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Original Research Article

Maternal serum lactate dehydrogenase level as a predictor of adverse pregnancy outcome in women with severe preeclampsia

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ABSTRACT

Background: Preeclampsia is a multisystem disorder causing vascular endothelial damage and leads to leakage of lactate dehydrogenase (LDH) into maternal serum. This study evaluated the serum LDH levels in severe preeclamptic women to detect any correlation with adverse pregnancy outcomes.
Methods: A prospective cohort study compared LDH levels of 68 severe preeclamptic women with 68 normotensives in the third trimester, matched for age, parity, and gestational age. The preeclamptic women were followed up until delivery to assess the maternal and neonatal outcomes. Data were analyzed with SPSS for Windows version 23. The level of significance was set at $p<0.05$.
Results: Both groups were comparable in their characteristics. The mean LDH level for severe preeclamptic group (717.40 IU/L) was higher than for the normotensive group (162.90 IU/L) and this was significant (p=0.001). Cesarean delivery was less likely when LDH was >600 compared to ≤600 (OR 0.31; p=0.049) indicating a potential protective effect. The likelihood of IUGR (OR 3.14; p=0.045), IUFD (OR 6.48; p=0.028), stillbirth (OR 7.06 p=0.007), perinatal mortality (OR 4.84; p=0.004) and low birth weight <2500 gm (OR 3.77; p=0.025) were all significantly higher with LDH levels >600 IU/L.
Conclusions: Maternal serum LDH levels were found to be significantly increased in pregnant women with severe preeclampsia compared to their normotensive counterparts, and elevated levels >600 IU/L in the third trimester was associated with adverse perinatal outcomes.

Keywords: Adverse pregnancy outcome, LDH, Severe preeclampsia

INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive disorder that develops in the second half of pregnancy and complicates 2-7% of pregnancies.[1] It is a multisystem disorder defined as new-onset hypertension and proteinuria occurring after 20 weeks of gestation in previously normotensive and non-proteinuric women.[2] It is characterized by an abnormal vascular response to placentation with increased systemic vascular resistance, a hypercoagulable state, and endothelial dysfunction.[3,4] It carries substantial risk for both fetus and mother, with a subsequent increase in perinatal and maternal morbidity and mortality.[5]

It is diagnosed by elevated blood pressure ≥140/90 mm of Hg taken on two consecutive occasions at least 6 hours apart and proteinuria after 20 weeks of gestation.[3,4] Preeclampsia is divided into two groups according to its severity as mild and severe, with a significant difference in their management. Blood pressure ≥160/110 mm of Hg and proteinuria >2 gm/24 hours urine or ≥2+ on dipstick are classed as severe preeclampsia.[6] The incidence of severe preeclampsia is estimated at 0.6-1.2% of all pregnancies.[7]

It has been shown that maternal vascular endothelial dysfunction is the key event, resulting in diverse clinical manifestations of preeclampsia.[8,9] LDH is an intracellular

enzyme, found in almost all body tissues, that converts lactic acid to pyruvic acid and an elevated level indicates cellular death and leakage of the enzyme from the cell.[10] A small quantity of LDH is always present in plasma. Normal LDH levels vary from 200 to 400 IU/L. Pregnancy itself does not affect the LDH levels. When tissues are damaged by injury or disease, there is an increase in the level of LDH in blood,[11] and as it is abundant in red blood cells, it can function as a marker for hemolysis.[12]

For a disease with the involvement of various systems, several potential candidate markers have been proposed.[13-17] Acute clinical symptoms that endanger life in pre-eclampsia correlate with the distinct activity of LDH.[18] Elevated LDH levels in preeclampsia indicate both tissue death and hemolysis.[12,19] LDH level has been suggested as a potential marker to predict the severity of preeclampsia and the indicator for multiorgan involvement.[20,21]

Previous studies have shown varying results for ability of LDH to predict adverse maternal outcomes. Some studies reported that serum LDH level increases with severity of preeclampsia and showed significant correlation with high BP and poor maternal and perinatal outcomes.[21-24] But some researchers did not find significant difference in serum LDH levels between preeclamptic women and healthy pregnant women.[25,26] This study, therefore, sought to evaluate serum LDH levels in severe preeclamptic and normotensive pregnant women and to detect any correlation between serum LDH levels and adverse maternal and fetal outcome in severe preeclamptic women. Being able to determine which woman and fetus are most at risk during severe pre-eclampsia would enable clinicians to tailor individual management more effectively and efficiently, with subsequent decrease in maternal and fetal morbidity and mortality.

