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Original Research Article

Lactate dehydrogenase levels in preeclampsia and its correlation with maternal and perinatal outcome

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ABSTRACT

Background: Hypertensive disorder of pregnancy occurs in approximately 6-8% of all pregnancies. The most serious consequences for the mother and the baby are the result of preeclampsia and eclampsia. Lactate Dehydrogenase (LDH) is an intracellular enzyme. Recently LDH has been suggested as potential marker to predict severity of pre-eclampsia. The objective of the present study was to compare the serum lactate dehydrogenase levels in women with preeclampsia and normal pregnant women and to correlate lactate dehydrogenase levels with maternal and perinatal outcome in preeclampsia.

Methods: An observational prospective study was conducted on 200 antenatal women attending the labour room emergency. Women with singleton pregnancy and cephalic presentation, from 28 weeks onwards were enrolled in the study. Out of 200, 100 were normal pregnant women and 100 were preeclamptic women. Serum LDH levels were measured in all women and maternal and perinatal outcome was assessed in terms of LDH levels.

Results: Higher levels of LDH was observed in pregnant women with preeclampsia (627.38±230.04 IU/l) as compared to normal pregnant women (224.43±116.61 IU/l). The maternal complications were found to be maximum in women with LDH > 800 IU/l. Abruption was the most common complication. The perinatal mortality and neonatal deaths were found to have significant correlation with high LDH levels.

Conclusions: Maternal and perinatal complications were associated with higher LDH levels in preeclampsia patients. Serum LDH levels can be offered to all patients of preeclampsia and can be used to predict the prognosis of preeclampsia.

Keywords: Maternal outcome, Lactate dehydrogenease, Preeclampsia, Perinatal outcome

INTRODUCTION

Preeclampsia is a multisystem disorder which complicates 5-8% of all pregnancies.[1] It is still regarded as disease of theories and its etiology has been poorly understood. There is increasing evidence that endothelial cell and altered endothelial cell function play an important role in the pathogenesis of preeclampsia.[2]

Preeclampsia account for approximately 63,000 maternal deaths annually worldwide.[3] In developed countries, the maternal death rate is reportedly 0-1.8%. The maternal mortality rate is as high as 14% in developing countries.[4,5] The fetal mortality rate varies from 13-30%. In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women.[6,7] Studies have shown that LDH activity and gene expression are higher in placentas of pre-eclampsia than normal pregnancy.[8,9]

The effects of LDH in pregnancy related complications like preeclampsia is now gaining attention. LDH is an intracellular enzyme and its level is increased in these

women due to cellular death. Though cellular enzymes in the extracellular space have no metabolic function, they are still of benefit because they serve as indicators suggestive of disturbance of cellular integrity induced by pathological conditions and is used to detect cell damage or cell death.

So, serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease.[10]

The major stimulants for LDH and its product, lactate, are pH and hypoxia. Hypoxia, when encountered in preeclampsia, increases glycolytic rate thereby increasing the activity of LDH which catalyses' the reversible reaction of pyruvate to lactate.[11-12]

This reaction largely occurs in anaerobic glycolysis (or hypoxic conditions) indicating fatigue in normal persons as lactate accumulates.

During fatigue or after strenuous exercise, serum proteins (e.g., LDH, aspartate aminotransferase, alanine amino transferase, albumin, and creatinine) have also been reported to change. In extreme cases or disease situations, cell death ensues as leakage of LDH outside of the cell occurs.[11-14]

Preeclampsia produces potentially lethal complications including placental abruption, hepatic failure, acute Renal failure and cardiovascular collapse. The analysis of a combination of biomarkers particularly markers related to vascular dysfunction such as LDH may enrich the ability to predict and prevent preeclampsia in near future.[15]

So the present study is aimed at comparing the LDH levels in normotensive and pre-eclamptic women and to correlate its levels with maternal and perinatal outcome in pre-eclampsia.

METHODS

This observational prospective study was conducted on 200 antenatal women who attended the labour room emergency in the department of Obstetrics and Gynaecology in collaboration with Department of Biochemistry at Pt. B.D. Sharma, PGIMS, Rohtak. Antenatal women with singleton pregnancy and cephalic presentation, from 28 weeks onwards were enrolled in the study randomly by computer generated randomization

Sample size was calculated using the formula :

n = 2Cp, power

d2

where

n was the number of subjects required in each group.

d was the standardized difference and

C p, power was the constant defined by the values chosen for the p-value and power.

Exclusion criteria

- Women with chronic hypertension, medical disorders and taking hepatotoxic drugs were excluded from the study.

Women were divided into two groups:

Group I comprised of 100 pregnant women with preeclampsia (study group) and were further subdivided into three categories on the basis of LDH levels.

