ORIGINAL RESEARCH PAPER

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STUDY TO CORRELATE THE OCCURRENCE OF ADVERSE MATERNAL AND PERINATAL OUTCOMES WITH VARIOUS LEVELS OF LDH AND URIC ACID IN PREGNANT WOMEN WITH PREECLAMPSIA

KEY WORDS: preeclampsia, maternal outcome, perinatal outcomes, LDH, uric acid,

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ABSTRACT

The most frequent pregnancy complication, which affects 7 to 15% of all gestations, is hypertensive disorders. Present study was aimed to correlate the occurrence of adverse maternal and perinatal outcomes with various levels of LDH and uric acid in pregnant women with preeclampsia at a tertiary hospital. Present study was single-center, prospective, observational study, conducted in Pregnant women with Gestational age >20 weeks, with proteinuria, with an average systolic BP >140 mm Hg and/or an average diastolic BP >90 mm Hg. The patients were be followed up every alternate day till they were discharged. During the above study period 118 patients were enrolled in the study. The mean age was 27.21 ± 6.15 years, with a range of 18 years 42 years. Majority (90%) of them were in the age group of 20-35 years. Preeclampsia was most commonly (60%) seen among primigravida. Early onset preeclampsia was found in 57 patients (48%) whereas 61 patients (52%) had late onset preeclampsia. 40% of the women in our study had mild preeclampsia, 52% had severe preeclampsia, and 8% had eclampsia. Among the 118 patients whose LDH and uric acid levels were correlated with the frequency of severe maternal and perinatal outcomes, high LDH levels (>600 IU/L) were linked with HELLP syndrome (p = 0.01) and acute renal damage (p value 0.03). High uric acid levels> 6mg/dL were shown to have a statistically significant connection with maternal outcomes such as HELLP syndrome (p=0.002) and perinatal outcomes such as low birth weight of 2 kg (p=0.001), preterm (p=0.03), poor APGAR scores (p=0.04), and NICU hospitalizations (p value 0.02). High levels of uric acid and lactate dehydrogenase (LDH) are connected with unfavourable maternal and perinatal outcomes.

INTRODUCTION

The most frequent pregnancy complication, which affects 7 to 15% of all gestations, is hypertensive disorders. According to WHO, hypertension accounts for 10 to 25 percent of direct maternal deaths in developing countries.[1] These maternal deaths from hypertensive disorders are roughly half preventable. The baby may also be at risk from hypertensive disorders. The leading single observable risk factor for stillbirth related to pregnancy is hypertension.[2] Fetal growth restriction, low birth weight, spontaneous or iatrogenic preterm labour, and neonatal intensive care unit hospitalisations are all significantly linked to preeclampsia.[3,4] LDH is an intracellular enzyme, and cellular death in PIH causes its level to rise. This may be used as a benchmark when deciding on management tactics to enhance the result for the mother and the fetus. Lactic dehydrogenase has been identified as a reliable biochemical marker for severe preeclampsia.[5,6,7]

The primary byproduct of purine metabolism is uric acid. Overproduction of uric acid is caused by increased purine breakdown in the placenta. In order to predict illness severity, renal function status, and fetal development retardation in women, it may thus be utilised as an effective and affordable marker. Present study was aimed to correlate the occurrence of adverse maternal and perinatal outcomes with various levels of LDH and uric acid in pregnant women with preeclampsia at a tertiary hospital.

MATERIALS & METHODOLY

Present study was single-center, prospective, observational study, conducted in department of Obstetrics and Gynecology, at Government Medical College, Jalgaon, Maharashtra, India. Study duration was of 2 years (July 2020 to June 2022). Study was approved by institutional ethical committee.

Inclusion Criteria

- Pregnant women with Gestational age >20 weeks, with proteinuria, with an average systolic BP >140 mm Hg and/or an average diastolic BP >90 mm Hg, willing to participate in present study

Exclusion Criteria

- Chronic hypertension – hypertension (BP >140/90 mmHg) before 20 weeks of gestation, before pregnancy
- Presence of Diabetes Mellitus, Heart diseases, Urinary tract infection
- Hyperuricemia due to other cause
- Renal diseases or chronic kidney diseases characterized by oliguria, creatinine >0.8

Study was explained to participants in local language & written informed consent was taken. Demographic details along with brief medical history was recorded using a preform designed questionnaire for data collection in this study. Also, they shall be evaluated for the other risk factor associated with pregnancy. The blood samples of each pregnant woman were collected at the time of admission. The patients were be followed up every alternate day till they were discharged.

