Lactate dehydrogenase as a biochemical marker for preeclampsia - eclampsia

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Abstract

Background: Lactate Dehydrogenase (LDH) is an intracellular enzyme required for the conversion of pyruvate to lactate. LDH activity and gene expression are higher in placentae in pre-eclampsia than normal pregnancy.

Aim: To correlate serum Lactate Dehydrogenase (LDH) levels in patients with Pre-eclampsia (PE) and eclampsia with severity of disease and maternal and neonatal outcomes.

Methods: This is a prospective observational study undertaken in the department of Obstetrics and Gynaecology at SNMC and HSK hospital and research centre, Bagalkot. Serum LDH levels were assessed in 200 women who were divided into the following groups (50 in each group): normal pregnancy, mild pre-eclampsia, severe pre-eclampsia and Eclampsia. LDH levels were compared with parameters like age, parity, gestational age, blood pressure, perinatal and maternal morbidity and mortality. Statistical analysis was done by Chi-square and one way ANOVA test.

Results: LDH levels were significantly elevated in women with mild pre-eclampsia, severe Pre-eclampsia and eclampsia groups ($p< 0.001$). Twenty women in mild PE group, 39 women in severe PE group and 44 women in eclampsia group had LDH > 600IU/ml. In the control group in only five women LDH levels were more than 600IU/ml. There was significant correlation between high blood pressure and high LDH levels ($p<0.001$). Higher LDH levels had poor maternal and perinatal outcome. Neonatal complications were found in 20 women with LDH <600IU/ml but there were 68 neonatal complications in women with LDH ≥600IU/ml which was found to be statistically significant.No maternal complications were found in women with LDH <600IU/ml, 10 women had complications whose LDH levels were >600IU/ml.

Conclusion: High serum LDH levels correlate well with the severity of the disease and poor outcomes in patients with Pre-eclampsia and Eclampsia.

Key words: Lactate dehydrogenase, Pre-eclampsia, Eclampsia, Maternal outcome, Perinatal outcome

Introduction

Lactate Dehydrogenase (LDH) is an intracellular enzyme required for the conversion of pyruvate to lactate. LDH is present in many organs and tissues like liver, kidney, heart, pancreas, skeletal muscle, lymph tissue and blood cells. It is a marker for common injuries and diseases.

Normal range of Serum LDH is 164-412 IU/L. It is increased in conditions such as liver disease, myocardial infarction, pre-eclampsia, progressive muscular dystrophy, many malignant conditions and almost any cause of hemolysis.[1]

LDH deficiency affects mainly muscle cells. It is very rare for a person to have low LDH levels. Two types of genetic mutations cause low levels. Type1 will experience fatigue and muscle pain especially after exercise while the type2 may have no symptoms at all. In addition, consumption of large amounts of ascorbic acid (vitamin C) leads to low level of LDH.[1]

Pregnancy causes profound anatomical, physiological, and metabolic changes in maternal tissues. These well-orchestrated changes can go wrong at some stage of pregnancy resulting in various feto-maternal complications. Pre-eclampsia and eclampsia is a multi-system disorder which leads to increased cellular death and various maternal and fetal complications.

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It complicates around 6-8% of all pregnancies. How pregnancy incites or aggravates hypertension remains unsolved despite decades of intensive research. Studies have shown that LDH activity & gene expression are higher in placentae in Pre-eclampsia than normal pregnancy. Hypoxia induces LDH isoenzyme activity in trophoblasts resulting in higher lactate production.[1]

LDH level >600IU/l has found to have significant maternal and perinatal morbidity and mortality. Elevated levels of LDH have also been seen in cases of HELLP syndrome. Many have used elevated total LDH (usually more than 600 U/L) as a diagnostic criterion for hemolysis. Among all five isoforms, only two of them (LDH1 and LDH2) are released from ruptured red blood cells and hence can be considered as markers of hemolysis. LDHA(4) seen in placentae with PE is most responsive to hypoxia. However, most laboratories do not specify the isoform of LDH that is estimated. Most authors also do not specify the type of LDH under evaluation in their work. The table below describes the various types found in the tissues[2].

LDH 1	Heart and red blood cells
LDH 2	Heart and red blood cells
LDH 3	Brain and kidney
LDH 4	Liver and skeletal muscle
LDH 5	Skeletal muscle and liver

Aims and objectives

1. To compare serum LDH levels in normal pregnancy and in women with Preeclampsia and Eclampsia
2. Correlation of LDH levels with severity of Preeclampsia and Eclampsia
3. Correlate maternal and perinatal outcome with serum LDH levels

MATERIAL AND METHODS

This was a prospective observational study conducted in the department of OBG, SNMC & HSK Hospital and research centre, Bagalkot. 200 pregnant women were enrolled at time of delivery and divided into 4 groups (50 in each group): (A) Normal pregnancy, (B)mild Pre-eclampsia, (C)severe Pre-eclampsia, (D)Eclampsia. Group A served as control group.

