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Original Research Article

## Role of LDH as a prognostic marker in preeclampsia/eclampsia: a comparative case control study

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### ABSTRACT

**Background:** Preeclampsia is a multisystem disorder which complicates 5-8% of all pregnancies. LDH is an intracellular enzyme and its level is increased in these women due to cellular death. Serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease in this group of women.

**Methods:** It was a prospective case control study. Data was analysed using SPSS 16.0. The sample comprised of approximately 154 cases. All patients were of gestational age 28 weeks and above. They were divided into three groups 45 normotensives, 40 mild pre-eclamptics, 41 severe pre-eclamptics and 28 eclamptics.

**Results:** Serum LDH levels consistently increased with increasing systolic and diastolic blood pressure, more so with diastolic blood pressure with a p value of <0.001. Most of the women with severe preeclampsia and eclampsia had severe proteinuria and serum LDH significantly increased with the severity of proteinuria (p<0.00). The incidence of operative delivery was moderately elevated with increased LDH level. The mean gestational age at the time of delivery in patients with serum LDH less than 600, 600 to 800 and more than 800 are 37.94 35.36 and 33.87 weeks. The mean baby weight in patients with serum LDH less than 600, 600 to 800 and more than 800 was 2.80, 2.62 and 1.81 kg.

**Conclusions:** Serum LDH values were significantly high in pre-eclamptic patients depending on the severity of the disease. Serum LDH levels had a good correlation with all the diagnostic components of preeclampsia like SBP, DBP and proteinuria, similarly with maternal and fetal morbidity and mortality.

**Keywords:** PIH, Pregnancy

### INTRODUCTION

Preeclampsia is a multisystem disorder which complicates 5-8% of all pregnancies.<sup>1</sup> The effects of lactate dehydrogenase (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.<sup>2</sup> Serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease in this group of women. This will help in making decision, about the management guidelines for better maternal and foetal outcome.<sup>3</sup> Though exact etiopathogenesis of pre-eclampsia is unknown, multiple

factors have been implicated to have a role in it; the factors being abnormal placental implantation, endothelial dysfunction, maternal immunological tolerance, cardiovascular, genetic, nutritional and environmental factors.<sup>4</sup>

Amongst these, endothelial dysfunction is considered to be the most important factor resulting in mild to moderate microangiopathy of target organs, leading to excessive leakage of LDH in serum.<sup>5</sup> Thus, presence of LDH signifies tissue damage and haemolysis.<sup>6</sup> Elevated LDH levels in pre-eclampsia reflect severity as well occurrence of complications in pre-eclampsia.<sup>7</sup> Being an intracellular

enzyme, 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 are 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.<sup>8</sup> 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.<sup>9</sup> 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.<sup>10</sup>

Hypoxia induces LDH isozyme activity in trophoblasts resulting in higher lactate production. Primary human trophoblast cells demonstrated an increase in LDH-A mRNA when exposed to hypoxic conditions confirming LDH-A isozyme presence in placental trophoblasts and their response to hypoxia.<sup>11</sup> LDH has five isoforms, and among all, LDHA4 seen in placenta with preeclampsia is most responsive to hypoxia.<sup>12</sup> Elevated levels of LDH are indicative of cellular damage and dysfunction, so it can be used as a biochemical marker since it reflects the severity of the disease, occurrence of complications, and foetal outcome. The levels of LDH in serum are increased in clinical situations associated with cell damage, leak, haemolysis, and cell death.<sup>13</sup>

### **Objectives**

To study perinatal and foetal outcome with increasing serum LDH levels. To compare LDH levels between PIH and normotensive pregnant women.

### **METHODS**

This study was conducted on antenatal women who attend the labour room emergency in the department of Obstetrics and Gynaecology SKIMS Medical College Bemina. It was comparative case control observational study and was conducted over a period of 2 years from 2019 to 2021.

All the antenatal women admitted in the Department of obstetrics and gynaecology Sher-I-Kashmir Institute of Medical Sciences, Medical College, Srinagar, with singleton pregnancy with term or near term were enrolled in the study randomly over a period two years.