Patients will be followed up till the time of discharge and the factors contributing to the outcome like eclampsia, HEELP Syndrome, abruption, postpartum hemorrhage, pulmonary edema, acute kidney injury, mortality will be analyzed. Neonates shall also be followed up till the time of discharge. Outcome will be analyzed based on gestational age at delivery, birth weight, APGAR score, Neonatal ICU (NICU) admission, need for ventilator support. Proportion and percentage of maternal and perinatal outcome in patients of preeclampsia will be calculated.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the

continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

During the above study period 118 patients were enrolled in the study. The mean age was 27.21 ± 6.15 years, with a range of 18 years 42 years. Majority (90%) of them were in the age group of 20-35 years. Preeclampsia was most commonly (60%) seen among primigravida. 40% of patients had no formal education and 34% had studied up to high school. Most of the patients included in our study were house wives (70%). 38% of patients belonged to upper middle, while 30% belonged to lower middle socioeconomic status.

Table 1- General Characteristics

Category	Subcategory	No. of subjects	Percentage
Age	<19	5	4
	20-34	106	90
	>35	7	6
Parity	Primipara	71	60
	Multipara	47	40

Among the population studied 16% had family history of hypertension. The onset of preeclampsia ranged from 22 weeks to 40 weeks. The mean week of onset of preeclampsia was found to be 31 weeks. Early onset preeclampsia was found in 57 patients (48%) whereas 61 patients (52%) had late onset preeclampsia.

Table 2– Other Characteristics

Characteristics	No. of subjects	Percentage
Family history of hypertension		
Present	19	16.1
Absent	99	83.9
mean week of onset of preeclampsia (weeks)	31	
Type of pre-eclampsia		
Early	57	48.31
Late	61	51.69

40% of the women in our study had mild preeclampsia, 52% had severe preeclampsia, and 8% had eclampsia. Deep tendon reflexes were exaggerated in 50% of the cases and normal in the other 50%. Proteinuria (1+) was found in 46% of the study population using the dipstick method. At the time of hospitalisation, sixteen (13%) of the patients had intrauterine fetal demise. Magnesium sulphate loading and maintenance doses were administered to 48 (41%) of the 118 patients. Among the 48 patients 72% received magnesium sulphate for impending symptoms and 28% received for fetal neuroprotection. Normal fundus was seen in 43% (50) patients, whereas 33% (39) patients had grade 1 hypertensive retinopathy. 8 (7%) patients had exudative retinal detachment.

Table 3– Pre-eclampsia Characteristics

Characteristics	No. of subjects	Percentage
Severity of hypertensive disorders of pregnancy		
Mild preeclampsia	47	39.83
Severe preeclampsia	71	60.17
Eclampsia	9	7.63
Proteinuria		
1+	56	47.46
2+	20	17.54
3+	32	28.07
MgSO4		
Not received	70	59.32
Received	48	40.68
• Received for Impending symptoms	35	72.92
• Received for Neuroprotection	13	27.08
Fundus examination		
Normal	51	43.22
Grade 1 retinopathy	39	33.05
Grade 2 retinopathy	18	15.25
Grade 3 retinopathy	2	1.69
Exudative retinopathy	8	6.78

Mean duration of hospital stay was 10.7 ± 5.1 days, with a range from 4 days to 21 days. 30% (35) patients did not require any antihypertensive drugs while 33% (39) required 2 drugs for hypertension control. 20% (10) patients required intravenous antihypertensive drugs for the initial stabilization of blood pressures.

Of the 118 patients, 73 (61%) were induced with prostaglandins E2/E1. 57% (67) of patients had caesarean sections, while 41% had vaginal deliveries. The most common reason for a caesarean section was fetal distress (non-reassuring CTG/meconium), which accounted for 42% of all cases. 75% of the intrapartum liquor was clear, while 20% was meconium stained. One patient had velamentous cord insertion.

9% (11) patients had eclampsia, 19% (22) developed HELLP syndrome, 5% had abruption, 5% had postpartum hemorrhage controlled by medical measures, none required surgical intervention, 9% (11) patients had acute renal failure, 2 of them required dialysis. Doppler changes, such as the absence and reversal of diastolic flow in the umbilical artery and the reversal of the cerebroplacental ratio, were observed in 13% (15) of the patients. In the study group, there were no cases of maternal mortality attributed to preeclampsia. 41% (48) of the babies required NICU admission, while 20% needed ventilator support. There were no reports of neonatal deaths.

