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MATERNAL MORTALITY AND MORBIDITY IN " HELLP" SYNDROME : A STUDY WITH 70 PATIENTS AND LITERATURE REVIEW

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Summary

The syndrome of haemolysis, elevated liver enzyme and low platelet is considered to be a complication of severe preeclampsia and eclampsia. Study design: This prospective study included 70 patients with " HELLP" syndrome managed in CMCH gynae and obstetric unit 2 from July 2005 to June 2007. "HELLP" syndrome was diagnosed clinically supported by laboratory findings of low platelets, increase AST, ALT , LDH and serum creatinine in patients with severe preeclampsia and eclampsia. Results : Out of 70 patients with "HELLP" 50(71%) patients were antepartum and 20 (29%) postpartum.Among antepartum 40(80%) developed "HELLP" less than 36weeks and 10(20%) between 37- 42weeks of pregnancy. Matrenal death 5(7%)were from complications like pulmonary oedema and acute renal failure. Serious maternal morbidity 56 (80%) included DIC 15(26%), abruptio 9(16%),acute renal failure10(17%) ,pulmonary 0edema 10(17%) and cerebro- vasculer accident (10%). Repeated blood transfusion needed in 14 (25%). There was no difference in laboratory findings of "HELLP" developing before and after delivery. Incidence of acute renal failure and pulmonary oedema were significantly higher in "HELLP" among patients with preeclampsia and postpartum eclampsia rather than "HELLP" in antepartum eclampsia. So it can be concluded that maternal mortality and morbidity is significantly higher when "HELLP"is complicated by pulmonary oedema and acute renal failure.

Key words

"HELLP" syndrome; eclampsia; acute renal failure

Introduction

Preeclampsia and eclampsia remains an important cause of maternal and perinatal mortality and morbidity through out the world specially in developing countries.

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Report 2010(BMMS-2010 Prcl.Report) maternal mortality from eclampsia have fallen to a lower level 20% of total (194/100000live birth) to date,still it remains the second largest individual cause of maternal mortality after postpartum haemmorrhage[1]. The spectrum of disease associated with preeclampsia is wide, ranging from relatively benign disease to more severe form[2]. One particular subtype is the multisystem form known as" HELLP" syndrome and was first escribe by Wensteen[3]. The syndrome "HELLP" is characterized by haemolysis, elevated liver enzyme and low platelet count was also described by Weinteen [3].Incidence varies from 0.2 to o.5% of all pregnancies, 4-12% of pregnancy with preeclampsia, eclampsia or PIH[4]. HELLP is more common in antepartum (69%) than postpartum (31%).Incidence and severity of HELLP syndrome varies with age,parity and ethnicity.Unlike preeclampsia HELLP is more common in elderly and multiparous women[5]. The pathogenesis and aetiology not yet known,it is suggested it starts with a failure in development of placenta .This changes begins as early as 18 to20 weeks. Generally the disorder is considered as placenta integrated ,liver targeted acute inflammatory condition with elements of disordered maternal immunological response and genetic modifying factor with a cascade that is terminated only by delivery. The purpose of the study was to

1. Describe from our experience the incidence of severe morbidity with HELLP syndrome.
2. To detect potential clinical and therapeutic factor that may affect mortality and morbidity.
3. To compare maternal morbidity in patients developing HELLP before and after delivery.

Materials and methods

Study design –Prospective study.
Place of study:-Gynae and Obstetric Unit 2 .
Sample size -70.
Duration :-July 2005 to june 2007.
Inclusion criteria- Patients of preeclampsia and eclampsia with clinical sign- symptoms of HELLP supported by laboratory findings of platelet < 100000/cumm,serum lactate dehydrogense>600 U/L, serum transaminase (ASTand ALT)>70 U/L, total billirubin >1.2mg/dl[2]. Routine laboratory investigation included serial measurement of liver function test, CBC, coagulation profile and renal function test .

Though not always the risk of severe morbidity correlates with severity of clinical symptom and laboratory abnormalities. Depending on the findings HELLP is classified in to three (3) class[2].

Disseminated intravascular coagulation was defined the presence of low platelet < 100000/cumm, low fibrinogen<300mg, positive fibrin split products and prolong prothombin time (>-14sec), and partial thromboplastin time (>40sec)[6].

Acute renal failure was diagnosed in the presence of oliguria-anuria in association with severe reduction in renal function (serum creatinine >1.2mg/dl)[6].

