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A Comparison of Severe Pre-Eclampsia/Edampsia in Patients with and without HELLP Syndrome

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Abstract

Background: The relationship of Haemolysis, Elevated Liver Enzymes and Low Platelets (HELLP) syndrome with maternal and perinatal health and its presentation in Pakistani population is not known.
Purpose: To determine the mode of presentation alongwith maternal and perinatal outcome of patients with HELLP syndrome.
Methods: Case records of patients with severe hypertension in pregnancy who delivered between January 1, 1989 and December 31,1994 at The Aga Khan University Hospital, Karachi. Out of 120 cases of severe pre-eclampsia/eclampsia, there were 36 cases of HELLP syndrome (Group-A). These were then compared with cases without HELLP syndrome (Group B) for their mode of presentation alongwith maternal and perinatal morbidity and mortality.
Results: The overall incidence of HELLP syndrome was 0.4%. In the antepartum factors; unbooked status (66% vs 30%; $p<0.05$), diastolic B.P. >120 mmHg (61% vs 16%; $p=0.05$) DIC (13% vs 2%; $p=0.03$), seizures (40% vs 16%, $p=0.01$) and ARF (11%. vs 1%, $p=0.07$) were significantly raised.In the intrapartum factors there were no significant differences between the two groups in mode of delivery and complications of delivery. Neonatal outcomes did not differ significantly in the two groups.
Conclusions: Women with severe hypertension in pregnancy manifesting with HELLP syndrome show a significantly greater frequency of developing DIC, seizures and acute renal failure. Therefore, their care necessitates intensive monitoring to preclude development of these complications (JPMA 48:29,1998).

Introduction

HIELLP syndrome represents a disease entity incorporating Hemolysis, Elevated Liver Enzymes and Low Platelets[1-4] is seen in sqme cases of pregnancy induced hypertension. Literature describes its two variants as HEL and ELLP[4]. The etiology is poorly understood and as yet no single precipitating factor has been isolated. HELLP syndrome is hypothesized to be a collection of various clinical and pathological nmnifestations secondary to an insult that leads to intravascular platelet activation and microvascular endothelial damage. The activation of platelets results in the release of thromboxane A2 and serotonin causing vasospasm, platelet aggregation and further endothelial injury. Progressive damage to the endothelial integrity leads to reduced prostacyclin production and enhanced surface mediated platelet activation. Thus a vicious cycle of progressively worsening DIC is generated which can only be disrupted by termination of pregnancy[5]. There is considerable paucity of literature in the subcontinent on the HELLP syndrome and its variants. It has been described as an early fonn of pre-eclanipsia[4]; as a unique variant of pre-eclampsia[6] and even as misdiagnosed pre-eclampsia[7]. There exists an urgent need to determine the significance of HELLP syndrome in maternal and perinatal mortality resulting from severe pre-eclampsia/eclampsia. Possible predisposing and aggravating factors for this syndrome need to be isolated and differences in the presentation and outcome of this disease, in Pakistan need to be elucidated. Considering these factors along'with the varied presentations of HELLP

syndrome and the delay in its early diagnosis and management, a retrospective study was conducted on all cases of pre-eclarnpsia/eclampsiawithandwithout HELLP syndrome. Specific objectives were consideration of the frequency, mode of presentation and the maternal and perinatal outcome of patients with severe pre- eclampsia/eclampsia.

Patients and Methods

The study population consisted of all women who delivered between January 1, 1989 and December31, 1994 at The Aga Khan University Hospital, Karachi. This is a tertiary health care centre which doubles as a teaching hospital, with approximately 2500 deliveries per year. The patients in the study were either being followed during their pregnancies at the antenatal clinics of the hospital (booked patients) or they were referred for pen and post parturn management from centres elsewhere in the city (unbooked patients). During the six year period 10,366 women were delivered at the institution, of these, 621 (6%) were identified to have pre-eclanipsia/eclampsia, of which 120 patients had severe pre-eclampsia/eclampsia (diastolic B.P.> 110 mrnHg). This group was subdivided into Group-A and Group-B. Patients with HELLP syndrome comprised Group-A, while those having severe pre-eclampsia/eclampsia without HELLP were designated Group-B. HELLP syndrome was diagnosed according to the criteria of Sibai et al[8] (Table 1).

Table I. Diagnostic criteria for HELLP syndrome.