Table 3– Pre-eclampsia Characteristics

Characteristics	No. of subjects	Percentage
Mean duration of hospital stay (days)	10.7 ± 5.1	
Antihypertensive drugs		
Not required	35	29.66
1 drug	37	31.36
2 drugs	39	33.05
3 drugs	7	5.93
Intravenous antihypertensive drugs	10	8.47
Mode of delivery		
Vaginal	48	40.68
LSCS	68	57.63
Instrumental	2	1.69
Maternal Outcome		
Eclampsia	11	9.65
HELLP syndrome	22	19.3
Abruption	6	5.26
PPH	6	5.26
Acute renal failure	11	9.65
Pulmonary edema	6	5.26
Fetal growth restriction	20	17.54
Doppler changes	15	13.16
Neonatal outcome		
NICU admission	48	42.11
Ventilator required	24	21.05
Low birth weight	58	50.88
Preterm birth	66	57.89
Low APGAR (<7)	34	29.82

Of the 118 patients tested over this time period, 12 (9%) had LDH levels more than 600 IU/l. LDH levels (>600 IU/L) are statistically related with increased severity of maternal

outcomes such as HELLP syndrome and acute kidney damage.

Uric acid levels more than 6 mg/dl were found in 59 (55%) of the patients in the study group. Uric acid levels (> 6 mg/dl) are statistically related with increased severity of maternal outcomes such as HELLP syndrome. Increased uric acid levels have been linked to various adverse maternal outcomes including as eclampsia, abruption, and acute renal damage, but no statistically significant link has been discovered.

Table 4- Maternal Complications

Maternal Outcome		LDH		P value	Uric acid		P value
		< 600 IU/L	≥ 600 IU/L		< 6 mg/dL	≥ 6 mg/dL	
Eclampsia	Yes	9 (7%)	0	0.623	0	9 (7%)	0.252
	No	97 (83%)	12 (10%)		46 (43%)	50 (49%)	
HELLP syndrome	Yes	12 (10%)	12 (10%)	0.01	0	23 (19%)	0.002
	No	94 (79%)	0		46 (43%)	29 (37%)	
Abruption	Yes	2 (1%)	2 (1%)	0.137	0	5 (3%)	0.517
	No	104 (87%)	5 (5%)		46 (43%)	61 (51%)	
PPH	Yes	5 (5%)	2 (1%)	0.163	2 (1%)	4 (3%)	0.972
	No	101 (85%)	9 (7%)		50 (41%)	61 (51%)	
Acute renal failure	Yes	5 (5%)	5 (5%)	0.03	0	9 (7%)	0.249
	No	101 (85%)	7 (6%)		46 (43%)	50 (49%)	
Pulmonary edema	Yes	5 (5%)	2 (6%)	0.392	2 (1%)	4 (3%)	0.993
	No	104 (87%)	9 (9%)		50 (41%)	61 (51%)	
Mode of delivery	Vaginal	42 (36%)	7 (5%)	0.359	28 (23%)	21 (19%)	0.162
	LSCS	64 (53%)	4 (5%)		23 (19%)	45 (39%)	

Just 7% of the 57 patients (50%) with a birth weight of <2 kg had LDH > 600 IU/L. There was no statistically significant relationship between rising LDH levels and perinatal outcomes. However higher uric acid levels were shown to have statistically significant connection with several perinatal outcomes including low birth weight, preterm, poor APGAR scores, NICU hospitalisations.

Table 5- Correlation between adverse perinatal outcome & levels of LDH & uric acid

Maternal Outcome		LDH		P value	Uric acid		P value
		< 600 IU/L	≥ 600 IU/L		< 6 mg/L	≥ 6 mg/L	
Birth weight <2 kg	Yes	50 (43%)	7 (7%)	0.521	12 (11%)	45 (39%)	0.001
	No	56 (47%)	4 (3%)		40 (33%)	21 (19%)	
Preterm	Yes	59 (51%)	9 (9%)	0.292	21 (17%)	47 (41%)	0.03
	No	47 (39%)	2 (1%)		31 (27%)	18 (15%)	
APGAR >7	Yes	13 (25%)	4 (3%)	0.474	7 (6%)	28 (23%)	0.04
	No	52 (45%)	7 (7%)		38 (32%)	38 (33%)	
NICU admission	Yes	40 (35%)	9 (8%)	0.183	7 (6%)	42 (35%)	0.02
	No	66 (53%)	2 (2%)		45 (39%)	24 (21%)	
Intra uterine death	Yes	14 (11%)	2 (1%)	0.965	7 (6%)	0	0.217
	No	92 (79%)	9 (9%)		45 (39%)	66 (57%)	

DISCUSSION

Preeclampsia is an idiopathic multisystem illness that occurs only during pregnancy. To avoid it, we must detect the sickness as soon as possible. Since the trinity of high blood pressure, oedema, and albuminuria is not specific nor sensitive enough, the hunt for a dependable marker is underway.