The diagnosis of pulmonary oedema was made on the basis of clinical and chest x-ray findings .Severe ascites was defined as the presence of ascitic fluid estimated >1000ml either clinically, USG or at cesarean section[6].

Patients with HELLP syndrome routinely received intravenous magnesium sulphate to prevent and control convulsion. Injection hydralizine to control hypertension. Fresh blood and blood products are transfused when needed. Dialysis was done in patients with acute renal failure. All patients were followed up closely monitoring the vital signs and maintaining intake output chart to find out stabilization usually within in 48 to 72 hours, marked by decrease in blood pressure, proteinuria as well as increase in urine output. Development of complications like pulmonary oedema, massive hepatic necrosis and acute tubuler necrosis in some patients also closely monitored. Statistical comparison was performed with the relative risk ratio, x^2 test and correlation with p value of <O.05 considered significant.

Results

During the study period 510 patients were admitted with mild to severe preeclampsia

(n- 418) and eclampsia (n-92).Among them 70 patients were complicated by HELLP (14%), incidence of HELLP in preeclampsia (n-60,86%) being about 6 times higher than eclampsia (n-10,14%). Maternal age ranges from 18 to 38 years, about 35(50%) being within 30 to 35 years. Four (4) patients had preexisting hypertension.There were no difference in maternal demographic characteristics and laboratory findings between women with antepartum and postpartum HELLP syndrome. About 53(76%) patients developing HELLP syndrome were multiparous, 20(29%) having four(4) children.

Table I : Presenting symptoms (n-70)

SYMPTOMS/SIGN	NO- 70	%
Right upper quadrants/ epigastric pain.	46	66
Nausea/Vomiting	40	57
Malaise	42	60
Headache	25	36
Visual change	40	21
Bleeding	15	21
Jaundice	16	23
Shoulder and neck pain	14	20
Ascites	6	1

Table I represents the common flu- like symptoms of HELLP present in 57 to 66% cases.

Table II : Times of onset/gestational age

Time of onset	Weeks of gestation.	Total n-70	%
Antepartum	28 t0 42 wk	50	71
	28 to32wks	08	11
	32 to36wks	32	46
	36 to 42 wks	10	14
Postpartum		20	29
	24 to 72 hr	20	
	72hrs or more	0	0
Preeclampsia			
Before delivery		16	23
After delivery		04	6

Table II, shows the time of onset of HELLP syndrome with respect to weeks of gestation and delivery. Most of the cases developed HELLP in antepartum period (71%), <36weeks (57%). In 4 patients (6%)(there were no evidence of preeclampsia and eclampsia either before or during labour.

Table III : Common laboratory findings and classifications of HELLP SYNDROME[5]

Laboratory test	Rang of findings	CLASS-1 20(30%)	2 35(50%)	3 15 (20%)
Platelet count	50000- 120000/ cumm	Less than 50000/cumm	50000 to 100000cumm	100000 to 150000/cumm
LDH	600 to 700U/L	More than 600U/L	More than 600U/L	More than 600U/L
AST	45 to 220 U/L	More than 70U/L	More than 70U/L	More than 40U/L
ALT	32 to 156 U/L	70U/L	70U/L	40U/L
Serum creatinine	1.6 to 4.8mg/dl			
Serum billirubin	2.4 to 28mg/dl			
Prothrombin time	15 to 20 sec			

Table III represents the laboratory findings in the patients with HELLP syndrome and on the basis of the findings patients were classed into 3 group to asses the severity of the disease, class 1 being the most severe forms. The laboratory finding do not differ in HELLP Syndrome before and after delivery.

Table IV : Serious complications and morbidity in patients with HELLP syndrome.

COMPLICATIONS	NO 56/70(80%)	%
DIC	15	26
Abruptio	9	16
Cerebral haemorhage	6	10
Acute renal failure	10	17
Pulmonary oedema	10	17
Ascites	6	10
Blood transfusion	14	25

Table IV represents the serious maternal complications on this group of patients before and after delivery. There was strong association among the complications and most of the patients experiencing multiple complications.

Table V : Relations of complications with time of onset of disease.

Complications	Antepartum n- 26/50 <36wks-13 >36wks-13	Postpartum n-30/20	Antepartum %	Postpartum %
Abruptio	9	0	18	0
Pulmonary oedema	3	7	6	35
Acute renal failure (ARF)	2	8	4	40
Cerebral haemorhage	2	4	4	20
Disseminated intra vascular coagulation	6	9	12	45
Ascites	4	2	8	10

Table represents the relations of complications in patients with HELLP before and after delivery. Postpartum HELLP was associated with higher incidence of DIC, cerebrovasculer disease, acute renal failure and pulmonary oedema compared to those developed HELLP before delivery.

