Hellp Syndrome, A Clincial Variant of Pre-Eclampsia

AHMED F.A., AMIN A., NAEEM N.K.
Correspondence: *Dr.Farhat ul ain Ahmed 32–B, St #1, Cavalry Ground Lahore: Email: aindoc2@yahoo.com*

Objective: of study the incidence and effects of complications on maternal and perinatal outcome in pregnancies complicated by HELLP syndrome in severe pre-eclampsia/eclampsia.

Material and Method: Retrospective survey of case records of 156 (1.17%) women admitted with pre-eclampsia/eclampsia during last 2 years (March 2005 –march 2007) in department of Obstetrics and Gynaecology, Fatima Memorial Hospital, Lahore was done.

Results: The incidence of severe pre-eclampsia/eclampsia was 1.17% (156/13336). Primigravidas constituted 44 and multigravidas 112. HELLP syndrome occurred in 6 primigravidas (13.63%) and 10 multigravidas (8.92%). Maternal deaths were 6.2% (1/16) in HELLP syndrome. Serious maternal morbidity in HELLP syndrome was abruptio placentae (25%), disseminated intravascular coagulation (62.5%), acute renal failure (18.75% of whom 33.3% needed haemodialysis) and postpartum hemorrhage (12.5%). Eighty women developed postpartum eclampsia, three developed adult respiratory distress syndrome. None had cerebral vascular thrombosis. Admissions to intensive care unit were 10, though none of patients required ventilator support. The perinatal mortality was 68.75% (11/16). The overall perinatal morbidity and neonatal ICU admissions were also significant.

Conclusion: HLLP syndrome is associated with increase in maternal and perinatal mortality & morbidity. The importance lies in early diagnosis, direct input by clinician with special expertise in the management. So the perinatal mortality and morbidity can be brought down with early reference to tertiary care level hospital.

Keywords: Maternal morbidity, perinatal mortality, HELLP syndrome, severe pre-eclampsia, eclampsia.

Pre-eclampsia / eclampsia is a disease peculiar to pregnancy that often results in multiorgan 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. It was first described by Weinstein in 1982 and is still the leading cause of maternal and perinatal morbidity and mortality.

HELLP syndrome complicates pre-eclampsia in 4-12% of cases.[1] Activation of endothelial cells may lead to release of von Willebrand factor multimers, which are highly reactive with platelets. Normally newly released multimers are cleaved by ADAMTS13 resulting in less reactive derivatives, whereas HELLP syndrome is characterized by increased amount of active VWF leading to thrombocytopenia and thrombotic microangiopathy[2].

Fetal disorder of mitochondrial fatty acid oxidation have recently been associated with obstetric complications including pre-eclampsia, HELLP syndrome, placental bed infarct and acute fatty liver of pregnancy. These disorders occur in about one-third of mothers who are heterozygous for a defect in the long chain hydroxylacyl – co- A dehydrogenase (LCHAD) enzyme and who bear a fetus homozygous for the defect[3]. The mechanism is not understood. Symptoms such as nausea, epigastric pain or right upper quadrant pain, headache and visual disturbance are in common with those of pre-eclampsia. Clinical deterioration may be rapid leading to disseminated intravascular coagulation, renal failure, adult respiratory distress syndrome and hepatic hemorrhage. Following delivery there may be serious initial deterioration rather than improvement.[4,5]

Maternal mortality was reported to be 1% in a large series from the USA[6], though it has varied form 1.1% to 24.2% in different studies[7, 8]. Reported perinatal mortality varies from 10 to 60% and is more commonly due to prematurity[9].

A randomized controlled trial in 40 antenatal patients with HELLP syndrome showed that intravenous dexamethasone (10 mg given 12 hourly) was more effective then intramuscular betamethasone (12 mg given 24 hourly) in improving liver dysfunction and thrombocytopenia, and stabilizing hypertension. Patients treated with dexamethasone exhibit longer time to delivery; this facilitates maternal transfer to a tertiary care center and postnatal maturity of fetal lungs. Steroids given antenatally do not prevent the typical worsening of laboratory abnormalities after delivery. However, laboratory abnormalities resolve more quickly in patients who continue to receive steroids postpartum.[10]

Patients with pre-eclampsia should be screened for HELLP syndrome with LFT and platelet count. With significant liver involvement, coagulation abnormalities develop. Fetal well being and growth assessed since placental insufficiency occurs in about 30% of pre-eclampsia patients. Eclampsia complicating HELLP and severe pre-eclampsia should be anticipated and prophylactic magnesium sulphate treatment should be considered.[11]

The importance lies in early diagnosis, direct input by clinicians with special expertise in the management. Its full treatment comprises the improvement of visceral perfusion, the control of blood pressure hematological decision and timing of delivery.