METHODS

Study site/area

This study was conducted at the antenatal clinic, medical laboratory and labor ward of the Rivers State university teaching hospital (RSUTH), a tertiary hospital owned and funded by the government of Rivers State of Nigeria. The hospital provides antenatal care and delivery services for low and high-risk pregnant women and serves as a referral center for neighboring hospitals. The hospital is well equipped and has the availability of a qualified team comprising obstetricians, pediatricians, and anesthetists. There was an average annual delivery of about 1700.

Study design

An observational prospective cohort study.

Study population

Sixty-eight (68) pregnant women from 26 weeks gestation, diagnosed with severe preeclampsia in the current pregnancy, were included in the study. Another 68 participants, apparently healthy normotensive women, were recruited as control group, matching for maternal age, parity, and gestational age. All consecutive, consenting women, meeting the inclusion criteria were recruited until the sample size was achieved, and this spanned between February 2022 to September 2023.

Sample size determination

This sample size was determined using the formula by Kotrlik et al at a confidence of 95%.[27]

$$\text{n/group} = 2x\frac{(Z_\alpha+Z_\beta)^2 x s^2}{\delta^2}$$

Where:

$Z\alpha$=value for alpha of 0.025 in each tail (1.96), Z_β= 0.84 (equivalent to 80% statistical power), S=standard deviation in the difference in serum LDH level in eclamptic women and normotensive women (136.92-28.09)=108.83 according to a study by Andrews et al.[28]

δ=is the difference likely to be detected/acceptable margins of error=18.0

$n=2\times(Z_\alpha + Z_\beta)^2 * s^2 / \sigma^2$

$n=2\times(0.025 + 0.84)^2 * 108.83^2 / 18.0^2$

$n=2\times0.7482) * 11843.97 / 324$

$n=17723.32/324$

n=54.70 approx. 55

Additional 10% for attrition: total sample size=(55 + 6), approx. 61, a total sample size of 68 was used for each study group.

Eligibility criteria

All eligible and consenting pregnant women aged ≥18 years, from gestational age of 26 weeks and meeting the diagnostic criteria for severe preeclampsia, were included. Exclusion criteria included women with chronic hypertension, diabetes mellitus, renal disorders, liver disorder, epilepsy, hemolytic anemia, thyroid disease, trauma/bone fracture, and the patient's refusal to give consent.

Sampling technique

Consecutive women with severe preeclampsia were recruited into the study until the sample size was achieved. The normotensive pregnant women were recruited at intervals based on the characteristics of the cases, matching for maternal age, gestational age, and parity. Nulliparous women with preeclampsia were matched with

apparently healthy nulliparous controls, while women with higher parities were matched within the intervals of para 1-3 and ≥4.

Study procedure

After an initial assessment in the antenatal clinic, or labour ward, for suitability, eligible women (cases and controls) were educated about the study, and informed consent obtained. A proforma was used to collect information on sociodemographic, past obstetric, and medical history. A systemic and obstetric examination was then done. Every participant had a dipstick urinalysis for proteinuria done and their blood pressure recorded using a calibrated mercury column sphygmomanometer and Littmann classic III stethoscope (with the woman seated and after a rest period of five minutes) by a resident doctor to reconfirm the initial findings. Severe preeclampsia was diagnosed when blood pressure was ≥160/110 mm of Hg or proteinuria ≥2+. Each participant had their blood sample taken for estimation of serum LDH levels in the hospital laboratory using clinical chemistry analyzer (Mindray BS-200 fully auto; Shenzhen Mindray bio-medical electronics Co. LTD, China). Treatment was started as indicated, using antihypertensives and sedatives.