Table VI : Clinical findings during maternal death (n-5)

Total no	Pregnancy complication	Complications Of HELLP	Cause of death
5	Preeclampsia No - 4		
	1	Ascites/ARF.	Acuterenalfailure/(ARF)
	1	Abruptio/ARF/ Pulmonary oedema.	Multi organ failure(MOF).
		Cadiac arrest	ARF/MOF.
	1	CVD/Pulmonary Oedem/ARF.	MOF/Hypoxic encephalopathy.
	1 Eclampsia No-1	Cerebro vascular Disease (CVD)/ARF.	Hypoxic encephalopathy.

Table table shows the cause of death of five (5) patients that died from different complications of HELLP syndrome,death being more common from preeclampsia in elderly multiparous patients mainly in postnatal period within first 48 to 72 hours.

Discussion

The study represents a fair number of HELLP, most of the patients met the criteria for HELLP syndrome suggested by senior authors[2]. In the study period 510 patients were admitted with preeclampsia mild to severe (n-418) and eclampsia (n- 92), Among them 70 (14%) developed HELLP diagnosed clinically and supported by laboratory abnormalities. Though it does not reflect the actual incidence in this sample, higher incidence is due to delayed diagnosis for vague flu like symptoms and delayed referral of more complicated patients from else where. Tendency to present with vague symptoms (90%)[2,16] for several days misdiagnose with medical and surgical problems like hepatitis,idiopathic purpura,acute fatty liver and appendicitis.

In the study HELLP was more common in antepartum (n-50,71%) than postpartum(n-20,29%), 16 (23%) post partum patients having severe preeclampsia before delivery[4,6]. So all health professional caring of pregnancy should have knowledge about HELLP. The incidence of HELLP were six times more in patients with preeclampsia (n-60, 86%) than eclampsia (n-20,14%) which is near similar to (10%)[6] but different to study, who reported strong association between HELLP and eclampsia (30%)[7]. The difference may be due to population studied (complicated reffered patients) and difference in diagnostic criteria of HELLP which differed in different study[6].

Severe preeclampsia though defined as presence of B.P >160 mmHg systolic and>110mm Hg diastolic along with oedema, proteinuria or both. But in some patients hypertension or proteinuria may be absent or missed. In the study 4 (6%) cases had hypertension and proteinuria and laboratory abnormalities for the first time after delivery and they suffered much more from pulmonary oedema and acute renal failure.

Laboratory findings of thrombocytopenia, prolong prothrombin time, partial thromboplastin time, low fibrinogen in this patients fulfill the criteria DIC[3]. That found one among the 26 patients of HELLP complicated by DIC.In our study we found 15 patients(26%) complicated by DIC, similar and except the above mention patient others do not have all the criteria of DIC[9]. None of 50 patients with HELLP, had abnormalities of prothrombin time or fibrinogen level. Presence of abruptio increased the risk of DIC[6].

In our study 10(14%) patients developed acute renal failure associated with abruptio, DIC, haemorrhagic complication, leading to hypovolumic shock were mainly responsible for acute renal failure and seven required dialysis. In the study incidence of acute renal failure was 8%[4]. Disseminated intra vascular coagulation was closely associated with acute renal failure.These could be avoided by reffering the patients earlier.

In the study 6 (9%) patients had documented evidence of severe ascites clinically ,USG or at cesarean setion.The presence of ascites was strongly associated with increase incidence cardiorespiratory complication, pulmonary oedema and acute renal failure[5]. In our study one Patient had huge ascites subsequently developed pulmonary oedema and anuria and died with 72 hours after admission.

Analysis of laboratory findings in relation to delivery revealed no difference in between antepartum and postpartum group, regarding platelet count, AST,ALT, LDH and serum billirubin and laboratory findings do not always correlated with severity of disease[8].

In our stiudy five patients (71/1000 live birth ,7.1%) died ,all in postnatal period,most were elderly multiparous[2] and delivered at or near term.There is also record of a 1-24% maternal mortality rate[4].Postpartum HELLP most likely to deliver at term and had increase evidence of DIC (R.R 3.75,p value <0.01),cerebrovasculer disease,acute renal failure and pulmonary oedema[4,5].