- A: < 600 IU/l
- B: 600-800 IU/l
- C: >800 IU/l

Group II comprised of 100 normotensive pregnant women (control group).

Serum lactate dehydrogenase levels was estimated in all the subjects. Collection of blood sample for estimation of LDH levels: Four ml venous blood was drawn under aseptic precautions from all subjects in a red vacutainer from antecubital vein. Serum was separated by centrifugation and used for estimation of LDH levels enzymatically by autoanalyzer.

Subjects were followed till delivery and discharge from the hospital. LDH levels of both the groups were compared and association of maternal and perinatal outcome was assessed in relation to LDH levels.

Statistical analysis

Statistical analysis was made using SPSS version 21.0, categorical data was compared between two groups by using Chi-square/Fisher exact test and quantitative data was compared by Student t-test. For multi-group comparison, One-way analysis of variance (ANOVA) was used.

RESULTS

Out of 100 preeclamptic women, 51 were mild preeclampsia and 49 were severe preeclampsia. The demographic profile of women with pre-eclmapsia and the normotensive women was similar in terms of age, parity and socioeconomic status as shown in Table 1. The maximum number of women belonged to the age group of 20-25 years followed by 25-30 years. Majority of women belonged to lower middle class followed by upper middle class and were nullipara. The maximum number of women in both the groups were unbooked (62% in study group and 65% in control group) and the difference was statistically insignificant (p>0.05). The mean LDH

levels were significantly higher in women with preeclampsia as compared to normotensive women as depicted in Table 2.

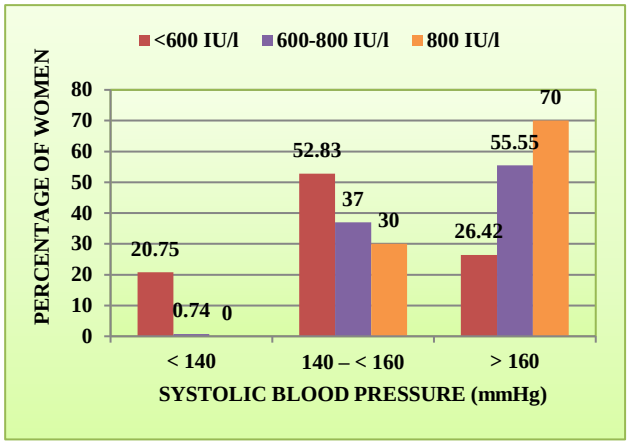

Figure 1: Association of systolic blood pressure and serum LDH levels.

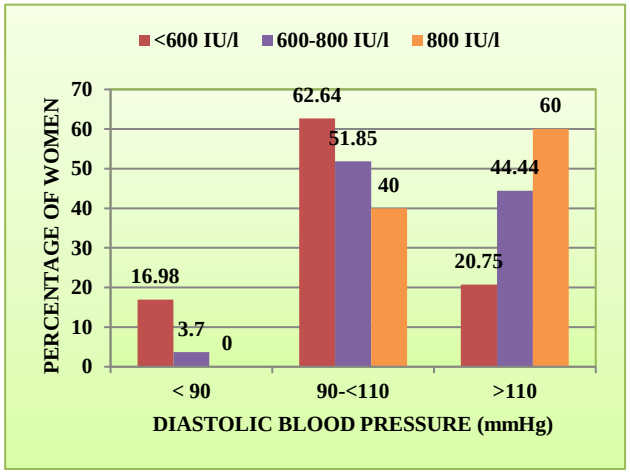

Figure 2: Association of diastolic blood pressure and serum LDH levels.

Table 3 shows the distribution of women with preeclampsia according to LDH levels into mild and severe eclampsia and there was significant increase in number of women with severe preeclampsia with higher LDH levels. The association of systolic and diastolic blood pressure with LDH levels is shown in Figure 1 and 2. Symptoms noted in the women with pre-eclmapsia were headache, blurring of vision, epigastric pain and nausea and vomiting. Headache was the most frequent symptom of pre-eclampsia. Though the symptoms were higher in patients with LDH levels >600 IU/l, there was no statistically significant difference (p >0.05) except blurred vision (p <0.01). Majority of women with preeclampsia (73.58%) with LDH levels <600 IU/l delivered vaginally. Among women with LDH levels > 600IU/l, 65.9% had ceasarean and rest delivered vaginally. The rate of caesarean section increased with LDH levels >600 IU/l and was statistically significant (p <0.001).

Table 1: Demographic profile.

