

## Serum Lactate Dehydrogenase (LDH) as an indicator of severity in preeclampsia

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**SUMMARY: Serum Lactate Dehydrogenase (LDH) as an indicator of severity in preeclampsia.**

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**Background.** Preeclampsia is one of the leading causes of maternal and perinatal morbidity and mortality. Lactate dehydrogenase levels are usually elevated in this condition and hence measuring LDH levels will help in identification of preeclampsia.

**Objectives.** To study the correlation of Lactate dehydrogenase levels with maternal and perinatal outcome in preeclampsia and to assess the severity of disease in association with LDH levels.

**Study Design.** Prospective comparative study.

**Material and methods.** Pregnant women diagnosed with preeclampsia were enrolled in the study conducted at hospitals attached to Kasturba Medical College, Mangalore from September 2015 to March 2017 after approval from the institutional ethical committee. Serum LDH levels were measured and the women were categorized based on its levels and they were monitored till delivery. Maternal and perinatal outcomes and severity of disease were analyzed according to the levels of serum LDH.

**Results.** A total of 90 patients with preeclampsia was studied. Mean LDH levels were found to be 646.95 IU/l. In mild preeclamptic women, LDH levels were < 600IU/L. In severe preeclampsia, 20 (44.25%) had LDH levels 800 IU/l. Higher LDH suggested increase in severity of disease which was found to be statistically significant. LDH was more than 600IU/L in 32(71%) of women with Systolic BP>160 mmHg and 14(31%) of women with Diastolic BP >110 mmHg. There was a significant association between serum LDH levels and fetal growth restriction, intra uterine fetal demise, low birth weight and low APGAR scores in neonates. Abruptio placentae, Eclampsia and disseminated intravascular coagulation were associated with LDH >800IU/L.

**Conclusion.** Preeclampsia is one of the most common causes for maternal and perinatal morbidity and mortality. Lactate Dehydrogenase (LDH) is a good indicator in assessing the severity in preeclampsia and also can help in early diagnosis and treatment and reducing the complications in mother and fetus.

**What is new in this Paper?** Preeclampsia is a condition which is difficult to diagnose. Serum markers like Lactate dehydrogenase levels are usually elevated in preeclamptic women. In our study, we found that higher levels of LDH are associated with complications like abruptio, eclampsia and DIC and perinatal morbidity.

KEY WORDS: Preeclampsia - Lactate dehydrogenase - Severity - Indicator - Perinatal outcome.

### Introduction

Preeclampsia and eclampsia complicate 6-8% of all pregnancies and lead to various maternal and fetal complications (1). It is an idiopathic multisystem disorder. A complex of endocrinological mechanisms is believed to be responsible for the multiorgan dys-

function. The multiorgan dysfunction in severe preeclampsia caused by vascular endothelial damage, including maternal liver, kidney, lungs, nervous system, blood and coagulation system will lead to excessive lactate dehydrogenase (LDH) leakage and elevated levels in serum due to cellular dysfunction (2-4).

Preeclampsia is one of the most common causes of maternal mortality. Despite improvements in the diagnosis and management of preeclampsia, severe complications can occur in both the mother and the fetus. Early detection and identification of pregnant women most at risk of developing the disease have

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proven challenging, but recent efforts combining biochemical and biophysical markers are promising (5). Several potential candidate biochemical markers have been proposed to predict the severity of preeclampsia. Among these biomarkers, lactate dehydrogenase (LDH) is confirmed as good marker associated with severe preeclampsia. LDH is an intracellular enzyme, its level is increased due to cellular death, which can be further used as a marker in decision making, regarding the management strategies to improve the maternal and fetal outcome in preeclamptic women (5).

## Objectives

1. To study the correlation of Lactate dehydrogenase levels with maternal and perinatal outcome in Preeclampsia.
2. To study the association of serum Lactate dehydrogenase levels with severity of preeclampsia.

## Material and methods

A prospective comparative study was conducted at a Tertiary care hospital in South India from September 2015 to March 2017 after approval from the institutional ethical committee.

All antenatal women diagnosed to have preeclampsia during third trimester in the age group (18-35 years) admitted in the hospital were enrolled in the study.

Subjects were divided into 2 groups:

- Group A: Mild preeclampsia
- Group B: Severe preeclampsia.