The written informed consent was obtained from all patients and ethical committee clearance was also sought. The sample comprised of approximately 154 cases.

A detailed history and physical and clinical examination were performed. Investigations performed were CBC, KFT, LFT, serum LDH, serum electrolytes (sodium and potassium), lactate levels, blood gas analysis, coagulogram, spot urine for proteins, 24-hour urinary protein and doppler ultrasonography and funduscopy.

### **Inclusion criteria**

Preeclamptic women with singleton pregnancy whose blood pressure was normal during first 20 weeks of gestation and no previous history of hypertension near term of their pregnancy.

### **Exclusion criteria**

Patients with history chronic hypertension, diabetes mellitus or smoking. Patient with pre-existing cardiac, liver or lung disease. Patients with multiple or molar pregnancies.

All the subjected included in this study were randomly divided into two groups: group A- healthy normotensive pregnant women as controls, group B- patients of preeclampsia and eclampsia (subjects). This was further subdivided into following subgroups: a) mild preeclampsia, b) severe preeclampsia, c) eclampsia. Further, all the patients were categorised into three groups according to serum LDH levels: LDH levels <600IU/l, LDH levels 600-800 IU/l, LDH levels >800 IU/l.

### **RESULTS**

A total of 154 patients were included in the study out of which 45 (29.2%) were normotensive who acted as controls. 109 (70.7%) patients acted as cases out of which 40 (26.0%) had mild preeclampsia, 41 (26.6%) had severe preeclampsia and 28 (18.2%) had eclampsia. Out of a total 109 patients with LDH levels <600 IU/l, 48 (44%) cases had normal SBP, 43 (39.4%) had SBP in the range of 140 to 159 mm of Hg and 18 (16.5%) had SBP of 160 and above. Out of 14 patients with serum LDH levels of 600 to 800 none had normal SBP, 8 (57.1%) had SBP in the range of 140 to 159 mm of Hg and 6 (42.9%) had SBP 160 and above. In the remaining 31 patients with serum LDH levels of 800 and above none had normal SBP, 11 (35.5%) had SBP in the range of 140 to 159 mm of Hg and 20 (64.5%) had SBP 160 and above (Table 2).

There was a significant rise in serum LDH in patients with abruptio placenta. Out of total of 154 women 17 had abruptio placenta. 6 (5.5%) had LDH values <600, 2 (14.3%) had LDH levels between 600 and 800.9 patients (29%) had LDH >800 (Table 3).

There was reduction in the mean GA with higher levels of LDH ( $p=0.001$ ). The mean gestational age at the time of delivery in patients with serum LDH less than 600, 600 to 800 and more than 800 are 37.94, 35.36 and 33.87 weeks (Table 4).

**Table 1: Comparison of serum LDH levels between normotensive and PIH patients.**

LDH levels	N	Mean	SD	Min	Max	P value
Controls	45	237.9	103.00	78	384	<0.001*
Mild pre-eclampsia	40	441.9	130.06	215	700	
Severe pre-eclampsia	41	605.8	422.94	256	1575	
Eclampsia	28	1141.0	352.89	720	1894	

\*Statistically significant (p value<0.05).

**Table 2: Correlation between serum LDH levels and systolic blood pressure.**

SBP (mmHg)	Serum LDH levels					
	<600		600-800		> 800	
	N	%	N	%	N	%
100-139	48	44.0	0	0.0	0	0.0
140-159	43	39.4	8	57.1	11	35.5
160 and above	18	16.5	6	42.9	20	64.5
<b>Total</b>	109	100	14	100	31	100

Chi-square=41.566; p value<0.001 (statistically significant).

**Table 3: Correlation between serum LDH levels and abruption.**

Abruption	Serum LDH levels					
	<600		600-800		>800	
	N	%	N	%	N	%
Yes	6	5.5	2	14.3	9	29.0
No	103	94.5	12	85.7	22	71.0
<b>Total</b>	109	100	14	100	31	100

Chi-square=13.771; p value=0.002 (statistically significant).

