for C section were IUGR and Status eclampticus followed by Oligohydramnios and foetal distress and severe pre Eclampsia.

Table 15: Distribution of study subjects based on birth weight

Birth weight	Partial help N(29)	Complete hellpN(21)	Total (%) N(50)
<1kg	0	4	4(8%)
1.1-1.5kg	6	4	10(20%)
1.6-2.0kg	10	9	19(38%)
2.1-2.5kg	3	3	6(12%)
>2.5kg	10	1	11(22%)

Majority of the babies were in range of 1.5 to 2.0 Kg birth weight followed by more than 2.5Kg and 1 to 1.5Kg. The birth weight of the babies having complete HELLP was significantly lower when compared to partial HELLP ($p<0.05$).

Table 16: Distribution of study subjects based on the maternal complications

Complications	No. of cases (%)	
	Partial help N(29)	Complete help N(21)
Abruptio placentae	2(4%)	5(14%)
Intracranial haemorrhage	0(0%)	1(2%)
Acute renal failure	1(2%)	2(6%)
Dic	0(0%)	3(6%)
Pleural effusion	1(2%)	2(4%)
Ards	0(0%)	1(2%)
Pulmonary embolism	0	0(0%)
Mortality	1(2%)	3(6%)

The most common maternal complication was Abruptio placenta, followed by maternal deaths and acute renal failure.

Table 17: Distribution of study subjects based on the perinatal outcome

Perinatal outcome	Partial help N(29)	Complete help N(21)	Total (%) N(50)
Live birth	20	12	32(64%)
Still birth	4	6	10(20%)
Iud	5	3	8(16%)

Table 18

Perinatal outcome	Partial help N(20)	Complete help N(12)	Total(%)N(32)
Nicu admission	11	8	19(59.37%)
Neonatal death	3	4	7(21.87%)
Take home baby	17	8	25(78.12%)

In our study, there were 38.09% of complete HELLP cases referred for NICU and 37.93% of partial cases needed NICU admission. Further, we encountered neonatal deaths in case of 19.04% and 10.34% cases respectively in complete and partial HELLP cases.

Table 19: Distribution of study subjects based on perinatal complications

Perinatal complication	Partial help N(20)	Complete help N(12)
Septicemia	1(3.12%)	5(15.62%)
Birth asphyxia	2(6.25%)	3(9.37%)
Rds	2(6.25%)	4(12.5%)
Preterm	13(40.62%)	9(28.12%)
Hyperbilirubinemia	3(9.37%)	3(9.37%)
Iugr	9(28.12%)	10(31.25%)
Mortality	3(9.37%)	4(12.5%)

In our study, 44% of cases delivered were preterm, 38% were having IUGR, 14% mortality, 12% each had septicaemia, RDS and hyperbilirubinemia and 10% cases suffered birth asphyxia.

Table 20: Distribution of study subjects based on the duration of hospital stay

Hospital stay (days)	Complete (n=21)		Partial (n=29)		P value
	No	%	No	%	
<5	3	15.00	2	6.90	0.2043
5 to 10	5	25.00	15	51.72	
10 to 15	10	50.00	8	27.59	
>15	2	10.00	4	13.79	
Total	21	100	29	100	
Mean	10.02				
SD	5.54				

The mean hospital stay was 10.02 ± 5.54 days.

Discussion

HELLP Syndrome occurs in approximately 0.2-0.6 percent of all pregnancies. Superimposed HELLP Syndrome develops in 4 to 12 percent of pregnancies. When preeclampsia is not present, diagnosis of the syndrome is delayed.

In our study complete HELLP syndrome constitutes about 42% and partial HELLP constitutes about 58%.

Table 21: HELLP Syndrome

Studies	Complete (%)	Partial (%)
Present study	42	58
Kumari S *et al.*(12)	27.1	72.9
Tandon A *et al.*(21)	19.09	80.91

Maternal age

In our study, the maternal age was 26.34 ± 4.92 years. The mean age of studies conducted by Mallesara A *et al.* (20) (21.34 ± 3.74 years) and Tandon A *et al.* (21) (23.6 ± 4.2 years). Bang NO *et al.* (22) also reported that majority of the patients of HELLP syndrome were less than 25 years. But higher means of age were reported by Campos a *et al.* (13) (Median of 31.3 years), Takrouri A *et al.* (16) (31 ± 7 years), Kirsanova T *et al.* (17) (32.6 ± 5.2 years), Bezikcloglu I *et al.* (18) (28.93 ± 7.90 years) and Cavkaytar S *et al.* (19) (26.8 ± 6.1 years)

Table 22: Parity distribution

Studies	Primi (%)	Multi (%)
Present study	34	66
William KP *et al.*(23)	35	65
Bang NO *et al.*(22)	57	43
Tiwari P *et al.*(15)	47.5	52.5

Compared to other studies, our study reported higher proportions of multi Gravida cases.