Hemolysis
Abnormal Peripheral Blood Smear with Nucleated RBC's
Total Bilirubin >1.2 mg/dl
Lactic Dehydrogenase (LDH) >600 U/L
Elevated Liver Function Tests:
Serum Glutamic Oxaloacetic Transaminase (SGOT) >70 U/L
Lactic Dehydrogenase (LDH) >600 U/L
Low Platelets:
Platelet Count <100,000/mm^3

Sibai et al[4]

Data was collected by reviewing the medical record files of these patients and their babies. Statistical analysis involved computing. the frequencies and percentages of our variables. Chi square tests of independence and Fisher Exact Two Tail tests were perfonned with 95% confidence interval and an alpha error of 0.5%, p value was significant if <0.05. The patients were managed in the labour room or in the emergency room at first contact. After stabilization they were transferred to the high risk antenatal ward for further management. First line therapy for controlling severe hypertension i.e., diastolic

Hernoiysis

Abnormal Peripheral Blood Smear with Nucleated RBC's

Total Bilirubin >1.2 mgfdl
Lactic Dehydrogenase (LDH)>600 UIL
Elevated Liver Function Tests:
Serum Glutamic Oxaloacetic Transaminase (SOOT) >70 U/L
Lactic Dehydrogenase(LDH)>600 U/L
Low Platelets:
Platelet Count <100,000/mm3
Sibai et al4
B.P. >110 mmHg was intravenous infusion of Hydralazine/sublingual Nifidepine. Subsequent control of hypertension was achieved by oral MethyldopafHydralazine/ Nifidepine depending upon the need for continuation of pregnancy. For seizures intravenous Magnesium sulphate or Diazepam was used depending upon the preference of the consultant. The management of Disseminated Intravascular micro Coagulation with haemorrhagic tendencies (DIC) involved symptomatic therapy depending upon the predominance of coagulopathy and bleeding diathesis.

Results

Of 120 patients with severe pre-eclampsia/eclampsia, 38 were cases of HELLP syndrome. The overall incidence of HELLP syndrome in 10,366 deliveries was 0.4%.

Table II. Mode of presentation of patients with severe pre-eclampsia/eclampsia.

Mode of presentation	Group-A (n=38)		Group-B (n=84)	
Maternal age (yrs) mean	27.8±5.4		27.6±5.5	
Gestational age (wks) mean	34.0±3.9		33.7±3.7	
	No.	%	No.	%
Preterm births	12	31.6	33	39.3
Term births	26	68.4	51	60.7
Primigravida	13	34.0	33	39.3
Multigravida	25	65.8	51	60.7
Antepartum	28	73.7	80	95.2*
Postpartum	10	26.3	4	4.8*
Right upper quadrant pain	8	21.1	4	4.7
Weight gain	11	28.9	27	32.1
Malaise/Headache	19	50.0	30	35.7
Nausea/vomiting	10	26.3	15	17.9
Diastolic B.P. >120 mmHg	23	60.5	13	15.5*
Marked Proteinuria >20g/L	8	21.1	8	9.5
Unbooked patients	25	65.8	25	29.8*

*$p<0.05$

Table II displays mean maternal age, gestational age, parity and mode of presentation with no significant statistical difference in these parameters. However, it was seen that women in Group-A (6 1%) had a significantly raised diastolic blood pressure (>120 mmHg) as compared to Group-B (16%). Significantly more patients with HELLP syndrome were unbooked as opposed to the control group (66% vs 30%).

Table III. Antepartum and intrapartum factors in patients with severe pre-eclampsia/eclampsia with and without HELLP syndrome.

	Group-A (n=38)	Group-B (n=38)	p value
Antepartum factors			
Seizures	15 (39.5%)	13 (15.5%)	0.004*
DIC	5 (13.2%)	2 (2.4%)	0.03*
Acute renal failure	4 (10.5%)	1 (1.2%)	0.03*
IUGR baby	9 (23.7%)	16 (19.0%)	0.56
Intrapartum factors			
SVD	19 (50.0%)	30 (35.7%)	0.14
Cesarean	19 (50.0%)	44 (52.4%)	0.81
Abruption	1 (2.6%)	2 (2.4%)	0.93
Liver hematoma	1 (2.6%)	0	0.31
ICU required	6 (15.8%)	6 (7.1%)	0.14

*p<0.05

Table III lists the various factors contributing to maternal morbidity associated with severe pre-eclampsia/eclampsia in patients with and without HELLP syndrome. In the antepartum factors DIC, seizures and acute renal failure significantly increased morbidity ($p<0.05$) in Group-A as compared to Group-B. Among the intnipartum factors no significant difference was seen in the mode of delivery between the two groups. There was no maternal mortality in either of the groups[5].

Table IV. Perinatal outcome of patients with severe pre-eclampsia with and without HELLP syndrome.