**Table 4: Correlation between serum LDH levels and gestational age.**

Serum LDH levels	N	Mean	SD	Min	Max	P value
<600	109	37.94	1.731	32	40	<0.001*
600-800	14	35.36	1.447	32	36	
>800	31	33.87	2.592	28	36	

\*Statistically significant (p value<0.05).

**Table 5: Correlation between serum LDH levels and mode of delivery.**

Mode of delivery	Serum LDH levels					
	<600		600-800		>800	
	N	%	N	%	N	%
LSCS	48	44.0	11	78.6	28	90.3
NVD	61	56.0	3	21.4	3	9.7
<b>Total</b>	109	100	14	100	31	100

Chi-square=24.092; p value<0.001 (statistically significant)

**Table 6: Correlation between serum LDH levels with fetal outcome.**

Variables	LDH<600 IU/l (n=22)	LDH 600-800 IU/l (n=27)	LDH>800 IU/l (n=32)
Average APGAR score	8.34	7.5	6.8***
Average weight of babies (kg)	2.8	2.6	1.8***
IUGR (%)	0	0	6.5**
IUFD (%)	0	0	9.7**

\*\*p<0.05, \*\*\*p<0.001

There was a significant rise in serum LDH in patients with operative delivery. Out of total 154 patients 87 delivered by LSCS, 67 delivered vaginally. Among the women who delivered by cesarean 48 (44%) had serum LDH less than 600, 11 (78.6%) had serum LDH between 600 and 800 and 28 (90.3%) had serum LDH above 800. Among the women who delivered vaginally 61 (56.0%) had serum LDH less than 600, 3 (21.4%) had serum LDH between 600 and 800 and 3 (9.7%) had serum LDH above 800 (Table 5).

There was a statistically significant difference between rise in serum LDH and fall in APGAR score. There was a reduction in the average weight of babies with higher level of LDH. There was a significant rise in serum LDH with incidence of intra uterine growth restriction. There was also a significant rise in serum LDH with intra uterine fetal deaths (Table 6).

## DISCUSSION

In our study serum LDH levels consistently increased with increasing systolic and diastolic blood pressure, more so with diastolic blood pressure with a p value of <0.001 similar to Jaiswar et al.<sup>14</sup>

Maternal complications including eclampsia, abruptio placenta, need for operative deliveries increased with increased LDH values. In our study patients with eclampsia had significantly higher levels of LDH compared to patients with normotension and preeclampsia (p<0.001). This was similar to findings by Jaiswar et al who found that in eclampsia group, majority of patients i.e., 25 (69.4%) had levels >800 IU/l.<sup>14</sup> Incidence of abruptio placenta was significantly higher in patients with LDH>800 in a study done by Qublan et al similar to the findings of our study.<sup>2</sup>

The incidence of operative delivery was moderately elevated with increased LDH levels and this explains the severity of the disease with increased LDH and the need for immediate delivery in them. Similar to our study, in a study done by Vidhya higher value of serum LDH level was associated with increased incidence of operative delivery.<sup>15</sup>

Mean GA and mean baby weight had negative correlation with S.LDH levels with p value <0.001 similar to Jaiswar et al whose mean GA at the time of delivery was significantly less in patients with increasing LDH levels (p value =0.025).<sup>16</sup> This fact could be explained by the increased preterm deliveries and the need for early termination of pregnancy to improve the maternal outcome in view of severity of disease.

Incidence of IUGR were significantly higher in pre-eclamptic women and their S. LDH levels compared to the controls (p value <0.001).<sup>16</sup> These findings were similar to the study done by Hak et al.<sup>17</sup>

This study included a smaller number of patients and had a shorter follow up period. For proper validation of these conclusions, a long term follow-up is required. In addition, further studies need to be done to confirm the results.

## CONCLUSION

After analysing the data and comparing the results following conclusion have been drawn from the study.

Serum LDH values were significantly high in pre-eclamptic patients depending on the severity of the disease indicating the increased cellular turnover in them.