Gestational age

The mean gestational weeks at admission in our study was 33.75 ± 3.06 weeks. Lower means were reported by Takrouri A *et al.* (16) (31 ± 1) and Cavkaytar S *et al.* (19) (31.8 ± 4.01 weeks). Higher means were reported by Tandon A *et al.* (21) (35 ± 2 weeks). But, Kumari S *et al.* (12) and Bang NO *et al.*(22) reported in their study the most common gestational weeks between 32-36 weeks and a study by Campos A *et al.*(13) reported it to be less than 34 weeks in their study.

Table 23: Presenting complaints

Studies	1st common	2nd common	3rd common
Present study	Malaise	Edema	Epigastric pain
Tandon A *et al.*(21)	Malaise	Epigastric pain	Headache
Cavkaytar S *et al.*(19)	Headache	Visual disturbances	Epigastric pain
Bezikcloglu I *et al.*(18)	Headache	Edema	Epigastric pain

Our study was in concordance with many studies stating that malaise is the most common complaint.

A study done by Kumari S *et al.*(12) reported that dizziness, nausea, vomiting, Epigastric pain and oliguria were more in complete compared to partial HELLP.

Table 24: At Admission investigations

Investigations	Present study		Bezikcluglo I *et al.*(18)		Tandon A *et al.*(21)	
	Mean	SD	Mean	SD	Mean	SD
Platelets	73500	41029.73	68584.09	32810.57	160590	55000
LDH	1551.88	1066.66	2644	1852	1016.4	383.7
AST	176.80	193.93	466.94	374.02	148.2	73.00
ALT	136.48	168.15	314.44	294.42	148.3	70.80

A study done by Campos a *et al.* (13) reported that on multivariate Platelets <1 lakh and LDH >1000 IU were important predictors for HELLP syndrome.

In our study, after 24 hours administration of corticosteroids, the LDH levels, AST and ALT levels dropped and Platelet levels improved in our study. Similar results were concluded by Campos A *et al.*(13) and Takrouri A *et al.*(16).

Table 25: Mode of delivery

Studies	C section (%)	Vaginal (%)
Present study	46.94	53.06
Bezikcloglo I *et al.*(18)	90.9	90.1
Cavykaytar S *et al.*(19)	73	27
Tandon A *et al.*(21)	72	28
Bang NO *et al.*(22)	35	65

Compared to other studies the c section rates in HELLP syndrome in our study was low.

Perinatal outcome

In our study, the most common perinatal complication was preterm followed by IUGR being the second most common and mortality in neonates being the third. In study conducted by Tandon A *et al.* (21), the most common complication was

neonatal deaths, followed by IUGR. They also found a significant difference between the proportions of neonatal deaths. ($p<0.05$) Mallesara A *et al.* (20) also found that the most common perinatal complication was preterm births and IUGR. Another study conducted by Kumari S *et al.* (12) showed Birth asphyxia to be the first most common perinatal complication followed by still births and IUGR.

Our study 38% babies were admitted to NICU after delivery. Higher rates were inferred by a study conducted by Tandon A *et al.*(21) and Bezikcloglo I *et al.*(18). But, lower rates were reported by Takrouri A *et al.*(16).

Our study reported 14% of neonatal deaths. Studies conducted by Kirsanova T *et al.* (17) and Tandon A *et al.* (21). Studies conducted by Takrouri A *et al.* (16) and Bezikcloglo I *et al.* (18) reported lower values compared to our study. The mean birth weight of complete HELLP cases was significantly lower than partial HELLP cases in our study. Studies conducted by Tandon A *et al.*(21) and Campos A *et al.*(13) also reported the overall mean birth weight in their study was lower and majority of them came into the category of low birth weight.

Maternal complications

The most common maternal complication in our study was Abruptio placenta followed by maternal mortality and acute renal failure, disseminated intravascular coagulation and pleural effusion. A study conducted by Kumari S *et al.* (12) found anaemia to be the most common maternal complication followed by Eclampsia, post-partum haemorrhage and abruption. Another study conducted by Bezikcloglo I *et al.* (18) found Eclampsia to be most common complication, followed by disseminated intravascular coagulation and post-partum haemorrhage. Cavkaytar S *et al.* (19) reported acute renal failure to be the most common complication followed by maternal deaths and disseminated intravascular coagulation.

Tiwari P *et al.* (15) showed that in their study there was no association between perinatal and maternal mortality and the HELLP syndrome. One study conducted by Takrouri A *et al.* (16) reported no maternal deaths.

Conclusions

Our study reflects many other studies conducted across the world. Majority of the cases were partial HELLP which at presentation are milder in the symptoms and give good improvement after administration of the specific treatment. The complete HELLP cases in our study had major maternal and foetal morbidity and mortality.

Malaise as described by other studies was the most common symptom.

There was a significant association between the platelets, ALT and LDH levels. The levels improved significantly after administration of corticosteroids.

Abruptio placenta was the most common maternal complication and preterm births were the most common perinatal complication.

We also reported 8% maternal mortality, 38% NICU admission and 14% neonatal deaths in our study due to HELLP. We also reported lower birth weights which was significantly lower in complete cases.

The mean duration of stay in hospital was also higher in our study compared to other studies.

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