Perinatal outcome	Group-A (n=38)		Group-B (n=84)	
Poor 5 min Apgar score i.e. (<7)	8	(21.1%)	12	(14.3%)
Neonatal sex	Male - 13	(34.2%)	Male - 38	(45.2%)
	Female - 25	(65.8%)	Female	45 (53.6%)
NICU care required	13	(34.2%)	17	(20.2%)
	RDS - 8		RDS- 7	
	Hyperbilirubinemia - 4		Hyperbilirubinemia - 6	
	Sepsis -	1	Sepsis-- 4	
Intrauterine death (IUD)	2	(5.2%)	3	(3.6%)
Neonatal death (NND)	4	(10.5%)	8	(9.5%)

Table IV presents a comparison of neonatal outcomes between Group-A and Group-B. The perinatal mortality rate in the 1{ELLP group was 15.7%, perinatal asphyxia was 21 .1%and the intrauterine death 5.2%. Of the patients with HELLP syndrome, 24% had small for gestational age babies. It was

seen that mothers in the HELLP syndrome group had a higherpercentage of babies with poor5 min Apgar scores, more babies requiring neonatal intensive care, a greater number of intrauterine deaths and higher neonatal mortality as compared to the control group of severe pre-eclanipsia/eclampsia. The percentage of female births as compared to male births was higher in both the groups.

Discussion

Literature reports over400 studies have been carried out on the HELLP syndrome but so far none from the developing countries of South East Asia. Pre-eclampsia and eclampsia form a major high risk group in the third world countries and there seems great likelihood of HELLP syndrome with high maternal and perinatal morbidity[8] complicating a large number of these cases. The description and the mode of presentation and severity as measured by maternal and perinatal outcome of HELLP syndrome in developing countries must be looked into. Our study gave an overall prevalence ofHELLP syndrome and the percentage of women with pre-eclampsia/eclampsia manifesting HELLP syndrome as comparable to previous studies in the obstetric literature[5,7,9,10,11,12] Although the literature reports the presence of HELLP syndrome even in patients without hypertension[13,14]. Our group targeted only patients with preeclampsia for the screening of HELLP syndrome. This study also showed that patients who received little or no antenatal care were at a higher risk of developing HELLP syndrome as opposed to those attending regular antenatal clinics. In the mode of presentation while diastolic blood pressure >110 mmHg was present in significantly more patients from Group-A than Group-B, right upper quadrant pain, marked proteinuria, malaise and headache were present in greater frequency among the group with HELLP syndrome as opposed to the severe pre-eclampsia/eclampsia group without HELLP syndrome[3,5,7,11,13].

This fact highlights the importance of early intervention in reducing morbidity from HELLP. Although right upper quadrant pain was present with greater frequency in Group-A as opposed to Group-B, nevertheless both right upper quadrant pain and nausea/vomiting were seen in only 26% of HELLP syndrome cases. Nearly one third of our patients with HELLP syndrome were pnmigravidae a percentage greater than seen in previous studies where multigravidae comprise the overwhelming majority of HELLP patients[8]. Mean maternal age and mean gestational age are comparable to those reported in the literature[8]. The outcome of our patients was again comparable with previous literature both in maternal and perinatal aspects. We observed that a significantly greater number of the patients with HELLP suffered from risk of developing seizures, acute renal failure (ARF) and disseminated intravascular coagulation (DIC), a trend seen previously[8]. The perinatal asphyxia rate, intrauterine death rate[15] and the perinatal mortality rate[16] closely reflected previously quoted figures for the group of patients with HELLP. However, these statistics did not differ significantly from those of severe pre-eclampsia eclampsia group. This shows that in future studies on perinatal outcome of HELLP patients should simultaneously look at patients with severe pre- eclampsia/eclampsia to pick out any significant differences between the two groups of patients with regards to pennatal parameters. Of our neonates from the HELLP group small for gestational age, incidence was similar to some previous literature[8], yet contrasting with our reports[15]. Although the risk for birth asphyxia. neonatal intensive care requirement, IUD and NND was higher in Group-A as opposed to Group-B, the difference was not significant.

In light of the various factors that have come forward from our study, we recommend that HELLP syndrome be treated as a serious clinical entity associated with an incidence of high maternal and perinatal morbidity and that it should receive the same serious attention in developing countries as it has received in the West. We also recommend that since all of our cases of HELLP were seen in the

group of severe pre-eclampsia/eclampsia, this group should be targeted as being at the highest risk for development of this syndrome. This will enable us to screen for HELLP in a manner which is both cost effective and resource efficient, a consideration that is of particular importance in a developing country. Nevertheless, we would like to point out that the section of the population represented by our study is highly skewed since we see only those cases referred from other centres or picked up through our own antenatal clinics. It is recommended that centres in other parts of the country and in South East Asia be motivated to study the incidence of HELLP syndrome since it has been shown that early recognition of this entity can help reduce maternal morbidity and perinatal mortality. It is important that physicians include this disease in the gamut of illnesses that they are likely to face in this part of the world.

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