

## Serum Lactate Dehydrogenase: A Biochemical Marker for the Prediction of Adverse Outcome in Pre-Eclampsia

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### Abstract

**Aims & Objectives:** To find out the role of serum LDH levels in prediction of adverse outcome of pre-eclampsia. Objectives: 1) To estimate the level of serum LDH in preeclampsia. 2) To study the correlation of LDH level and severity of the disease. 3) To study the correlation of LDH level and occurrence of complications. 4) To identify the better severity indicator in maternal and perinatal outcomes.

**Materials & Methods:** A study was conducted over a period of 6 months in the department of Obstetrics and Gynaecology, Bharati Vidyapeeth medical college and hospital, Sangli. Women with pre-eclampsia were studied who satisfied the inclusion and exclusion criteria of the study. Demographic, hemodynamic, laboratory data were compared among 2 groups. The symptoms and complications of severe pre-eclampsia along with the fetal outcome were analysed according to serum LDH levels.

**Results:** Severely pre-eclamptic women patients were significantly younger, with low gravidity and parity. Higher LDH levels have significant correlation with high BP. The symptoms and complications of pre-eclampsia along with perinatal mortality were increased significantly in pt with LDH > 800 IU/L compared with those who had lower levels.

**Conclusion:** Serum LDH is useful biomarker and can be considered as a supportive prognostic tool that reflects the severity of disease and complications of pre-eclampsia. Identification of high-risk patient with increased level of LDH mandate their close monitoring and correct management may prevent these complications.

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### Introduction

Hypertensive disorders of pregnancy are one of the most common complications in pregnancy and contribute greatly to maternal and perinatal morbidity and mortality rates. Hypertension is a sign of an underlying pathology which may be pre-existing or appears for the first time during pregnancy. These conditions, however, are largely preventable and once detected, they are treatable. Hypertension during pregnancy is diagnosed when the systolic

pressure is 140 mmHg or more, and /or diastolic pressure of 90 mmHg or more, measured on two occasions at least 4 hours apart within 7 days. Preeclampsia is a multisystem disorder which complicates 5-8% of all pregnancies. [1] It lead to a lot of cellular death. Pre-eclampsia, is a pregnancy induced disorder characterized by hypertension and proteinuria. 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 preeclampsia than normal pregnancy. [8,9]

The effects of LDH in pregnancy related complications like preeclampsia is now gaining attention. Lactate dehydrogenase (LDH) is an intracellular enzyme which converts pyruvic acid to lactic acid during the process of glycolysis. Glycolysis is the major energy pathway in the placenta. Hypoxia in PE further enhances glycolysis and increases LDH activity. 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. Studies have shown that LDH activity & gene expression are higher in placentas of PE than normal pregnancy. Hypoxia induces LDH isoenzyme activity in trophoblasts resulting in higher lactate production. Elevated levels of LDH are indicative the cellular damage and dysfunction, so it can be used as a biochemical marker because it reflects the severity of the disease, occurrence of complications and fetal outcome. [10] Its estimation would prove useful because these complications are preventable.

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 amino transferase, alanine aminotransferase, 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 preeclamptic women and to correlate its levels with maternal and perinatal outcome in preeclampsia.

### Material & Methods

A retrospective observational study was conducted over a period of 6 months in the department of Obstetrics and Gynaecology, Bharati Vidyapeeth medical college and hospital, Sangli. Women with preeclampsia were studied who satisfied the inclusion and exclusion criteria of the study. Demographic, hemodynamic, laboratory data were compared among 2 groups. The symptoms and complications of severe preeclampsia along with the fetal outcome were analysed according to serum LDH levels.

The records of women with preeclampsia having singlet on pregnancy, age 18-30years, preeclamptic women whose blood pressure was normal during first 20 weeks of gestation, no previous history of hypertension, all the cases were in the third

trimester of pregnancy were included in this study. Records of women with history of chronic hypertension, diabetes mellitus, drugs intake, smoking, alcoholism, liver, cardiac or renal diseases or any other major illness were excluded from the study.

### Results

Out of 70 pre-eclamptic women, 54 were mild preeclampsia and 16 were severe

preeclampsia. The demographic profile of women with pre-eclampsia 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 20-30 years followed by 30-35 years. Severely pre-eclamptic women patients were significantly younger with low gravidity and parity.

**Table 1: Distribution according demographic variables.**

Variables	Frequency	Percentage (%)
<b>Age</b>		
<20 years	4	5.7
20-35 years	58	82.9
>35 years	8	11.4
<b>Mode of delivery</b>		
LSCS	41	58.6
Vaginal delivery	29	41.4
<b>Birth weight – LBW</b>		
Yes	52	74.3
No	18	25.7
<b>Gravidity</b>		
Primi	48	68.5
Multi	22	31.4

As mentioned in table 2, 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. Symptoms noted in the women with pre-eclampsia 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 ( $p < 0.001$ ), 65.9% had caesarean and rest delivered vaginally. The rate of caesarean section increased with LDH levels >600 IU/l and was statistically significant ( $p < 0.001$ ).

**Table 2: Distribution according to LDH level in various groups according to severity.**

S. LDH	Mild Pre-eclampsia	Severe Pre-eclampsia
<600IU/L	33	5
600-800IU/L	16	4
>800IU/L	5	7

As shown in Table 3, 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. HELLP was the most common complication followed by eclampsia.

**Table 3: According to maternal complications.**

Complications	Frequency (n)	Percentage (%)
Eclampsia	2	2.9%
Abruptio placenta	1	5.8%
Postpartum hemorrhage	0	0%
HELLP	5	7.1%
CVA	0	0%

No maternal death was observed in the both 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 according to LDH levels in the study group are depicted in Table 1. 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.

### 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 preeclampsia ( $p < 0.01$ ). Qublan et al [10] found in their study that the mean LDH levels in controls was  $299 \pm 79$  IU/l, in patients with mild preeclampsia was  $348 \pm 76$  IU/l and in severe preeclampsia was  $774 \pm 69.61$  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 [16], Hazari et al [17] and Gandhi et al. [18]

Present study demonstrated that LDH level  $< 600$  IU/l was observed in 86% patients of mild preeclampsia and 41.7% patients of

severe preeclampsia whereas 13.20% patients with mild preeclampsia and 58.30% 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]

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 al [10] 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. HELLP 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  $2.42 \pm 0.79$  kg. In women with LDH levels 600- 800 IU/l, the mean baby weight was  $1.99 \pm 0.68$  kg while in the subgroup with LDH levels  $> 800$  IU/l, it was  $1.979 \pm 0.787$  kg ( $p = 0.019$ ). [16] Umasatysi et al [21] found 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  $2.36 \pm 0.60$  kg, with LDH levels 600-800 IU/l, it was  $2.20 \pm 0.52$  kg and the patients with LDH levels  $> 800$  IU/l, it was  $1.99 \pm 0.59$  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] 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, abruption, HELLP syndrome and perinatal complications like low birth weight 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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