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A study to detect HELLP syndrome and partial HELLP syndrome among preeclamptic mothers and their impact on fetomaternal outcome

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Abstract: *Objective:* The purpose of the study was to detect & evaluate the feto-maternal outcome of HELLP syndrome & partial HELLP syndrome among preeclamptic mothers. *Materials and methods:* This cross sectional observational study analysed feto-maternal outcome in 44 patients with HELLP syndrome and 32 patients with partial HELLP syndrome and compared with 556 patients having preeclampsia without features of HELLP syndrome. *Results:* 600 patients were included in this study. The 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, haematological 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. Eclampsia was significantly increased in both HELLP syndrome and partial HELLP syndrome. *Conclusion:* Both HELLP and partial HELLP syndrome must be diagnosed as soon as possible in pregnant or post partum women with preeclampsia. HELLP syndrome is severe than preeclampsia in terms of maternal and perinatal outcome. Partial HELLP syndrome is almost as grave as HELLP syndrome.

Keywords: Preeclampsia, HELLP syndrome, partial HELLP syndrome.

Introduction

HELLP syndrome, a life threatening obstetric complication in the later half of pregnancy, considered to be a variant of preclampsia, characterized by hemolysis, elevated liver enzymes and low platelet count was first described by Pritchard et al [1] in 1954. HELLP syndrome develops in 1 in 1000 pregnancies and 4–12% of the patients with severe preeclampsia or eclampsia [2]. HELLP syndrome can be classified into complete and partial HELLP syndrome based on the number of abnormalities [3].

Complete HELLP syndrome is defined as having the following laboratory abnormalities:

a) *Hemolysis:* Characteristic peripheral blood smear, decreased hemoglobin and hematocrit, total bilirubin ≥ 1.2mg/dl, serum lactate dehydrogenese (LDH) ≥ 600/ul.

b) *Elevated liver enzymes:* aspartate aminotransferase (AST) ≥ 70 u/l, alanine aminotransfarase (ALT) ≥ 50u/l .

c) *Low platelet count:* class 1 HELLP with a maternal platelet nadir ≤50000/ cmm., class 2 HELLP with a platelet nadir between 50000 and 100000/cmm and class 3 HELLP with >100000 to ≤ 150000/cmm.

Lynda J Salheim [4] observed that presenting symptoms of HELLP syndrome include epigastria or right upper quadrant abdominal pain (65%), nausea and vomiting (50%) a malaise (90%) and nonspecific viral syndrome like symptoms.

It has been observed that the mothers with pre-eclampsia do not always reveal the full picture of HELLP syndrome, but there are alterations in hematological indices and/or liver function which adversely affect

fetomaternal outcome. This category of women with at least two features of the complete HELLP Syndrome, are separately detected by Ching Ming Liu et al [3] as partial HELLP syndrome. Therefore, partial HELLP could be an appropriate diagnosis when all the criteria for HELLP are not met. The purpose of this study is to compare maternal and perinatal outcome among women with HELLP syndrome, partial HELLP syndrome and women with pre-eclampsia having normal haematological and bio- chemical parameters.

Material and Methods

The study was conducted from 1st June 2007 to 31st December 2010 in the Department of Obstetrics and Gynaecology, IPGME&R, Kolkata after obtaining ethical approval. 600 subjects were selected from the study population which comprised of antenatal patients attending the out patient department and those admitted in the antenatal ward as booked cases or referred from outside. Inclusion criteria included blood pressure 140/90 mm of Hg or more and proteinuria of 300 mg/24 hrs or more after 20 weeks period of gestation for preeclampsia group; for HELLP Syndrome group above mentioned abnormal laboratory parameters along with criteria for preeclampsia and at least two abnormal parameters of HELLP with preeclamptic criteria for partial HELLP Syndrome.

Exclusion criteria included known heart disease leading to hypertension, known case of essential hypertension, known renal disease, previous history of jaundice or liver disease, coarctation of aorta, pheochromocytoma, systematic lupus erythromatosus and subjects not willing to undergo the study. The patients were subjected to detailed history, clinical examination and appropriate investigations. Every individual were allocated into one of the following groups:

1) Pregnant mothers with preeclampsia having the features of HELLP syndrome, which included both complete and partial HELLP syndrome.
2) Mothers with preeclampsia having only partial HELLP syndrome.
3) Mothers with preeclampsia without the features of complete HELLP syndrome or partial HELLP syndrome.