All the severe preeclamptic women were monitored closely to note worsening clinical parameters, development of imminent eclampsia, pulmonary edema, HELLP syndrome, and fetal growth/wellbeing. Also, a note was made about the mode of delivery, gestational age at delivery, birth weight of baby, Apgar score, admission to neonatal intensive care unit (NICU), and perinatal morbidity and mortality. Because levels of serum LDH <400 IU/L are common in normal pregnancy and only levels >600 IU/L were reported to be associated with complications, the severe preeclamptic women were divided into three categories based on serum LDH levels (<400, 400-600, and >600 I.U/L) and analyzed as a Cohort.[29] They were compared in terms of sociodemographic variables, and fetomaternal outcomes.

Data collection instruments

A structured proforma was used to collect data from each participant. This included personal information (age and parity), complications in current pregnancy (eclampsia, acute renal failure, HELLP syndrome, intrauterine growth restriction (IUGR), intrauterine fetal death (IUFD), abruptio placenta, primary postpartum haemorrhage (PPH), maternal mortality), and fetal outcome (gestational age (GA) at delivery, birth weight, asphyxia (Apgar score <7 at 5 mins), NICU admission, perinatal mortality).

Data analysis

Coded data was entered into an excel spreadsheet and analyzed with SPSS (statistical package for social sciences) for Windows version 23 software (SPSS Inc., Chicago, IL, USA). The initial analysis examined the baseline characteristics of the women to check the comparability of the groups. The mean LDH levels of the preeclamptic and normotensive women was compared. The differences in sociodemographic and pregnancy outcomes, and serum LDH parameters of the preeclamptic group were evaluated using student's t test for quantitative, and Mann-Whitney, Chi-square, or Fischer's exact tests for categorical variables, as appropriate. The level of significance was set at 5%. Independent variables were analyzed using bivariate analysis, and the variables with an association were fitted into a multivariate logistics regression analysis.

RESULTS

An examination of the baseline characteristics of the participants is provided in Table 1 and reveals the comparability of both groups. The mean maternal age of the severe preeclamptic women was 32.13±5.74 with a range of 18-45 years, while that of the normotensive control was 32.72±5.59 with a range of 18-42 years, and the difference was not statistically significant (p=0.546). The median parity was 1 for both groups, with no statistically significant difference (p=0.784) in the distribution. Likewise, no statistically significant difference was observed between both groups in terms of gestational age distribution (p=0.841) with a mean of 33.84±4.56 and 34.74±3.98 for the severe preeclamptic and normotensive group respectively. However, a significant difference was observed in the levels of LDH with more of the severe preeclamptic women having LDH levels above 400 compared to the controls. The mean LDH level for severe preeclamptic group (717.40 IU/L) was substantially higher than for the normotensive group (162.90 IU/L) and this difference was statistically significant (p=0.001).

The analysis presented in Table 2 compares the associations between LDH levels and various maternal characteristics and pregnancy complications among the severe preeclamptic women. Two of the women were lost to follow up and only 66 women were analyzed. Regarding maternal age, parity, and gestational age at delivery, there were no significant differences observed between severe preeclamptic women with LDH levels <400, 400- 600 and >600 (p=0.788, 0.207, and 0.455 respectively). Majority of the women, 50(75.8%), had cesarean delivery (CD) while only 16 had spontaneous vaginal delivery (SVD), but the proportion that had SVD increased with rising LDH levels, from 6.25% to 31.25% and 62.50% for LDH levels <400, 400-600 and >600 respectively, the differences in the mode of delivery between the LDH groups was statistically significant (p=0.026). Pregnancy complications showed varied associations with LDH levels, with a notable significant difference (p=0.03) observed for intrauterine fetal death (IUFD), with increasing proportion of 0.0%, 22.22% and 77.78% occurring with increase in the LDH group from <400, to 400-600 and >600 respectively. There was no significant difference between the three LDH groups in the

occurrence of IUGR (p=0.124), fetal distress (p=0.652) and others (p=0.545) which included abruptio placenta, eclampsia, and oligohydramnios.