	Group I (Study) N(%)	Group II (Control) N (%)	Statistical significance (p value)
Mean age ±SD (years)	24.38±3.68	25±2.99	>0.05 NS 95% CI -0.32 to 1.56
Parity			
P0	61 (61%)	43 (43%)	>0.05 NS
P1	28 (28%)	34 (34%)	
P2	6 (6%)	17 (17%)	
P3	3 (3%)	4 (4%)	
>P4	2 (2%)	2 (2%)	
Socioeconomic status			
Lower	6 (6%)	18 (18%)	p=0.06 >0.05 NS
Upper lower	13 (13%)	13 (13%)	
Lower middle	53 (53%)	43 (43%)	
Upper middle	28 (28%)	26 (26%)	

Table 2: Mean LDH levels in both groups.

Group I (Study) LDH levels		Group II (Control) LDH levels	Statistical significance (p value)
Mild preeclampsia	**Severe preeclampsia**		
531.73±168.33 IU/l	726.93±244.53 IU/l	224.43±116.61 IU/l	<0.01 HS 95% CI -453.81 to -352.09
Total mean = 627.38±230.04 IU/l			

HS: Highly significant

Table 3: Distribution according to LDH levels in study group.

LDH range (IU/l)	Mild preeclampsia (n=51)	Severe preeclampsia (n=49)	Total preeclampsia (n=100)	Statistical significance (p value)
< 600	35(66.03%)	18(33.96%)	53	<0.001 Sig.
600 to 800	11(40.7%)	16(59.2%)	27	>0.05 NS
> 800	5(25%)	15(75%)	20	<0.01 Sig.

Table 4: Maternal outcome according to LDH levels in study group.

	LDH levels	LDH level	LDH levels	Statistical analysis
	<600 IU/l (n=53)	**600-800 IU/l (n=27)**	**>800 IU/l (n=20)**	**P value**
Eclampsia	0	3 (11.11%)	6 (30%)	<0.001 HS
Abruption	5 (9.43%)	3 (11.11%)	6 (30%)	>0.05 NS
HELLP syndrome	0	1 (3.7%)	4 (20%)	<0.001 HS
DIC	0	1 (3.7%)	2 (10%)	>0.05 NS
Transfer to RICU/ICU	0	3 (11.11%)	3 (15%)	<0.05 Sig.
Renal failure	0	1(3.7%)	2 (10%)	>0.05 NS
Mortality	0	0	1 (5%)	-
Total	8	14	28	

Table 5: Perinatal outcome according to LDH levels in study group

	LDH levels Subgroup A	LDH levels Subgroup B	LDH levels Subgroup C	Statistical significance (p value)
	<600 IU/l (n=53)	**600-800 IU/l (n=27)**	**>800 IU/l (n=20)**	
Mean birth weight (kg)	2.36±0.60	2.20±0.52	1.99±0.59	<0.05 Sig.
Apgar 1 min <7	40 (75.47%)	24 (88.88%)	19 (95%)	>0.05
Apgar 5 min <7	7 (13.20%)	4 (14.81%)	6 (30%)	>0.05
LBW	21(39.6%)	18(66.66%)	17(85%)	<0.01 Sig.
Prematurity	18(33.96%)	9(33.33%)	6(30%)	>0.05 NS
VLBW	3(5.66%)	5(18.51%)	8(40%)	<0.01 Sig.
Neonatal sepsis	2(3.77%)	2(7.40%)	5(25%)	<0.01 Sig.
NICU admission	12(22.64%)	8(29.62%)	10 (50%)	>0.05 NS
Perinatal mortality	4(7.54%)	3(11.11%)	8(40%)	<0.001Sig.

Table 4 shows the maternal outcome in women with preeclampsia according to LDH levels. The maternal complications were found to be maximum in women with LDH > 800 IU/l. Abruption was the most common complication followed by eclampsia. Only one maternal death (5%) was observed in women with LDH levels >800 IU/l and no maternal death was observed in the other two groups. On statistical analysis, eclampsia, HELLP syndrome and rate of transfer to RICU/ICU was found to be significantly associated with high LDH levels. Perinatal outcome and various complications according to LDH levels in the study group are depicted in Table 5. There was fall in Apgar score at 1 minute and 5 minutes with increase in LDH levels, but no significant difference was found (p >0.05) and there was significant association with raised LDH levels with low birth weight of the babies, neonatal sepsis and perinatal mortality.

DISCUSSION

Pre-eclampsia is considered an idiopathic multisystem disorder. The prevention of pre-eclampsia is necessary to prevent the complications, so it must be diagnose the disease at the earliest. The effects of LDH in pregnancy related complications like preeclampsia is now gaining attention. In the present study, authors observed a significant rise in the LDH levels in preeclampsia patients as compared to control group and that there is an increase in LDH value with increasing severity of preeclamsia (p <0.01).

