Maternal Perinatal Outcome Associated with the Syndrome of Hemolysis, Elevated Liver Enzymes and Low Platelets in Pre-eclampsia / Eclampsia

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OBJECTIVE – To study the incidence and the effects of complications on maternal and perinatal outcome in pregnancies complicated by HELLP syndrome in severe pre-eclampsia / eclampsia. **MATERIAL AND METHODS** – A survey of case records of 188 (5.18%) women admitted with pre-eclampsia or eclampsia during the year 2000-2001 was done. **RESULTS** – The incidence of severe pre-eclampsia / eclampsia was 5.18% (188/3627). Primigravidas constituted 119 and multigravidas 69. HELLP syndrome occurred in 23 primigravidas (19.32%) and 20 multigravidas (28.98%). Maternal deaths were 1.3% (2/145) in pre-eclampsia and 6.97% (3/43) in HELLP syndrome. Serious maternal morbidity in HELLP syndrome was abruptio placentae (39.5%), disseminated intravascular coagulation (60%), acute renal failure (25.58%; of whom 63% needed hemodialysis) and postpartum hemorrhage (13.9%). One woman developed cerebral venous thrombosis, two developed postpartum eclampsia and two developed respiratory distress syndrome. Admission to intensive care unit and ventilatory support were needed in 13.95%. The perinatal mortality was 42.2% (19/45). The overall perinatal morbidity and neonatal ICU admissions were also significant. **CONCLUSION** – HELLP syndrome is associated with increase in maternal and perinatal mortality and morbidity. The perinatal mortality and morbidity can be brought down with early reference to tertiary care level hospitals.

Key words : maternal morbidity, perinatal mortality, HELLP syndrome, severe pre-eclampsia, eclampsia.

Introduction

Pre-eclampsia / eclampsia is a disease peculiar to pregnancy that often results in multi-organ failure. The syndrome of hemolysis, elevated liver enzymes and low platelets has been recognized as a complication of severe pre-eclampsia / eclampsia for many years. The incidence of HELLP syndrome among pre-eclampsia ranges from 4% to 14%[1,2]. Pregancies complicated by this syndrome are associated with poor maternal and perinatal outcome. There is considerable controversy regarding the nature, incidence, clinical significance and management protocol of this syndrome. Goodlin et al[3] described this syndrome as EPH (edema, proteinurea, hypertension) and claimed that this syndrome had been reported in the obstetric literature for about 100 years. Weinstein[4] considered this as a unique variant of severe pre-eclampsia and called it HELLP syndrome in reference to laboratory abnormalities. Here we report the observations from 43 women of severe pre-eclampsia / eclampsia complicated by HELLP syndrome.

Aims and Objectives

1. To describe the incidence and the effects of serious obstetric complications on maternal and perinatal outcome in pregnancies complicated by HELLP syndrome in pre-eclampsia / eclampsia
2. To determine the influence of age, parity and gestational age on the frequency of this syndrome

Material and Methods

This retrospective study surveyed a 2 year period (2000-2001). A good number of our severe pre-eclampsia and eclampsia patients were unbooked or booked elsewhere and referred to us due to high risk factors. Hence our incidence may be on the higher side as compared to that in the general population around. We reviewed the case records of 188 women admitted to our hospital with severe pre-eclampsia and eclampsia. Severe pre-eclampsia was diagnosed if the diastolic blood pressure was 110 mm of Hg more and proteinuria 2 + or more, and eclampsia if convulsion was present. We studied the incidence of HELLP syndrome (i.e. platelet count < 100,000 µl, LDH> 600 U/L and AST/ALT > 70U/L) and distribution of maternal age, parity and gestational age among these women. Maternal and perinatal outcome were separately studied in terms of mortality and serious morbidity. The data were analysed statistically by Chi square method and P value of <0.05 was considered significant. Regression analysis was used for perinatal outcome (apgar >< gestational age) and the correlation co-efficient 'r' was found out.

Results

The incidence of severe pre-eclampsia / eclampsia was 5.18% (188/3627). It was higher in primigravidas viz.

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119/ 188 (63.29%) than in multigravidas viz. 69/188 (36.71%) with a P value of < 0.000387. HELLP syndrome occurred in 23 primigravidas (19.32%) and 20 mutigravidas (28.98%). Higher incidence in multigravidas was not statistically significant (P<0.539), (Table I). Table II and III summarize the distribution of maternal age and gestational age in pre-eclampsia/eclampsia and HELLP syndrome respectively. In HELLP syndrome, 37.5% (6/16) were below 28 weeks of gestation, 16.9% (10/59) between 28-34 weeks of gestation and 23.8% (27/113) above 34 weeks of gestation. Table IV depicts the number of deaths and the complications in these women. We had three maternal deaths (6.97%) two of them died of DIC and PPH, the third had acute renal failure with pulmonary edema and died of multi-organ failure. Disseminated intravascular coagulopathy was the most frequent complication (60.4%) followed by abruptio plaentae (39.6%). Both these complications were strongly associated with intrauterine fetal death. Acute renal failure developed in 25.58% of women, 63% of whom required hemodialysis. Six women (13.9%) had postpartum hemorrhage. One woman developed cerebral venous thrombosis, two had postpartum eclampsia and two had adult of respiratiory distress syndrome. Admission to intensive care unit and ventilatory support were needed in 13.95%.

The 43 pregnancies resulted in 45 births (two sets of twins). There were 17 still births and two neonatal deaths for a perinatal mortality rate of 422 per 1000. Table V depicts the distribution of intrauterine deaths and apgar scores at different gestational ages. Regression analysis of 191 babies of 188 pregnancies (three sets of twins) in pre-eclampsia / eclampsia group was done (r-0.76). Table VI summarizes the distribution of apgar scores at various gestational ages in 191 babies of 188 women with severe pre-eclampsia and eclampsia (three sets of twins). Regression analysis showed that the correlation co-efficient 'r' = 0.49 which is significant for a positive corelation i.e. as the gestational age increases, apgar score increases.