While all the severe preeclamptic mothers in this study survived, there were 13 stillbirths (SB) and 53 live births as depicted in Table 3, giving an SB rate of 19.7%. LDH levels showed a significant association with stillbirths (p=0.011), with increasing proportion of 7.69% to 15.38% and 76.92% occurring in the <400, 400-600 and >600 LDH groups respectively. Of the live births 10 babies had early neonatal death (ENND), giving a total perinatal mortality of 23 (34.8%). The perinatal mortality was also significantly higher (p=0.012) with increasing LDH levels. There were no statistically significant differences in other perinatal outcomes between the <400, 400-600 and >600 LDH groups in terms of fetal birth weight categorization (p=0.176), perinatal asphyxia (p=0.293), NICU admission (p=0.524), preterm LBW (p=0.948), small for gestational age (SGA) babies (p=0.378), and others (p=0.127) made up of macrosomia (1) and HIV exposure (1).

The data were further analyzed in a bivariate logistics regression along LDH levels categorized as >600 and ≤600 against maternal characteristics and pregnancy complication (Table 4), as well as perinatal outcomes (Table 5). For the mode of delivery, CD was found to be less in the >600 LDH group as compared to the ≤600 group (p=0.044). Pregnancy complications such as IUGR (p=0.041) and IUFD (p=0.015) occurred more in the LDH >600 group compared to LDH ≤600 group. With regards to perinatal outcomes, the occurrence of stillbirth (p=0.005), poor baby outcome (p=0.003) and lower fetal birth weight (p=0.048) were all significantly higher in the LDH >600 group.

Table 6 shows a multivariate logistics regression analysis using crude odds ratios for maternal and perinatal outcomes based on LDH levels >600 among the severe preeclamptic women. Cesarean delivery was found to be less likely in the >600 LDH group as compared to the reference (SVD) with an odds ratio (OR) of 0.31 (p=0.049), indicating a potential protective effect the higher the LDH level.

The likelihood of IUGR (OR 3.14; p=0.045), IUFD (OR 6.48; p=0.028), stillbirth (OR 7.06 p=0.007), perinatal mortality (OR 4.84; p=0.004) and low birth weight <2500 gm (OR 3.77; p=0.025) were all significantly higher in the >600 LDH group. After adjusting for confounding variables (Table 7), we found a statistically significant correlation between IUGR and maternal serum LDH level >600 IU/L (OR 19.08; p=0.013); intrauterine growth restriction was 19-fold more likely to occur in severe preeclamptic pregnancies when the LDH level was >600 IU/L.

Table 1: Distribution of participant characteristics and LDH values among severe preeclamptic and normotensive women.

Variables	Groups		χ2 (P value)
	Cases (Preeclamptic), (n=68) (%)	Control (Normotensive), (n=68) (%)	
Maternal age (In years)			
18-25	10 (14.71)	8 (11.76)	
26-34	35 (51.47)	31 (45.59)	1.16 (0.561)
≥35	23 (33.82)	29 (42.65)	
Mean ± SD	32.13±5.74	32.72±5.59	0.60 μ
Range	(18-45)	(18-42)	(0.546)
Parity			
0	31 (45.59)	28 (41.18)	
1-3	31 (45.59)	35 (51.47)	0.49 (0.784)
≥4	6 (8.82)	5 (7.35)	
Median (IQR)	1.0 (0-2.5)	1.0 (0-2.0)	0.059α
Gestational age (In weeks)			
<37	51 (75.0)	52 (76.47)	0.040
≥37	17 (25.0)	16 (23.53)	(0.841)
Mean ± SD	33.84±4.56	34.74±3.98	1.22 μ
Range	(26-41)	(26-41)	(0.224)
LDH level			
<400	22 (32.35)	65 (95.59)	
400-600	19 (27.94)	3 (4.41)	0.001*γ
>600	27 (39.71)	0 (0.0)	
Mean ± SD	717.40±425.19	162.90±108.09	10.42 μ
Range	(115.0-1630.0)	(30.0-421.0)	(0.001)*