Material and Methods

This retrospective study surveyed a 2 years period (March 2005-2007). Patients admitted with severe pre-eclampsia

and eclampsia with HELLP syndrome whether booked or unbooked (booked elsewhere and referred to us due to high risk factors) were further studied for maternal and fetal outcome.

A total of 156 cases of severe pre-eclampsia and eclampsia were reviewed. Severe pre-eclampsia was diagnosed if the diastolic blood pressure was 110 mm Hg or more and proteinuria 2+ or more and eclampsia if convulsions were present in a woman who meets criteria of severe pre-eclampsia. Criteria for HELLP syndrome included platelet count < 100,000 ml, LDA > 4500/L and AST / ALT > 70 U/L. Maternal and perinatal outcome was studied with distribution of maternal age, parity and gestational age among these women. Maternal and perinatal mortality and serious morbidity was studied. The data was analyzed statistically by Chi square method. A P value of < 0.05 was considered significant.

Regression analysis was used for perinatal outcome (APGAR >< gestational age) and correlation co-efficient "r" was found out.

Results

The frequency of severe pre-eclampsia / eclampsia was 1.17% (156/13336). It was higher in primigravidas (112/156) 71.7% then in multigravidas (44/156) 28.2% with a P value of < 0.51. HELLP syndrome complicated 16 women with pre-eclampsia and eclampsia with distribution among multigravidas (10/16) 62.5% and (6/16) 37.5% primigravidas (Table 1).

Table 2 summarizes the distribution of maternal age and gestational age in women with HELLP syndrome. In women with HELLP syndrome (4/16)25%were below 28 weeks of gestation, (5/16) 31.25% were between 28-34 wks of gestation and 43.75% were above 34 wks of gestation.

Table 3 depicts the complications and maternal death among women with HELLP syndrome. There was one maternal death due to rupture of liver capsule and intraperitoneal bleed diagnosed on USG, who presented with severe acute abdominal pain and died within 6 hours of admission. Eclampsia occurred in 8 patients 5 were antepartum and 3 were postpartum eclamptic fits. DIC was the most frequent complication (10/16) 62.5% followed by abruptio-placentae (4/16) 25%.Both these complications were strongly associated with intrauterine fetal death. Acute renal failure developed in (3/16) 18.75% with only 1 patient requiring haemodiaysis. Only (2/16) 12.5% had Post-Partum Hemorrhage. Adult respiratory distress syndrome was seen in (3/16) 18.75% patients.

Intensive care admissions were 10, though none of the patients required ventilatory support.

HELLP syndrome complicating 16 pregnancies resulted in 17 births (1 set of twins). There were 4 intrauterine demise before the age of 26 wks (4/16) 25%, 2 (2/16) 12.5% between 25-34 wks and (2/16) 12.5% after 34 weeks of gestation. There were three early neonatal deaths.

Table 1: Parity Distribution in Pre-eclampsia / Eclampsia and HELLP syndrome.

Disease	Multigravida		Primigravida		P-Value
	No.	%	No.	%	
Pre-eclampsia and Eclampsia	112	71.79	44	28.21	<0.51
HELLP syndrome	10	8.92	6	13.63	<0.51

Table 2: Aternal age, Parity and Gestational age in HELLP syndrome.

Maternal Age (Years)	< 28 wks		28-34 wks		> 34 wks	
	Multi	Primi	Multi	Primi	Multi	Primi
< 20	0	1	-	-	-	-
21-25	1	0	2	0	2	1
26-30	2	-	1	1	2	1
> 30	-	-	-	1	-	1

Table 3: Aternal outcome with HELLP Syndrome.

Maternal outcome	Number of cases
Abruptio-placentae	4
Eclampsia	8
DIC	10
Acute Renal Failure	3
Dialysis required	1
PPH	1
Cerebral vascular thrombosis	0
ARDS	3
ICU Admission	10
Death	1

Table IV: Neonatal Outcome

Gestational age	IUD	ALIVE	
		APGAR <5	APGAR>5
<28 weeks	4	-	-
28 – 34 weeks	2	1	2
> 34 weeks	2	2	3

Neonatal death = 3
Correlation co-efficient r = 0.48 P value < 0.19

Discussion

HELLP, a syndrome characterized by hemolysis, elevated liver enzyme levels and a low platelet count, is an obstetric

complication that is frequently misdiagnosed at initial presentation. Many investigators consider the syndrome to be a variant of preeclampsia, but it may be a separate entity. The pathogenesis of HELLP syndrome remains unclear. Early diagnosis is critical because the morbidity and mortality rates associated with the syndrome have been reported to be as high as 25 percent. Platelet count appears to be the most reliable indicator of the presence of HELLP syndrome.

