

HELLP Syndrome Associated AKI -Single centered study from South India

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Abstract: *Background:* Despite significant advances in obstetric management and therapeutics, pre eclampsia - eclampsia is still a serious complication of pregnancy with high morbidity and mortality. Approximately 10-20% of women with PIH have underlying HELLP Syndrome. HELLP Syndrome can have varied clinical presentations, including acute kidney injury (AKI). *Methods:* This is a retrospective, observational study. The study duration was from January 2002 to December 2015. Details regarding demographic characteristics, clinical profile, laboratory parameters, renal manifestations and outcome, maternal and fetal complications were studied. *Results:* A total of 79 patients were studied. HELLP syndrome occurred most commonly during the antenatal period (81%). AKI was seen in 32 patients (40.5%). Proteinuria was largely present but for 13 patients. Patients with HELLP syndrome were divided into 3 classes based on the Mississippi 2006 classification. Further analysis reveals incidence of AKI is more in Class I (81.25%) compared to the class II and class III, 12.50% and 6.25% respectively. Furthermore, when the incidence of AKI was analyzed, a total of 32 patients suffered from AKI of which 19 required renal replacement therapy. 25% of the patients who had AKI died. *Conclusions:* HELLP syndrome is one the important cause of maternal and perinatal morbidity and mortality. AKI in HELLP syndrome is quite common, it has to be diligently sort for has its treatment has serious implications for both short and long term morbidity and mortality of the mother and neonate.

Keywords: HELLP syndrome, Acute kidney injury, Renal failure, Dialysis, Proteinuria.

Introduction

Despite significant advances in obstetric management and therapeutics, pre eclampsia - eclampsia is still a serious complication of pregnancy with high morbidity and mortality. Approximately 10-20% of women with preeclampsia and eclampsia have underlying HELLP Syndrome. The HELLP Syndrome was first defined by Veinstein in 1982 while describing a case of severe preeclampsia complicated by haemolytic anaemia, elevated liver enzymes and low platelets [1]. HELLP Syndrome can have varied clinical presentations, including acute kidney injury (AKI). Most of the patients with AKI have a spontaneous recovery of renal function and rarely AKI can be severe enough requiring dialysis [2-3].

Maternal mortality appears to be related to consumption coagulopathy, pulmonary and cerebral edema, AKI, Liver rupture/ infarction, cerebral infarction/ haemorrhage and hypovolemic shock.

Background: Since 1960, the incidence of acute kidney injury (AKI) in pregnancy has been reduced significantly and currently affects 1 in 20,000 pregnancies. The legalisation of abortion contributed to this decline in most countries. The first peak of AKI is during the first trimester and dominated by infections and illegal abortions especially in low resource countries.

The second peak occurs during the third trimester and is related to preeclampsia - eclampsia, HELLP Syndrome, Acute fatty liver of pregnancy or post-partum haemorrhage. HELLP Syndrome is a leading cause of pregnancy related AKI (PR-AKI), AKI occurs in 3%-15% of cases of HELLP syndrome, and HELLP syndrome accounts for 40 % of all cases of PR-AKI and up to 60 % of severe cases [4-7]. AKI associated with HELLP Syndrome even in its severe form requiring RRT, usually retains a favourable outcome. Only few Indian studies have looked

into this aspect. So this study was designed to study the characteristics of HELLP related AKI and factors associated for unfavourable outcome.

Material and Methods

This is a retrospective, observational study of 79 patients with diagnosis of HELLP syndrome who were undergoing treatment at M.S. Ramaiah Medical College Hospitals were included in the study. The study duration was from January 2002 to December 2015. Details regarding demographic characteristics, clinical profile, laboratory parameters, renal manifestations and outcome, maternal and fetal complications were studied. Patients with pre-existing hypertension, diabetes mellitus, chronic kidney disease and renal transplant recipients were excluded from the study.