Qublan et al10 found in their study that the mean LDH levels in controls was 299±79 IU/l, in patients with mild preeclampsia was 348±76 IU/l and in severe preeclampsia was 774±69.61 IU/l. This demonstrated that there is significant association of LDH levels with severe preeclampsia. Similar results were depicted in studies conducted by Jaiswar et al Hazari et al and Gandhi et al.[16-18]

Present study demonstrated that LDH level <600 IU/l was observed in 66% patients of mild preeclampsia and 36.73% patients of severe preeclampsia whereas 9.8% patients with mild preeclampsia and 30.61% patients with severe preeclampsia had LDH levels >800 IU/l. LDH levels were found to be significantly higher in severe preeclampsia than mild preeclampsia. These findings were similar to those of Demir et al and Sarkar et al.[19,20]

In the present study, it was observed that systolic blood pressure (SBP) and diastolic blood pressure(DBP) was significantly higher with higher serum LDH levels. These results correlate with the studies conducted by Umasatyashri et al, Bhave et al and Jaiswar et al.[16,21,22] In the study conducted by Jaiswar et al 61.11% patients with LDH levels > 800 IU/l had systolic blood pressure ≥160 mmHg.[16] Jaiswar et al found in his study that 61.11%

patients had diastolic blood pressure ≥110 mmHg in patients with LDH levels >800 IU/l.[16] Most of the symptoms increased with increasing LDH levels >600 IU/l. Headache was the most frequent symptom followed by pedal edema and the findings were comparable with studies conducted by Hazari et al and Mary et al.[17,23] The association of mode of delivery with higher LDH levels was not significant in the study done by Qublan et al10 and Mary et al. This is in contrary to our present study in which authors found that with increasing LDH values, rate of cesarean delivery increases significantly. Various maternal complications observed were eclampsia, abruption, DIC, HELLP syndrome and renal failure. Abruption was the most common complication observed among all the subgroups followed by eclampsia.

Statistically increased incidence of eclampsia, HELLP syndrome and rate of RICU/ICU transfer was found on comparing the three subgroups of patients with LDH levels <600, 600-800 and >800 IU/l. It was also observed that maximum number of complications were observed in preeclamptic women with LDH levels >800 IU/l and more than one complication was present in one patient. Umasatyasri et al observed increase in maternal morbidity with increasing serum LDH levels. They observed higher serum LDH levels were associated with increased incidence of maternal complications like abruption, renal failure, HELLP syndrome (p <0.05). Qublan et al and Demir et al concluded that there was a statistically significant relation between maternal complications and high LDH levels.[10,19,21]

Studies have shown association of low birth weight of infants with increase in serum LDH levels. Jaiswar et al noted with LDH levels <600 IU/l, the mean baby weight was 2.42±0.79% kg. In women with LDH levels 600-800 IU/l, the mean baby weight was 1.99±0.68 kg while in the subgroup with LDH levels >800 IU/l, it was 1.979±0.787 kg (p 0.019).[16] Umasatysi et al21found that there was reduction in the average birth weight with increase in LDH levels as also depicted from the present study with significant p value of <0.05. The mean birth weight in the present study in patients with LDH <600 IU/l was 2.36±0.60 kg, with LDH levels 600-800 IU/l, it was 2.20±0.52 kg and the patients with LDH levels >800 IU/l, it was 1.99±0.59 kg. The mean Apgar score at 1 min and 5 min was found to be less in cases with high LDH levels in a study conducted by Umasatyasri et al and Jaiswar et al. In the present study, though there was fall in Apgar score <7 at 1 minute and 5 minutes with increase in LDH levels but no significant association was observed.[16,21]

Significant increase in the incidence of perinatal mortality was observed by Qublan et al in patients with increasing levels of serum LDH (p <0.001).[10] The effect on perinatal outcome was also studied in Jaiswar et al and Bhave et al study demonstrating a significant increase in still births, neonatal deaths and perinatal mortality with increase in serum LDH levels.[16,22] In present study, similar results were observed showing a significant increase in neonatal deaths (p <0.05) and perinatal mortality (p<0.001) but no significant increase in still birth was found with higher LDH levels (p >0.05). It was observed that maternal and perinatal morbidity and mortality had significant association with increasing LDH levels. It showed that LDH levels have significant correlation with increasing severity of preeclampsia with poorer maternal and perinatal outcome.

CONCLUSION

Lactate dehydrogenase levels were found to be significantly increased in patients of preeclampsia. Maternal complications like eclampsia, disseminated intravascular coagulopathy, abruption, HELLP syndrome and perinatal complications like low birth weight and perinatal mortality were associated with higher LDH levels in preeclampsia patients. Thus, LDH levels reflect the severity of preeclampsia and the occurrence of complications.

In patients with higher LDH levels, vigilant monitoring and prompt management may decrease maternal and perinatal morbidity and mortality. Serum LDH levels can be offered to all patients of preeclampsia and can be used to predict the prognosis of preeclampsia.

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