Serum LDH levels had a good correlation with all the diagnostic components of preeclampsia like SBP, DBP and with maternal and fetal morbidity and mortality

Hence diagnostic and management strategies may be considered based on serum LDH levels and further studies on a larger sample can be done to substantiate our observations on the utility of this parameter as a diagnostic and prognostic component of preeclampsia. Development of new management strategies based on serum LDH levels may help in appropriate decision making thereby avoiding unwanted maternal and fetal deaths.

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## REFERENCES

1. Lain KY, Roberts JM. Contemporary concepts of the pathogenesis and management of preeclampsia. *JAMA.* 2002;287(24):3183-6.
2. Qublan HS, Amarun V, Bateinen O, Al-Shraideh Z, Tahat Y, Awamleh I, et al. LDH as biochemical marker of adverse pregnancy outcome in severe preeclampsia. *Med Sci Monit.* 2005;11:393-7.
3. Jaiswar SP, Gupta A, Sachan R, Natu SN, Shaili M. Lactic-dehydrogenase: a biochemical marker for preeclampsia-eclampsia. *JOGI.* 2011;61(6):645-8.
4. Qublan HS, Amarun V, Bateinen O, Al-Shraideh Z, Tahat Y, Awamleh I, et al. LDH as biochemical marker of adverse pregnancy outcome in severe preeclampsia. *Med Sci Monit.* 2005;11:393-7.
5. Trends in maternal mortality: 1990 to 2010. WHO, UNICEF, UNFPA and the World Bank estimates. Available from: [http://whqlibdoc.who.int/publications/2012/9789241503631\\_eng.pdf](http://whqlibdoc.who.int/publications/2012/9789241503631_eng.pdf). Accessed on 12 July 2012.
6. Butt AA, Michaels S, Greer D, Clark R, Kissinger P, Martin DH. Serum lactate [8] dehydrogenase level as a clue to the diagnosis of histoplasmosis. *AIDS Read.* 2002;12(7):317-21.
7. Malik KK, Akmal N, Akhter N. Correlation of lactate dehydrogenase levels with the severity of pre-eclampsia. *Tohoku J Exp Med.* 2004;202:87-92.

8. Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health Volume 3, Issue 2, Pages 58-59, April 2013.
9. Kamath R, Nayak R, Shantharam M. Serum uric acid level in preeclampsia and its correlation to maternal and fetal outcome. *Int J Biomed Res.* 2014;5(1):22.
10. Lu H, Forbes RA, Verma A. Hypoxia-inducible factor 1 activation by aerobic glycolysis implicates the Warburg effect in carcinogenesis. *J Biol Chem.* 2002;277(26):23111-5.
11. Demir SC, Evruke C, Ozgunen FT, Urunsak IF, Candan E, Kadayifci O. Factors that influence morbidity and mortality in severe preeclampsia, eclampsia and hemolysis, elevated liver enzymes, and low platelet count syndrome. *Saudi Med J.* 2006;27(7):1015.
12. Bournères PF, Rocchiccioli F, Nurjhan N, Zeller J. Stable isotope determination of plasma lactate conversion into glucose in fasting infants. *Am J Physiol.* 1995;268:E652-9.
13. Munde SM, Hazari NR, Thorat AP, Gaikwad SB, Hatolkar VS. Gamma glutamyl transferase and lactate dehydrogenase as biochemical markers of severity of preeclampsia. *Int J Med Health Pharm Biomed Eng.* 2014;8:50-3.
14. Jaiswar SP, Gupta A, Sachan R, Natu SN, Shaili M. Lactic-dehydrogenase: a biochemical marker for preeclampsia-eclampsia. *JOGI.* 2011;61(6):645-8.
15. Vidhya, Muthuramalingam. "Lactate dehydrogenase as surrogate marker of preeclampsia and eclampsia." *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, vol. 9, no. 5, May 2020, pp. 1924s.
16. Jaiswar SP, Gupta A, Sachan R, Natu SN, Shaili M. Lactic-dehydrogenase: a biochemical marker for preeclampsia-eclampsia. *JOGI.* 2011;61(6):645-8.
17. Hak J, Gupta S. LDH levels in pregnancy and its association with severity of the disease and fetomaternal outcome in pre-eclampsia and eclampsia. *JK Sci.* 2015;17(3):110.

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