Definitions: AKI was defined as serum creatinine level > 1.3mg/dl [8]. Preeclampsia was defined as blood pressure reading > 140/90 mmHg diagnosed for the first time after twenty weeks of gestation with 2+ proteinuria on dipstick. Severe preeclampsia was defined as the association of severe arterial hypertension (SAP exceeding 160 mm Hg and DAP exceeding 110 mm H) or proteinuria ≥5 g/L or > 3+ or signs of visceral involvement (headaches, visual disturbances, epigastric or right upper-quadrant pain) [9].

Eclampsia is defined as the presence of new-onset grand mal seizures in a woman with preeclampsia. HELLP syndrome was diagnosed as: thrombocytopenia (<100.10⁹ cells/L), elevated liver enzymes [Aspartate Aminotransferase (AST)>70 IU/L], and hemolysis [10, 11]. Sepsis was defined as per criteria laid down by American College of Chest Physicians [12]. Post-partum hemorrhage was defined as a blood loss of ≥500 mL after vaginal delivery or ≥1000 mL after cesarean delivery, or as noted in the medical records.

Statistical analysis: Data was analyzed using SPSS software version 18.0. Statistical significance was tested at P value of < 0.05. Risk estimate was calculated and its 95% CI was analyzed. Results are given as number, mean, median, and interquartile range for quantitative variables, and percentages for nominal variables.

Results

A total of 79 patients satisfied the criteria for HELLP syndrome were studied between a periods of January 2002 to December 2015. Majority of the patients were in the age group of 26-30 (41.7%) years (Table 1, 2 & 3).

Table-1: Age group	
Age (Years)	Number
15 – 20	08
21 - 25	28
26 – 30	33
More than 30	10
Total	79

Table-2: Period of pregnancy	
Pregnancy period	Number
Antenatal	64
Postnatal	15
Total	79

Table-3: Gestational age	
Gestational Period	Number
Before 27 weeks	08
Between 27 to 37 weeks	48
After 37 th week	23
Total	79

HELLP syndrome occurred most commonly during the antenatal period however in our study 19% of HELLP syndrome was noted in the post natal period as well. When analyzed based on the gestational period majority of the HELLP syndrome were seen between 27 and 37 weeks of pregnancy (MEDIAN) and it was least common before 27th week gestation. HELLP syndrome was predominantly seen in multiparous women when compared to primigravida (Table 4) and this has been substantiated by earlier studies, the pathogenesis of which still remains unknown [13].

Parity	Number
Primi	23
Multi	56
Total	79

PIH	Number
Mild preeclampsia	47
Severe preeclampsia	19
No Proteinuria	13

Pain in the upper quadrant of the abdomen and nausea were the predominant symptoms, patients often complained of malaise and headache, visual disturbances was seen in 21 patients this further enforces our previous knowledge of pre eclampsia being closely related to HELLP syndrome (Table 5). Severe pre eclampsia was seen in 19 patients. And the remaining of 47 patients suffered from mild pre eclampsia. AKI was seen in 32 patients (40.5%). Proteinuria was largely present but for 13 patients. Complications were noted in most of our studied population, AKI was second only to DIC (Disseminated Intravascular Coagulation), and the other notable complications were wound infection, abruptio placenta, hepatic infarction, cerebral hemorrhage and cerebral edema (Table 6).

Symptom	Number
Upper quadrant / epigastric pain	69
Nausea / vomiting	57
Malaise	38
Headache	27
Visual disturbances	21

Patients with HELLP syndrome were divided into 3 classes based on the Mississippi 2006 classification [14-16]. Analysis revealed 47 patients (50.63%) of the patients had Class 1 HELLP syndrome of which 26 patients had AKI. Further analysis reveals incidence of AKI is more in Class 1 (81.25%) compared to the class II and

class III, 12.50% and 6.25% respectively. Furthermore, when the incidence of AKI was analyzed, a total of 32 patients suffered from AKI of which 19 required renal replacement therapy. 25% of the patients who had AKI died.