Exclusion criteria were pre-existing diabetes mellitus, renal disease, thyroid disorder, epilepsy, liver disorders.

In addition to the investigations specific to their condition, all participants also underwent Serum LDH estimation.

All subjects were further divided according to LDH levels into following groups

a) < 600 IU/ml
b) 600-800 IU/ml
c) > 800 IU/ml

For statistical analysis appropriate tests of significance like Chi-square test for proportional data and one way ANOVA test for continuous data were used to find out the association between LDH levels and various outcome parameters.

Results

Total of 200 women were studied out of which 50 normal pregnant women served as control group. Remaining women had mild Preeclampsia (50), severe Preeclampsia (50) and Eclampsia (50).

Table 1. Distribution by age and parity

Parameter	Control	Preeclampsia
Mean age (in years)	25.46	25.44
Primigravida	48%	46%
G2	28%	26%
G3 and above	24%	28%

As shown in table 1, mean age was comparable in each group. Distribution according to parity was similar in both groups.

In the control arm, only 5% had raised LDH levels. In mild Preeclampsia group 40% had raised LDH levels. In severe preeclampsia group 78% had raised LDH levels and in eclampsia group 88% had raised LDH levels. Hence it is clearly observed that there is a significant rise in LDH levels with increasing severity of disease (p value < 0.001). There was significant rise on comparison of each group with the other (Table 2).

Mean LDH values were raised in the study groups as compared to the control group which was shown to be statistically significant (p value <0.001). This was again found to be significant on comparison across the group (Table 3).

On statistical analysis, high systolic and diastolic BP was associated with higher levels of serum LDH (p value <0.001) (Table 4).

Mean gestational age at the time of delivery was 38.5±2.14weeks in cases with LDH levels <600IU/l. It was significantly less in patients with LDH level between 600-800 IU/l which was 37.30± 2.96 and 36.36± 3.56 in women with LDH > 800 IU/l. It was found that in cases with LDH levels <600 IU/l, the mean baby weight was 2.5± 0.38 kg. In the group with LDH levels 600-800 IU/l, the mean baby weight was 2.27± 0.61 kgs.

The mean weight in the third group i.e, with LDH>800IU/l was 2.06± 0.59kg. This observation indicates that there is a reduction in the average weight of babies with higher level of LDH (p<0.001) (Table 5).

Table 2. Comparison of LDH levels among subjects in each group

Groups 50 in each	LDH < 600 IU/ml n=92	LDH 600-800 IU/ml n=38	LDH > 800 IU/ml n=70	P value (chi square test)
Normal pregnancy	45(95.0)	3(6.0)	2(4.0)	< 0.001
Mild pre-eclampsia	30(60.0)	6(12.0)	14(28.0)	
Severe pre-eclampsia	11(22.0)	18(36.0)	21(42.0)	
Eclampsia	6(12.0)	11(22.0)	33(66.0)	

Table 3. LDH levels among various groups

	Normal pregnancy Mean±SD	Mild pre-eclampsia Mean±SD	Severe pre-eclampsia Mean±SD	Eclampsia Mean±SD	P value (one way ANOVA test)
No of cases	50	50	50	50	<0.001
Mean	434.9±172.5	557.0±464.9	1094.0±111.5	981.2±555.2	
Range	224-1036	65-2640	136-6028	189-3110	

Table 4. Association of systolic and diastolic blood pressure with LDH levels

Parameters	LDH < 600 IU/ml N=92 Mean ±SD	LDH 600-800 IU/ml N=38 Mean± SD	LDH > 800 IU/ml N=70 Mean± SD	P value (ANOVA test)
Systolic BP	135.91± 21.36	164.63± 21.42	150.94± 18.48	<0.001
Diastolic BP	88.59± 15.18	106.47± 13.50	99.14± 12.54	<0.001

Table 5. Comparison of LDH levels with gestational age at delivery and birth weight

Outcome	LDH < 600IU/ml N= 92 Mean ± SD	LDH600 -800 IU/ml N=38 Mean ± SD	LDH > 800 IU/ml N=70 Mean ± SD	P value (one way ANOVA test)
Gestational Age	38.5± 2.14	37.30± 2.96	36.36± 3.56	< 0.001
Birth Weight	2.5± 0.38	2.27± 0.61	2.06± 0.59	< 0.001