The vague nature of the presenting complaints can make the diagnosis of HELLP syndrome frustrating to physicians. Approximately 90 percent of patients present with generalized malaise, 65 percent with epigastric pain, 30 percent with nausea and vomiting, and 31 percent with headache. Because early diagnosis of this syndrome is critical, any pregnant woman who presents with malaise or a viral-type illness in the third trimester should be evaluated with a complete blood cell count and liver function tests.

Clinical and laboratory criteria have been developed to differentiate severe pre-eclampsia from mild pre-eclampsia, HELLP syndrome from severe pre-eclampsia and to determine the severity of pre-eclampsia.[12,13] The disease process is only reversed by termination of pregnancy.

It has been observed that HELLP syndrome occurs in approximately 0.2 to 0.6 percent of all pregnancies. In comparison, preeclampsia occurs in 5 to 7 percent of pregnancies. Superimposed HELLP syndrome develops in 4 to 12 percent of women with preeclampsia or eclampsia. When preeclampsia is not present, diagnosis of the syndrome is often delayed.

HELLP syndrome complicating severe pre-eclampsia / eclampsia in this study was 10.2% which is almost similar to a study conducted by Retiman TM in which HELLP complicated pre-eclampsia in 4-12% of cases[14] and by Sibai BM in which it was 9.7%[15] .62.5% multigravida and 37.5% of the primigravidas developed this syndrome. Some experience is shared by Wehbe G[16]. In women with HELLP syndrome 25% were below 28 wks of gestation, 31.25% between 28-34 wks and 43.75% were above 34 wks of gestation. Women with pre-eclampsia/eclampsia at a lower gestational age < 28 wks are more prone to develop this complication.

HELLP syndrome is associated with increased maternal mortality and morbidity[17]. Serious maternal morbidity was DIC 62.5% followed by abruptio placentae 25%. Subai et al observed DIC only in <5%. Acute renal failure developed in 18.75%. Only one patient required haemodialysis. Observation showed the presence of DIC was associated with increased frequency of renal complications. Sub capsular haematoma is a life threatening but rare complication of HELLP syndrome and was seen in one woman who died in our study.

Infant morbidity and mortality rates have seen to range from 10 to 60 percent, depending on the severity of maternal disease. Infants affected by HELLP syndrome are more likely to experience intrauterine growth retardation and respiratory distress syndrome. Pregnancies complicated by severe pre-eclampsia / eclampsia and HELLP syndrome are associated with poor fetal outcome. The reported mortality ranges from 7.7 to 60%.[18,19] In our study the overall perinatal morbidity and neonatal ICU admissions were also significant.

Regression analysis of the perinatal mortality showed correlation co-efficient 'r' very significantly (Pvalue <0.19) having a positive relationship such that as the gestational age increases the APGAR score increases leading to a better neonatal outcome.

HELLP syndrome is associated with increase in maternal perinatal mortality and morbidity. Because of the serious associated morbidity and mortality, family physiccians and health care providers who provide maternity care need to be aware of HELLP syndrome so that they can identify it early for referral and management. The increase in maternal – perinatal mortality and morbidity can be brought down with early reference, timely intervention and a good tertiary level care for both mother and newborn.

Conclusion

Severe pre-eclampsia and HELLP syndrome are still the leading causes of maternal perinatal morbidity and mortality. The aim of this report is to draw attention to the life threatening complications that may occur in cases of pre-eclampsia and HELLP syndrome. The importance lies in early diagnosis, direct input by clinicians with special expertise in the management of pre-eclampsia, anaesthetists and haemotologists.

Pregnant women with headache of sufficient severity to seek medical advice or with a new epigastric pain should have their blood pressure measured and urine tested for protein as a minimum requirement.

Clear written, management protocols for severe pre-eclampsia should give initial and continuing treatment in hospital.

There should be early engagement of intensive care specialist in the care of women with severe pre-eclampsia.

The administration of glucocorticoids to patients with HELLP syndrome, both antenatally and postnatally can shorter the disease course, reduces recovery time and decreases morbidity.

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