In 4(80%) casess HELLP syndrome developed patients with severe preeclampsia and were complicated by severe life threatening complications like pulmonary oedema, acute renal failure and multi organ failure. One patient aged 38 years had preexisting chronic hypertension and she delivered at term and died due to hypoxic encephalopathy with multi organ failure. "HELLP" syndrome may develop de novo most commonly in the first 48 hours postpartum though can take up to 7 days to manifest and increase the risk of acute renal failure and pulmonary oedema[5].These support our previous observation that HELLP syndrome is associated with increase maternal mortality & morbidity mostly in the postpartum period[5].

Once HELLP syndrome is diagnosed irrespective of gestational age our aim was to immediate delivery, the true cure of the syndrome[4,5]. Prolongation of pregnancy with steroid for foetal lung maturation do not improve preinatal and maternal outcome in terms of mortality and morbidity like abruptio, pulmonary oedema,acute renal failure rather than increase the risk of stillbirth substantially[10].

The administration of steroid is followed by transient rapid improvement of clinical and laboratory parameters, allowing an extension of time period between hospital admission and induction of delivery.[11,12]. The improvement of thrombocytopenia has been more frequently observed for low doses of steroid compared to the high doses[11].

HELLP syndrome is not an indication of cesarean section but it was observed that HELLP syndrome was associated with increase rate of cesarean section. Mode of delivery depends on gestational age and Bishop score. Severe maternal complications are more frequent when induction of delivery is delayed for more than 12 hours but labour should not be prolong beyond six hours[13]. Cesarean section is done if gestational age is less than 34 weeks with Bishop score less than 5,in absence of labour,as well as intrauterine growth retardation and oligohydroamnios .In cesarean section intraperitoneal subcutaneous closed suction drain were given through a separate incision to prevent haematoma formation[5].

Inj.magnesium sulphate and inj hydralazine were used to control convulsion and hypertension respectively. Fresh blood and blood products were given to correct coagulation defect.Vit k was given if needed.The patients might have10% or 50% dextrose to prevent hypoglycaemia which is dangerous[5]. If platelet count is less than 75000/cumm general anesthesia preffered to regional anesthesia[14]. Platelet count should be maintained grater than 20000/cumm in vaginal delivery and 40000/cumm in cesarean section by platelet transfusion if count is beyond the range[15].

Though HELLP is associated with increase mortality and morbidity, outcome of most patients with HELLP syndrome is generally good. With early detection and good supportive care a majority patients recover completely. It is important to continue monitoring of fluid balance, laboratory abnormalities, and pulse oximetry closely into the immediate postpartum period .Maternal platelet count decreases immediately after delivery,then rises starting in day 3 postpartum,reaching >100000 cumm^3 after day 6 postpartum.The lack of an increase in platelet level after 96 hours from delivery indicates a severe disorder,with the possible development of multi organ failure[4].

HELLP syndrome is not an indication of permanentcontraception.If needed subsequent pregnancy could be allowed. In subsequent pregnancy recurrence rate for preeclampsia is 20%, HELLP less than 5% but 20to 27% if class 1 HELLP[4].

In subsequent pregnancy there are also increase chance of preterm labour, intrauterine growth retardation, abruptio and foetal death is higher even in absence of preeclampsia and HELLP syndrome. So close follow up is crucial in subsequent pregnancy by observing flu like prodormal syndrome in second trimester of pregnancy, colour Doppler at 22weeks to 24 weeks of pregnancy[2,5] and taking preventing measure with tablet aspirin 75mg, increasing dietary protein and calcium supplementation.Hyaluronic acid levels increase in preeclampsia to >100ug/L,being a reliable marker for HELLP syndrome. Increased serum fibronectin, higher alpha-fetoprotein, human chorionic gonadotrophin values in second trimester of pregnancy increase the risk of HELLP syndrome up to 47 times[16]. Serum amyloid A, at values >3.5mg/L by proteome analysis is selected with predictive value as a marker of HELLP syndrome.Anti phospholipid syndrome is also a predisposing factor for HELLP syndrome[4]. Trends toward early postnatal discharge possibility of HELLP after normal pregnancy and delivery should be kept in mind. As contraception oral contraceptive pill can be prescribed in absence of thrombophillia[5].

Conclusion

HELLP a generalized microangiopathy in older multigravid in third trimester, is associated with increase mortality and morbidity .Predicting high risk cases, adopting preventive measure ,early diagnosis and referral can improve the outcome to a great extent.

Disclosure

All the authors declared no competing interestes

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