*Statistically significant (p≤0.5); χ2=Chi-square; γ=Fisher's Exact p: μ=Student t test; IQR=Interquartile range; α=Mann-Whitney test.

Table 2: Comparison of maternal characteristics and pregnancy complications based on LDH levels among the severe preeclamptic women.

Variables	LDH			Total, (n=66)	χ2 (P value)
	<400, (n=22) (%)	400-600, (n=17) (%)	>600, (n=27) (%)		
Maternal age (In years)					
18-25	4 (40.0)	2 (20.0)	4 (40.0)	10 (100.0)	0.788γ
26-34	10 (29.41)	11 (32.35)	13 (38.24)	34 (100.0)	
≥35	8 (36.36)	4 (18.18)	10 (45.45)	22 (100.0)	
Parity					
0	9 (30.0)	7 (23.33)	14 (46.67)	30 (100.0)	0.207γ
1-3	13 (41.94)	9 (29.03)	9 (29.03)	31 (100.0)	
≥4	0 (0.0)	1 (20.0)	4 (80.0)	5 (100.0)	
Gestational age (In weeks)					
<37	16 (32.65)	11 (22.45)	22 (44.90)	49 (100.0)	1.57 (0.455)
≥37	6 (35.29)	6 (35.29)	5 (29.41)	17 (100.0)	
Mode of delivery					
CD	21 (42.0)	12 (24.0)	17 (34.0)	50 (100.0)	0.026*γ
SVD	1 (6.25)	5 (31.25)	10 (62.50)	16 (100.0)	
Pregnancy complications					
IUGR					
Yes	4 (22.22)	3 (16.67)	11 (61.11)	18 (100.0)	0.124γ
No	18 (37.5)	14 (29.17)	16 (33.33)	48 (100.0)	
IUFD					
Yes	0 (0.0)	2 (22.22)	7 (77.78)	9 (100.0)	0.03*γ
No	22 (38.60)	15 (26.32)	20 (35.09)	57 (100.0)	
Foetal distress					
Yes	3 (50.0)	1 (16.67)	2 (33.33)	6 (100.0)	0.652γ
No	19 (31.67)	16 (26.67)	25 (41.67)	60 (100.0)	
Others					
Yes	4 (36.36)	4 (36.36)	3 (27.27)	11 (100.0)	0.545γ
No	18 (32.73)	13 (23.64)	24 (43.64)	55 (100.0)	

*Statistically significant (p≤0.5); χ2=Chi-Square; γ=Fisher's Exact p.

Table 3: Comparison of perinatal outcomes based on LDH levels among the severe preeclamptic women.

Variables	LDH			Total (n=66)	χ2 (P value)
	<400, (n=22) (%)	400-600, (n=17) (%)	>600, (n=27) (%)		
Baby status					
Live birth	21 (39.62)	15 (28.30)	17 (32.08)	53 (100.0)	0.011*γ
Stillborn (SB)	1 (7.69)	2 (15.38)	10 (76.92)	13 (100.0)	
Baby weight (gm)					
<2500	12 (27.91)	9 (20.93)	22 (51.16)	43 (100.0)	0.176γ
2500-3900	8 (40.0)	7 (35.0)	5 (25.0)	20 (100.0)	
≥4000	2 (66.67)	1 (33.33)	0 (0.0)	3 (100.0)	
Apgar score					
Normal	18 (43.90)	12 (29.27)	11 (26.83)	41 (100.0)	0.293γ
Asphyxia	3 (25.0)	3 (25.0)	6 (50.0)	12 (100.0)	
NICU admission					
Yes	13 (39.39)	7 (21.21)	13 (39.39)	33 (100.0)	0.524γ
No	9 (27.27)	10 (30.30)	14 (42.42)	33 (100.0)	
Fetal complications					
Preterm LBW					
Yes	9 (34.62)	7 (26.92)	10 (38.46)	26 (100.0)	0.11 (0.948)
No	13 (32.50)	10 (25.0)	17 (42.50)	40 (100.0)	
Small gestational age (SGA)					
Yes	2 (40.0)	0 (0.0)	3 (60.0)	5 (100.0)	0. 378γ
No	20 (32.79)	17 (27.87)	24 (39.34)	61 (100.0)	