For all study patients, the following parameters were assessed: maternal age, parity, gestational age on admission, gestational age at delivery, systolic blood pressure (SBP), diaslotic blood pressure (DBP), laboratory parameters like Hb%, packed cell volume, bilirubin level, peripheral blood smear, reticulocyte count, platelet count, LDH level, AST level, ALT level, antenatal & postpartum maternal complications, mode of delivery, type of anaesthesia, placental changes. The following perinatal factors were analysed: birth weight, Apgar score at 1 min of birth, NICU admission and neonatal complications.

Statistical Methods: This is a cross sectional observational study. Demographic and clinical variables were summarized by descriptive statistics. Numerical parameters were compared among the groups by student's unpaired t test. Categorical variables were compared by Fisher's exact test or Chi square test.

Results

Total 600 patients were screened. There were 44 cases of HELLP syndrome. Out of 44 cases –complete HELLP syndrome were found in 12 cases and remaining 32 patients presented with features of partial HELLP syndrome. Table 1 depicts the distribution of HELLP syndrome, partial HELLP syndrome and preeclampsia, according to maternal age, parity, SBP, DBP, gestational age on admission and at delivery, no. of booked cases and laboratory parameters. No significant differences in age and parity were found among the HELLP syndrome, partial HELLP syndrome and preeclampsia group. Majority of the subjects in the three groups did not present with severe hypertension. Both the systolic and diastolic blood pressure were higher in those with HELLP syndrome than those with preeclampsia. Gestational age (GA) on admission and at delivery in patients with HELLP syndrome and partial HELLP syndrome were found to be significantly less than in patients with preeclampsia.

Booked cases in both HELLP syndrome (63.64%) and partial HELLP syndrome (47.25%) were significantly less than in those

with preeclampsia (74.82%). The haematolgical and biochemical variables in HELLP and partial HELLP syndrome were found to be significantly different than in preeclampsia group. In patients with partial HELLP syndrome 6.25% had haemolysis and low platelet count, while 56.25% had haemolysis and elevated liver enzymes and 37.5% had low platelet count and elevated liver enzymes.

Table-1: Distribution of Preeclampsia , HELLP syndrome (complete & partial) and partial HELLP syndrome, according to maternal age , parity, SBP, DBP, GA on admission , GA at delivery , booked cases and laboratory parameters

	Preeclampsia (n=556)	HELLP syndrome (n= 44)	P value (between PE & HS)	Partial HELLP syndrome (n = 32)	P value (between PE & PHS)
Age (in yrs)	23.7±5.19	23.7± 4.7	0.92	24.3 ?± 5.25	0.62
Parity Primi Multi	 370 (66.55%) 186 (33.45%)	 28 (63.64 %) 16 (36.36%)	0.423	 18 (66.55 %) 14 (33.45 %)	0.816
SBP (in mm of Hg)	168.3 ±14.13	175.6 ± 15.14	0.02	177.3 ± 16.18	0.15
DBP(in mm of Hg)	104.6± 5.07	107.3±7.26	0.02	106.6 ±7.07	0.13
GA on admission	36 wks 3 d ± 2 wks 2d	35 wk± 2 wks	0.01	35 wk± 3 wks	0.03
GA at delivery	36 wks 5 d± 2 wks	35 wks ± 3 wks	.00	35 wk± 3 wks 2 d	0.003
Booked cases	416 (74.82%)	28 (63.64%)	0.001	14 (43.75%)	0.016
Hb (gm %)	10.3 ± 1.21	9 1.48	.00006	9.4 ± 1.31	.005
PCV (%)	31.4± 2.6	23.9± 4.23	.000	25.1± 4.08	.000
Reticulocyte count (%)	1.3 ±7.7	2.8 ± 1.45	.000	2.4 ± 1.4	.000
Platelet count (cmm)	273449± 80021.31	170590 ± 56000	.000	196637 ± 78218.14	.002
LDH (u/l)	893± 359.3	1018.5± 383.7	.000	996.1 ± 246.3	.000
Total bilirubin (mg /dl)	.9± .45	2.7± 1.61	.000	2.4 ± 1.64	.000
AST (u/l)	56.3 ±11.03	150.2 ±72.88	.000	145.8± 71.3	.000
ALT (u/l)	42 ±7.53	149.3 ±70.89	.000	144.6± 67.71	.000
Haemolysis in peripheral blood smear	64 (11.51%)	30 (68.18 %)	.001	18 (56.25%)	.001
Haemolysis & low platelet count				1 (6.25%)	
Haemolysis & elevated liver enzymes				9 (56.25%)	
Low platelet count & elevated liver enzymes				6 (37.5%)	