In present study average age was 27.21 ± 6.15 years, ranging from 18 to 42 years. The vast majority (90%) of them were between the ages of 20 and 35. Preeclampsia was most prevalent (60%) in primigravida, which is consistent with previous research.8

Increased levels of LDH were shown to be related with poor maternal outcomes in this investigation. Maternal problems increased statistically significantly with rising LDH levels (P 0.001). In contrast, we found no statistically significant link between postpartum hemorrhage and greater LDH levels in patients.

In the study of Qublan HS et al.,9 severely preeclamptic women with LDH levels of >800 IU/l had a significant increase in complications in terms of abruption placenta, postpartum hemorrhage, and other complications compared to women with lower serum LDH levels. level of LDH (>1,400 IU/l) was shown to have a high predictive value for significant maternal morbidity. In a study conducted by Martin JN Jr Cantanzerite et al.8 discovered that a subset of individuals with higher LDH levels exhibited hemolysis, HELLP syndrome characteristics, and were at significant risk for maternal morbidity. The findings of these investigations were congruent with our findings.

There was no statistically significant relationship between rising levels of LDH and manner of delivery in our research. 42% of women gave birth vaginally, whereas 58% had LSCS. Sreelatha S et al.10 discovered that 54 (90%) of the women had LSCS, whereas 6 (10%) delivered vaginally. The increasing caesarean rates were ascribed to concerns that the period between induction and delivery may fluctuate, resulting in deteriorating mother and neonatal outcomes.

According to Sarada et al.,11 patients with LDH levels more than 800 had a higher risk of serious maternal problems such as abruption 15%, eclampsia 26%, HELLP 10%, acute renal failure 5.2%, pulmonary oedema 10%, DIC 15%, newborn difficulties 42%, and neonatal fatalities 26%. It was determined that increased LDH levels were associated with worse mother and fetal outcomes.

Higher blood LDH levels, according to Jaiswar SP et al,12 was related with an increased risk of perinatal fatalities, premature births, IUGR, and LBW. With rising serum LDH levels, there was a substantial increase in perinatal mortality (P 0.001). When LDH levels >600 IU/l were found in preeclampsia moms, perinatal death was 48(55.8%), IUGR was 19(47.5%), LBW 1.5Kg was 26(74.2%), and premature delivery was 40(62.5%).

In their investigations, He S et al.13 and Ababio et al.14 found that LDH is a prognostic sign for small for gestational age newborns in the preeclamptic group, particularly in those with normal liver functions. Yet the connection between LDH and birth weight in preeclampsia seemed to be concentration dependent, requiring predictors such as p H, platelet count, and diastolic blood pressure for causality. Bera et al.15 shown that LDH is a strong predictor of preeclampsia severity and poor fetal outcomes.

In contrast to the previous research, there was an increase in perinatal morbidity in our study in terms of low birth weight less than 2 kg, preterm deliveries, low APGAR 7, and NICU hospitalisations with elevated levels of LDH, although none of

them were statistically significant. In our research, however, there were no newborn fatalities. There were seven occurrences of intrauterine fetal fatalities, however only one was connected with LDH levels more than 600 IU/L.

Increased uric acid levels have been linked to various adverse maternal outcomes including as eclampsia, abruption, and acute renal damage, but no statistically significant link has been discovered.There was no statistically significant relationship between rising LDH levels and perinatal outcomes. However higher uric acid levels were shown to have statistically significant connection with several perinatal outcomes including low birth weight, preterm, poor APGAR scores, NICU hospitalisations.

Koopman et al.16 discovered that elevated uric acid levels were linked to an increased risk of eclampsia. According to Kamath et al.,17 lower gestational age and higher serum uric acid levels at the onset of hypertension were significantly associated with the risk of progression to severe disease and adverse maternal and fetal outcomes such as HELLP (12%), eclampsia (2%), perinatal deaths (2%), and fetal growth restriction (20%). Each standard deviation rise in uric acid levels was related with a 2.3 fold increased risk of severe disease progression and a 1.5 fold increased risk of maternal and perinatal problems.

Uric acid is a more accurate predictor of perinatal outcomes, such as preterm delivery, low birth weight, growth limitation, and NICU hospitalisation. A careful monitoring of blood uric acid level and LDH throughout pregnancy may aid in the early diagnosis and treatment of preeclampsia, hence minimising maternal and fetal problems associated with preeclampsia.

CONCLUSIONS

The leading cause of maternal and neonatal morbidity and death is preeclampsia. High levels of uric acid and lactate dehydrogenase (LDH) are connected with unfavourable maternal and perinatal outcomes, according to the findings of this research. LDH is also a stronger indication of the severity of maternal outcomes such as HELLP syndrome, abruption, and acute kidney damage. Nevertheless, there was no correlation between LDH levels and delivery method.

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