Table 6. Comparison of LDH levels and perinatal outcome

Outcome	LDH levels			P value
	< 600IU/ml N= 92 N(%)	600 -800 IU/ml N=38 N (%)	> 800 IU/ml N=70 N (%)	
NICU admission	2 (2.2)	5(13.2)	15(21.4)	0.00048
IUGR	14(15.2)	6(15.8)	22(31.4)	0.0292
Perinatal death	4(4.3)	8(21.1)	12(17.1)	0.00743

Table 7. Comparison of LDH levels and maternal complications

Complications	LDH levels			P value
	LDH < 600IU/ml N= 92 N (%)	LDH 600 -800 IU/ml N=38 N (%)	LDH > 800 IU/ml N=70 N (%)	
Yes	0(0.0)	2(5.3)	8(11.4)	0.00421
No	0(0.0)	36(94.7)	62(89.6)	

Table 8. Description of maternal complications

Complications	LDH levels			P value
	< 600IU/ml n= 92 N(%)	600 -800 IU/ml n=38 N (%)	> 800 IU/ml n=70 N (%)	
Abruption	0 (0.0)	1(2.6)	3(4.3)	0.148
HELLP	0 (0.0)	0(0.0)	3(4.3)	0.0591
Hemiparesis	0 (0.0)	0(0.0)	1(1.4)	0.393
Maternal death	0(0.0)	1(2.6)	1(1.4)	0.561

Figures in parenthesis are percentages

There were 2 babies requiring NICU admission in mothers whose LDH values were < 600IU/ml but there were 20 babies for NICU admission in mothers whose LDH values were ≥ 600 IU/ml which was statistically significant. The occurrence of neonatal complications, IUGR, and perinatal deaths were significantly higher in mothers who had increased serum levels of LDH (Table 6).

There was statistically significant increase in the maternal complications with increasing LDH levels (p= 0.00421) (Table 7).

When the LDH levels were in the normal range there were no maternal complications. Where LDH levels were between 600-800IU/l there were 2 maternal complications, which were one abruption and one maternal death due to PPH. In the third group where the LDH levels were more than 800IU/l there were 3 with abruption, 3 with HELLP, one with hemiparesis and one maternal death due to PPH (Table 8).

Discussion

Qublan et al[3] found in their study that the mean LDH levels in controls was 299± 79 IU/l, in women with mild preeclampsia was 348 ±76IU/l and in patients with severe preeclampsia was 774± 69.61 IU/l. Thus they demonstrated a significant association of serum LDH levels with severe preeclampsia (p <0.001). In the present study also, the LDH levels were significantly raised with the severity of the disease (< 0.001) and this was in accordance with the above study.

The association of low birth weight babies with increase in serum LDH levels was suggested by Dacaj R et al in their study[4]. This was in contradiction to Qublan et al[3] who did not find any significant association. In the present study it was observed that there was a significant association of low birth weight with increasing LDH levels (p=0.00048).

Increase in the incidence of perinatal deaths was observed by Qublan et al[3] in patients with increasing levels of serum LDH levels (p < 0.001). Intrauterine death was seen in 4.8% of cases, intrauterine growth restriction in 33.9% and prematurity in 77.9%. Similar findings were also seen in the present study showing significant increase in neonatal complications.

A high level of LDH (> 1400IU/l) was shown to have a high predictive value for significant maternal morbidity in a study conducted by Beena et al[5]. Kozic JR et al[6] reported a subgroup of patients who had elevated level of LDH manifested with hemolysis, elevated liver enzymes, HELLP syndrome and were at a high risk for developing maternal mortality. Demir et al[6] concluded that there was a statistically significant relation between maternal complications and high LDH levels. It was noted that in early onset severe preeclampsia, LDH levels before delivery were significantly higher in the abruption group by Vinitha Padmini et al[7].

Present study has shown significant increase in the maternal complications with increase in LDH levels (p value = 0.00421).

Conclusion

Systolic and diastolic BP were significantly higher in patients with higher serum LDH levels. Serum LDH levels were significantly raised with the severity of the disease. Mean gestational age at the time of delivery and birth weight was less in patients with increasing LDH levels. Statistically significant increase in the perinatal and maternal complications was seen with increasing LDH levels.

Limitation of the study

- Specific isoforms of LDH were not identified.
- Variations in the LDH values were not assessed over time in the same women.
- Contributory reasons for maternal and perinatal morbidity and mortality were not assessed.

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