Table-2: Characteristics of Preeclampsia, HELLP syndrome and partial HELLP syndrome according to mode of delivery, type of anaesthesia, macroscopic features of placenta, maternal and perinatal outcome

	Preeclampsia (n=556)	HELLP syndrome (n=44)	P value (between PE & HS)	Partial HELLP syndrome (n = 32)	P value (between PE & PHS)
Mode of Delivery					
LUCS	416 (74.82%)	32 (72.72%)	.423	22 (68.75%)	.564
Emergency	358 (64.38%)	32 (72.72 %)	.138	22(68.75%)	.368
Elective	60 (10.79%)	0		0	
VD	140 (25.17%)	12 (27.27 %)		10(31.25%)	
Spontaneous	48 (8.63%)	0	.029	0	.007
Induced	92 (16.18%)	12 (27.27 %)		10(31.25%)	
Type of Anaesthesia					
Spinal anaesthesia	382 (68.7%)	18 (40. 09%)	< .001	14 (43.75%)	.011
General anaesthesia	34 (5.75 %)	14 (31.87 %)		8 (25 %)	
Placental Changes					
Abruption	12 (2.15%)	6 (36.36%)	.572	4 (12.5%)	.363
Calcification	56 (10.71%)	6 (36.36%)		4 (12.5%)	
Infarction	18 (3.23%)	4 (9.09%)		2 (6.25%)	
Preinatal Outcome					
BW (in gm)	2477.5 ±425.33	1913 ±628.86	.000	2022.6 ±666.64	.007
Apgar score (at 1 min)	5.4 ±2.73	5 ±2.69	.139	5.1 ±2.53	.28
IUD	12 (2.15 %)	8 (18.18%)	.003	6 (18.75%)	.009
IUGR	110 (19.78 %)	12 (27.27%)	.412	8 (25%)	.337
Neonatal death	8 (1.14%)	6 (31.31%)	.001	4 (12.5%)	.038
Admission in NICU	150 (26.97%)	30 (68.18%)	.001	20(62.5%)	.011
Maternal Outcome					
Eclampsia	42 (7.55%)	16 (36.36%)	.001	10 (31.25%)	.008
MOD	20 (3.59%)	4 (9.09%)		2 (6.25%)	
ARF	22 (3.96%)	8 (18.18%)		4 (12.5%)	
Placental abruption	12 (2.15%)	6 (13.63%)		4 (12.5%)	
DIC	12 (2.15%)	4 (9.09%)		2 (6.25%)	
Sepsis	18 (3.23%)	4 (9.09%)		2 (6.25%)	
Death	10 (1.79%)	8 (18.18%)		2 (6.25%)	
Onset of Complications					
Antepartum	62 (11.15%)	14 (31.81%)		8 (25%)	
Postpartum	24 (4.31%)	12 (27.27%)		10 (31.25%)	

Table 2 reveals the characteristics of HELLP syndrome, partial HELLP syndrome and preeclampsia, according to mode of delivery, type of anaesthesia, macroscopic features of placenta, perinatal and maternal outcome. Majority of patients in all the three groups underwent caesarean section. Emergency caesarean sections outnumber elective cases in all three groups .But the rate of emergency and elective caesarean section did not differ significantly among the three groups. Spontaneous vaginal delivery rates were significantly different among them.

However, spontaneous vaginal delivery rates were less than induced ones in all categories of patients. Patients with HELLP and partial HELLP syndrome mostly underwent general anaesthesia during caesarean section but spinal anaesthesia was predominanant in preeclampsia group. Rate of spinal anaesthesia were significantly less in HELLP syndrome (40.09%), partial HELLP syndrome (43.75%) than preeclampsia (68.7%). Birth weight (BW) was significantly reduced in HELLP and partial HELLP syndrome in comparison to preeclampsia. All the perinatal complications except intra uterine growth restriction and Apgar score at one minute were found to be statistically increased in HELLP syndrome and partial HELLP syndrome than preeclampsia. The range of maternal complications in our study included eclampsia, acute renal failure (ARF), placental infarction, multiorgan dysfunction (MOD), sepsis, disseminated intravascular coagulation (DIC) and maternal mortality.