Continued.

Variables	LDH			Total (n=66)	χ2 (P value)
	<400, (n=22) (%)	400-600, (n=17) (%)	>600, (n=27) (%)		
Others					
Yes	2 (100.0)	0 (0.0)	0 (0.0)	2 (100.0)	0.127γ
No	20 (31.25)	17 (26.56)	27 (42.19)	64 (100.0)	
Baby outcome					
Alive	18 (41.86)	13 (30.23)	12 (27.91)	43 (100.0)	0.012*γ
Dead (SB+ENND)	4 (17.39)	4 (17.39)	15 (65.22)	23 (100.0)	

*Statistically significant (p≤0.5); χ2=Chi-Square; γ=Fisher's Exact p.

Table 4: Association between maternal characteristics and pregnancy complications with LDH levels >600 among the severe preeclamptic women.

Variables	LDH		Total, (n=66)	χ2 (P value)
	>600 (n=27), (%)	≤600 (n=39), (%)		
Maternal age (In years)				
18-25	4 (40.0)	6 (60.0)	10 (100.0)	0.864γ
26-34	13 (38.24)	21 (61.76)	34 (100.0)	
≥35	10 (45.45)	12 (54.55)	22 (100.0)	
Parity				
0	14 (46.67)	16 (53.33)	30 (100.0)	0.068γ
1-3	9 (29.03)	22 (70.97)	31 (100.0)	
≥4	4 (80.0)	1 (20.0)	5 (100.0)	
Gestational age (in weeks)				
<37	22 (44.90)	27 (55.10)	49 (100.0)	1.25 (0.263)
≥37	5 (29.41)	12 (70.59)	17 (100.0)	
Mode of delivery				
CD	17 (34.0)	33 (66.0)	50 (100.0)	4.0728 (0.044)*
SVD	10 (62.50)	6 (37.50)	16 (100.0)	
Pregnancy complications				
IUGR				
Yes	11 (61.11)	7 (38.89)	18 (100.0)	4.18 (0.041)*
No	16 (33.33)	32 (66.67)	48 (100.0)	
IUFD				
Yes	7 (77.78)	2 (22.22)	9 (100.0)	0.015*γ
No	20 (35.09)	37 (64.91)	57 (100.0)	
Fetal distress				
Yes	2 (33.33)	4 (66.67)	6 (100.0)	1.00γ
No	25 (41.67)	35 (58.33)	60 (100.0)	
Others				
Yes	3 (27.27)	8 (72.73)	11 (100.0)	0.503γ
No	24 (43.64)	31 (56.36)	55 (100.0)	

*Statistically significant (p≤0.5); χ2=Chi-Square; γ=Fisher's Exact p.

Table 5: Association between perinatal outcomes with LDH levels >600 among the severe preeclamptic women.

Variables	LDH		Total, (n=66)	χ2 (P value)
	>600 (n=27) (%)	≤600 (n=39) (%)		
Baby status				
Live birth	17 (32.08)	36 (67.92)	53 (100.0)	0.005*γ
Stillborn (SB)	10 (76.92)	3 (23.08)	13 (100.0)	
Baby weight (gm)				
<2500g	22 (51.16)	21 (48.84)	43 (100.0)	0.048*γ
2500-3900	5 (25.0)	15 (75.0)	20 (100.0)	
≥4000	0 (0.0)	3 (100.0)	3 (100.0)	
Apgar score				
Normal	11 (26.83)	30 (73.17)	41 (100.0)	2.29 (0.130)
Asphyxia (<7)	6 (50.0)	6 (50.0)	12 (100.0)	

Continued.