Complications	Number
Eclampsia	19
Abruptio Placentae	17
DIC	47
AKI	32
Severe ascities	16
Wound infection / Haematoma	11
Pulmary edema	04
Cerebral haemorrhage	01
Cerebral edema	03
Sub capsular liver hematoma	02
Maternal death	13

Class	Parameters	Number	AKI
I	Platelets <50000 LDH >600 IU/L AST / ALT > 70 IU/L	40	26
II	Platelets 50000 to 100000 LDH 600 IU/L AST / ALT > 70 IU/L	22	04
III	Platelets 100000 to 150000 LDH 600 IU/L AST / ALT > 40 IU/L	17	02

On analysis of the cohort using the RIFLE classification, majority of the study population were classified into failure followed by Injury and Risk. (Table7). The mortality rate was

directly proportional to the RIFLE class where patients with Failure had 29.41% mortality rate. A number of fetal complications were noted in patients with HELLP syndrome. 49 patients had pre term delivery, 33 patients had intra uterine growth retardation. Perinatal death was seen in 24 patients and 4 patients had Intra uterine death. (Table 8). These patients also had higher incidences of low birth weight, 52 of the 79 delivers had a birth weight of less than 2500 grams (MEDIAN).

Discussion

Acute kidney injury remains a serious, though uncommon, medical complication of pregnancy. It has historically been described in association with haemorrhagic or septic shock, but is also known to occur in severe pre-eclampsia [17]. The HELLP syndrome, a condition thought to be closely linked to pre eclampsia has more recently been identified as a significant risk factor in the development of severe renal dysfunction. In our cohort of HELLP patients all of them suffered either from mild or severe pre eclampsia further concreting the evidence of close association. However, in 20% of cases there may be no evidence of pre-eclampsia before or during labour, as in this pregnancy which was regularly controlled [18-19].

Even though HELLP syndrome predominantly is a feature of pregnancy there have been reports of up to 30% of all patients develop HELLP syndrome after parturition, typically within 48 hours of this occurrence in the post-partum period. In our cohort 16% of the women had HELLP syndrome in the post natal period. DIC was the most common complication seen in our patients, 60.2% of the studied cohort suffered from this. In a series of 442 pregnancies complicated by hemolysis, elevated liver function tests, and low platelets (HELLP syndrome), 92 had DIC (21 percent) (20-21).

In our study a total of 32 patients developed AKI of which 19 required regular renal replacement therapy. 1 patient reached ESRD requiring regular renal replacement therapy. In the largest study done on AKI in HELLP syndrome by Beller et al stated acute tubular necrosis as the most common cause for AKI explaining the return of renal function after the acute insult has

settled. In his paper biopsy of the kidney revealed glomerulonephritis in 3 patients, endotheliosis in 4 patients, nephrosclerosis in 2 patients, haemolytic ureic syndrome in 1 patient and normal in 1 [22], others have also reported acute cortical necrosis as well [23]. Approximately 10%-46% of pregnant women with AKI associated with HELLP syndrome need dialysis in the acute phase but even these cases typically show a complete recovery of kidney function.

The perinatal mortality rate ranges between 7% and 34% and depends on gestational age and maternal disease severity [24]. In a retrospective study where 111 patients with HELLP were matched with 467 patients in the severe preeclamptic group according to maternal and neonatal complications and morbidities found that the overall neonatal mortality and morbidities was greater in infants of women with the HELLP syndrome, and there was a greater need for mechanical ventilation, neonatal intensive care, and longer times in the neonatal intensive care unit, the mean gestational age at delivery and fetal body weight was significantly lower in the HELLP group. In our study 49 births were pre term and IUGR as noted in 33 deliveries. 11 infants weighed between 500-1500 grams requiring neonatal intensive care and 41 infants weighed between 1500 grams to 2500 grams.

Conclusions

HELLP syndrome is one the important cause of maternal and perinatal morbidity and mortality. It can present either in antepartum, peripartum or in the postpartum period. One has to be very vigilant in identifying these patients at the earliest, as early diagnosis can to some extent prevent development of serious complications. AKI in HELLP syndrome is quite common, it has to be diligently sort for has its treatment has serious implications for both short and long term morbidity and mortality of the mother and neonate. Renal involvement in HELLP syndrome has varied manifestations which require careful clinical and biochemical expertise to identify the nature of renal involvement.

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