Eclampsia was increased significantly in HELLP syndrome (36.36%) and partial HELLP syndrome (31.25%) than preeclampsia (7.55%). The complications were distributed in the antepartum and postpartum period in both HELLP and partial HELLP syndrome groups. Placental changes like calcification, infarction and abruption were found in HELLP syndrome, partial HELLP syndrome and preeclampsia.

Discussion

Although the term HELLP syndrome was coined in 1982 using the acronym of laboratory tests, but controversies persist regarding the diagnosis and prognosis of this enigmatic disease. Our study used standardized strict laboratory criteria for the diagnosis of the disease. Partial HELLP syndrome may be underestimated unless the physician is aware of it. HELLP or partial HELLP syndrome can be diagnosed during pregnancy or after delivery in women with preeclampsia. Our study calculated the prevalence of HELLP syndrome as 7.3% in preeclampsia while the prevalence of partial HELLP syndrome came out as 5.3%. Ching Ming Liu et al [3] found that complete HELLP syndrome occurred in 2.3% of cases of severe preeclampsia, partial HELLP syndrome in 17.4% of cases.

Most of the patients in our study were primigravida and less than 25 years old. Similar results had been reported by American Academy of Physicians 2 and Chabra et al [5]. Mean DBP for HELLP syndrome, partial HELLP syndrome and preeclampsia were 107.3, 106.6 and 104.6 mm of Hg respectively. Therefore, even though HELLP syndrome is considered to be a variant of severe preeclampsia its severity is reflected in its laboratory parameters but not in the usual clinical parameter of blood pressure that typically reflects disease severity of preeclampsia. This is similar to the finding of Satpathi Hemant K et al [6].

The cesarean section rate in HELLP and partial HELLP syndrome were very high in our study as the pregnancy was terminated as soon as the disease was diagnosed to avoid worsening of maternal and perinatal outcomes. Such decisions resulted in increased cesarean section rates and preterm delivery. According to Ching Ming Lui et al [3] the overall cesarean delivery rate was 83.3%, 89.1% and 86.3% in complete HELLP syndrome, partial HELLP syndrome and severe preeclampsia respectively with p value 0.874 thereby ruling out any significant difference among the values. Joelcio Fransisco Abbade et al [7] proved in their study that the overall caesarean section delivery rate was significantly higher in the Partial HELLP syndrome group (70.7%) than in the hypertension group (57.7%). Women with partial HELLP syndrome have significant maternal and perinatal complications which are almost as grave as in HELLP syndrome. It emphasizes the

importance of recognizing HELLP syndrome as well as partial HELLP syndrome as distinct entities which are associated with serious maternal and perinatal morbidities. The distribution of all perinatal variables except Apgar score are corroborated by the results of the studies of of Joelcio Fransisco Abbade et al [7].

The rate of eclampsia in HELLP syndrome group and partial HELLP syndrome group were significantly higher than that in preeclampsia, as shown in our study, was well supported by the study of Ching Ming Liu et al [3]. Placental findings corroborated with the bad perinatal prognosis in both HELLP and partial HELLP syndrome. Usually mothers with altered liver function received Fresh Frozen Plasma (FFP) and mothers with low platelet count (≤40,000/cu mm) received Platelet concentrate. In crisis fresh whole blood were also transfused. Sepsis were observed mainly in referred cases with poor antenatal care. Maternal deaths were due to disease itself or its complications. A significant number of patients with HELLP syndrome (36.36%) and partial HELLP syndrome (56.25%) were referred from outside without receiving adequate antenatal care. This underlies the importance of awareness of the diagnosis of both HELLP and partial HELLP syndrome, prompt referral to tertiary care hospital for further investigations and appropriate intervention.

Conclusion

Both HELLP and partial HELLP syndrome must be diagnosed as soon as possible in pregnant or post partum women with preeclampsia. The study suggests that all pregnant or post delivery women with hypertension should have a complete blood count, platelet count and liver enzyme determination. This strategy helps us to make an early diagnosis of partial HELLP or HELLP syndrome and thus intervene in time to get the best possible maternal and perinatal outcome. HELLP syndrome is severe than preeclampsia in terms of maternal and perinatal outcome. Partial HELLP syndrome is almost as grave as HELLP syndrome. However, large prospective multicentric trials are urgently needed to calculate the exact prevalence in our country and to formulate the optimal line of management.

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