Table I : Parity Distribution in Pre-Eclampsia/Eclampsia and HELLP Syndrome

Disease	Primigravidas		Multigravidas		P value
	No.	%	No.	%	
Pre-eclampsia and eclampsia	119	63.29	69	36.71	<0.000387
HELLP syndrome	23	19.32	20	28.98	<0.539 NS

Table II : Maternal Age >< Parity and Gestational Age in Pre-Eclampsia/Eclampsia

Maternal age	< 28 Weeks		28-34 Weeks		> 34 Weeks		Total
	Primi	Multi	Primi	Multi	Primi	Multi	
<20 yrs	6	1	15	1	26	1	50
21-25 yrs	6	1	16	8	30	18	79
26-30 yrs	0	2	6	6	9	23	46
> 30 yrs	-	-	2	5	3	3	13
Total	12	4	39	20	60	45	188

Table III : Maternal Age >< Parity and Gestational Age in HELLP Syndrome

Maternal Age	< 28 Weeks		28-34 Weeks		> 34 Weeks		Total
	Primi	Multi	Primi	Multi	Primi	Multi	
< 20 yrs	1	-	2	-	3	-	6
21-25 yrs	2	1	3	1	8	5	20
26-30 yrs	-	1	2	-	2	7	12
>30 yrs	-	1	-	2	-	2	5
Total	3	3	7	3	13	14	43

Table IV Maternal Outcome in HELLP Syndrome

Maternal Outcome	Gestational age < 28 weeks	Gestational age 28-34 weeks	Gestational age >34 weeks
Abruptio placentae	3	7	7
DIC	1	9	16
Acute renal failure	2	2	7
Dialysis required	1	2	4
PPH	2	2	2
Cerebral venous thrombosis	-	-	1
Pulmonary edema	-	-	1
Adult respiratory distress syndrome	1	1	-
Post-partum eclampsia	-	1	-
MICU – admissions and ventiliation	1	3	2
Death	1	-	2

Table V : Perinatal Outcome in 45 Babies in HELLP Syndrome

Gestational Age	Apgar		Apgar
	0 (still birth)	< 5	>5
< 28 weeks	4	3	-
28-34 weeks	5	1	5
> 34 weeks	8	2	17
Total	17	6	22

Correlation coefficient r = 0.76, P = < 0.001

Table VI : Perinatal Outcome in 146 Babies in Pre-eclampsia / Eclampsia

Gestational Age	Apgar		
	0 (Still birth)	<5	>5
< 28 weeks	6	1	2
28-34 weeks	24	8	18
> 34 weeks	15	3	69
Total	45	12	89

Correlation coefficient r = -0.69, P = < 0.001

Discussion

Clinical and laboratory criteria have been developed to differentiate severe from mild pre-eclampsia, HELLP syndrome from severe pre-eclampsia and to determine the severity of pre-eclampsia[5,6]. The disease process is reversed only by termination of pregnancy. Saving the mother's life should be the primary goal of any management protocol followed by delivery of a live mature newborn in optimal condition[7]. The incidence of HELLP syndrome among severe pre-eclampsia / eclampsia in this study was 22.87% (43/185). 19.32% (23/119) primigravidas and 28.98% (20/69) of the multigravidas developed this syndrome. The higher incidence in multigravidas is not statistically significant. Gestational age was < 28 weeks in 6 (37.5%) women, 28-34 weeks in 10 (17.5%) and > 34 weeks in 27 (23.89%). Women with pre-eclampsia / eclampsia at a lower gestational age i.e. < 28 weeks are more prone to develop this complication. Sibai et al[8] reported an incidence of 18.9% among severe pre-eclampsia / eclampsia. Our high incidence is because of high percentage of referrals of complicated cases to our institution.

HELLP syndrome is associated with increased maternal morbidity and mortality[7,8]. Maternal deaths were 3/43 (6.97%) in our study. Serious maternal morbidity was disseminated intravascular coagulation i.e. 60% (20/43) with abnormal laboratory values of PT/APTT. Majority of these cases occurred in women who had accidental hemorrhage (39.5%). If these cases were excluded, then the incidence of DIC developing denovo in HELLP syndrome was 20.9% in our study.

Sibai et al[8] observed DIC only in <5% in their study. Our higher incidence could be attributed in part, to the differences in the populations studied. Our study showed that the presence of DIC was associated with an increased frequency of renal complications, 11 patients had acute renal failure of whom seven required dialysis. Many of these patients were managed initially at local hospitals and were referred subsequently because of deteriorating renal function. Hence it is possible that this complication could have been avoided if some of these patients had been referred earlier. Subcapsular liver hematoma is a life-threatening but rare complication of HELLP syndrome. We had no woman with this complication.

Pregnancies complicated by severe pre-eclampsia/ eclampsia and HELLP syndrome are associated with poor fetal outcome. The reported perinatal mortality ranges from 7.7% to 60%[9,10]. In our study, the perinatal mortality was 42.2%. The overall perinatal morbidity and neonatal ICU admissions were also significant. Regression analysis of the perinatal morbidity showed the correlation co-efficient 'r' (0.76) very significant (P value < 0.001) having a positive relationship such that as the gestational age increases, the apgar score increases and brings out a better perinatal outcome.

HELLP syndrome is associated with increase in maternal-perinatal mortality and morbidity. The incidence is more in multiparas and the complications are more when it occurs at a lower gestational age. The increase in maternal-perinatal mortality and morbidity can be brought down with early reference, timely intervention and good tertiary level care for both mother and newborn.

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