Variables	LDH		Total, (n=66)	χ2 (P value)
	>600 (n=27) (%)	≤600 (n=39) (%)		
NICU				
Yes	13 (39.39)	20 (60.61)	33 (100.0)	0.063 (0.802)
No	14 (42.42)	19 (57.58)	33 (100.0)	
Fetal complications				
Preterm LBW				
Yes	10 (38.46)	16 (61.54)	26 (100.0)	0.11 (0.744)
No	17 (42.50)	23 (57.50)	40 (100.0)	
Small gestational age (SGA)				
Yes	3 (60.0)	2 (40.0)	5 (100.0)	0.82 (0.366)
No	24 (39.34)	37 (60.66)	61 (100.0)	
Others				
Yes	0 (0.0)	2 (100.0)	2 (100.0)	0.509γ
No	27 (42.19)	37 (57.81)	64 (100.0)	
Baby outcome				
Alive	12 (27.91)	31 (72.09)	43 (100.0)	8.63 (0.003)*
Dead (SB+ENND)	15 (65.22)	8 (34.78)	23 (100.0)	

*Statistically significant (p≤0.5); χ2=Chi-Square; γ=Fisher's Exact p.

Table 6: Bivariate logistics regression using crude odds ratios for maternal and perinatal outcomes based on LDH levels >600 among the severe preeclamptic women.

Variables	LDH		cOdds ratio, (95% CI)	P value
	>600, (n=27) (%)	≤600, (n=39) (%)		
Mode of delivery				
CD	17 (34.0)	33 (66.0)	0.31 (0.096-0.995)	0.049*
SVD[R]	10 (62.50)	6 (37.50)		
IUGR				
Yes	11 (61.11)	7 (38.89)	3.14 (1.02-9.65)	0.045*
No [R]	16 (33.33)	32 (66.67)		
IUFD				
Yes	7 (77.78)	2 (22.22)	6.48 (1.22-34.16)	0.028*
No [R]	20 (35.09)	37 (64.91)		
Baby status				
Stillborn (SB)	10 (76.92)	3 (23.08)	7.06 (1.72-29.01)	0.007*
Live birth [R]	17 (32.08)	36 (67.92)		
Baby weight (gm)				
<2500	22 (51.16)	21 (48.84)	3.77 (1.19-11.98)	0.025*
≥2500g [R]	5 (21.74)	18 (78.26)		
Baby outcome				
Dead (SB+ENND)	15 (65.22)	8 (34.78)	4.84 (1.63-14.36)	0.004*
Alive [R]	12 (27.91)	31 (72.09)		

*Statistically significant (p≤0.5); cOR=Crude odds ratio; [R]=Reference value

Table 7: Multivariate logistics regression using adjusted odds ratios for maternal and perinatal outcomes based on LDH levels >600 among the severe preeclamptic women.

Variables	LDH		aOdds ratio (95% CI)	P value
	>600, (n=27) (%)	≤600, (n=39) (%)		
Mode of delivery				
CD	17 (34.0)	33 (66.0)	0.89 (0.12-6.57)	0.917
SVD [R]	10 (62.50)	6 (37.50)		
IUGR				
Yes	11 (61.11)	7 (38.89)	19.08 (1.86-195.56)	0.013*
No[R]	16 (33.33)	32 (66.67)		
IUFD				
Yes	7 (77.78)	2 (22.22)	0.97 (0.042-22.50)	0.987
No[R]	20 (35.09)	37 (64.91)		

Continued.

Variables	LDH		aOdds ratio (95% CI)	P value
	>600, (n=27) (%)	≤600, (n=39) (%)		
Baby status				
Stillborn (SB)	10 (76.92)	3 (23.08)	8.59 (0.49-149.33)	0.140
Live birth [R]	17 (32.08)	36 (67.92)		
Baby weight (gm)				
<2500	22 (51.16)	21 (48.84)	0.27 (0.02-3.35)	0.309
≥2500[R]	5 (21.74)	18 (78.26)		
Baby outcome				
Dead (SB+ENND)	15 (65.22)	8 (34.78)	5.63 (0.56-56.92)	0.143
Alive [R]	12 (27.91)	31 (72.09)		

*Statistically significant (p≤0.5); aOR=Adjusted Odds Ratio; [R]=Reference value.

DISCUSSION

We conducted a matched case-control analysis to compare the serum LDH levels in severe preeclamptic women and normotensive controls. The participants were matched as regards maternal age, parity, and gestational age at delivery. As was expected, we found no significant difference in these characteristics between both groups, and therefore, both groups were comparable and the difference in LDH levels found is not likely attributable to other extraneous factors.

This study found a significantly higher serum LDH level among the severe preeclamptic women compared with matched normotensive women, with a mean LDH level of 717.40 IU/L and 162.90 IU/L respectively. Similar findings have been reported by other studies. Qublan et al reported 774.9 and 299 IU/L for severe preeclamptic and normotensives respectively, while Bhati et al reported 629.7 and 169.3 and Deshmukh et al reported 646.79 and 280.98 respectively for severe preeclamptic and normotensives. These studies that compared the LDH levels in women with varying severity of the disease have also reported a significant rise in LDH levels with increasing severity of preeclampsia.[23,30,31]

We then proceeded to analyze the cohort of severe preeclamptic women according to their level of serum LDH. This study found a significant association between LDH levels and the mode of delivery in these women, with cesarean delivery less likely to occur with LDH levels >600 IU/L, which suggest a possible protective effect. This was contrary to a previous study that reported significantly higher CD rate with higher levels of LDH, as it was expected that, with increase in severity of the disease, the maternal morbidity including CD will increase.[31] Unlike that study, that included all degrees of severity of preeclampsia in their analysis, our study only included cases of severe preeclampsia, and coupled with the high proportion of CD cases (75.8%) in our study, may explain our observation. Moreover, the severity of the blood pressure and adequacy of control measures, as well as many other factors influence the decision to deliver these women by cesarean section.

Significant results were obtained from analysis of the perinatal outcomes among the severe preeclamptic women on the basis of LDH levels. Severely preeclamptic women with LDH levels >600 IU/L showed a significant increase in IUGR (3-fold), IUFD (6-fold), low birth weight babies (3-fold), stillbirth (7-fold) and overall perinatal mortality (4-fold) compared to those with LDH levels ≤600 IU/L. After adjusting for confounding variables, we found IUGR to be the most important factor associated with these findings. Qublan et al reported a 5-fold increase in perinatal mortality, with prematurity and IUGR as the most important risk factor responsible for the increase.[23] Despite the cut-off of serum LDH level applied (>600 or >800), similar poor perinatal outcomes have been reported by Jaiswar et al, Bhati et al, Deshmukh et al, Kharb et al, Dave et al, Moharana et al, and Jharia et al.[24,30-35] These poor perinatal outcomes are indicative of chronic hypoxia in the fetus, as a result of placental insufficiency and hypoperfusion, resulting from endothelial dysfunction.

We did not find any significant difference following comparison of the mean gestational age at delivery, as well as maternal age and parity, on the basis of LDH levels, suggestive that these factors are not predictive for severity of the disease, and this has been corroborated by other studies.[23,30,32]

CONCLUSION

Maternal serum LDH levels were found to be significantly increased in pregnant women with severe preeclampsia compared to their normotensive counterparts, and elevated levels >600 IU/L in the third trimester was associated with adverse perinatal outcomes. Detection of increased LDH levels should warrant close monitoring and appropriately timed delivery to decrease the occurrence of serious adverse outcomes.

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