Informed written consent was obtained. Detailed history was taken and examination done. Demographic and anthropometric data was recorded. Blood samples was collected before initiation of medical therapy.

**Exclusion Criteria:** chronic hypertension, overt diabetes mellitus, liver disease, renal disease, thyroid disorder, epilepsy.

Subjects were studied according to the serum LDH levels into subsequent groups:

- a) 600 IU/l
- b) 600 – 800 IU/l
- c) >800 IU/l

Maternal and perinatal outcomes were analyzed and severity of the disease were studied according to the serum LDH levels.

Subjects were followed up till delivery and early postnatal period and newborn outcome was also noted.

**Maternal outcome:** gestational age at delivery, maternal complications: eclampsia, abruption, HELLP syndrome, DIC, acute renal failure and pulmonary edema and maternal death.

**Perinatal outcome:** low birth weight, fetal growth restriction, still birth, intrauterine fetal demise, preterm birth, low Apgar score and early neonatal death.

### Normal serum LDH values (6):

Group	Serum LDH level
Non pregnant women	115 to 211 IU/L
First trimester	78 to 433 IU/L
Second trimester	80 to 447 IU/L
Third trimester	82 to 524 IU/L

The statistical analysis was done by Chi-square test (for proportional data). Differences were considered significant when  $p < 0.05$ .

## Results

A total of 90 patients was studied, 45 with mild preeclampsia (Group A) and remaining 45 with severe preeclampsia (Group B). Maximum number of patients belonged to age group of 21-30 years (Table 1). Parity distribution was similar in both the groups (Table 2).

Mean LDH levels were found to be 646.95 IU/l. In mild preeclamptic women, serum LDH levels were < 600 IU/L. In severe preeclampsia, 20 (44.25%) had LDH levels <600 IU/l, 12 (26%) LDH levels between 600 and 800 IU/l and 13 (28.8%) had levels >800 IU/l. Higher serum LDH levels suggested increase in severity of disease which was found to be statistically significant (Table 3).

TABLE 1 - DISTRIBUTION OF STUDY POPULATION ACCORDING TO AGE.

Age (yrs)	Mild preeclampsia(n=45)	Severe preeclampsia(n=45)
<20	7 (15.8%)	0
21-25	20 (44.6%)	21 (46.7%)
26-30	11 (24.9%)	15 (33.3%)
>30	7 (15.8%)	9 (20%)

TABLE 2 - DISTRIBUTION OF STUDY POPULATION ACCORDING TO PARITY.

Parity	Mild preeclampsia (n=45)	Severe preeclampsia (n=45)
Primi	22 (48.5%)	27 (59.5%)
Multi	23 (51.5%)	18 (40.5%)

TABLE 3 - DISTRIBUTION OF STUDY POPULATION ACCORDING TO LDH LEVELS.

Study Group	Serum LDH level (IU/L)			P value
	<600	600 - 800	>800	
Mild preeclampsia (n=45)	45 (100%)	0	0	0.001 *
Severe preeclampsia (n=45)	20 (44.25%)	12 (26%)	13 (28%)	

Of the 90 cases, 45 had systolic BP in the range of 140-160 mm of Hg and 45 had systolic BPs more than 160 mmHg. Serum LDH was more than 600 IU/L in 32 (71%) of women with systolic BP more than 160 mmHg. Diastolic BP more than 110 mmHg was noted in 14 (31%) of women with serum LDH more than 600 IU. Upper levels of serum LDH ( $P<0.001$ ) was found to be associated with higher systolic and diastolic blood pressures on statistical analysis (Table 4).

The mean baby weight was 2.526 kg with LDH levels <600 IU/l, 2.392 kg with LDH between 600-800 IU/l and 1.879 kg with LDH levels >800 IU/l. According to this observation, there is a decrease in the mean weight of newborns with increasing levels of LDH. Rate of fetal growth restriction, fetal demise, Low APGAR score were higher with upper levels of serum LDH levels (Table 5).

Severity of disease i.e. thrombocytopenia and Renal sufficiency was observed in 26 (29%) women with LDH >800 IU/L suggesting that higher levels of serum LDH levels was associated with increase in severity of preeclampsia (Table 6).

There was a significant association between serum LDH levels and maternal complications. Abruption placentae and eclampsia was observed in women with serum LDH between 600-800 IU/L. DIC, Abruption and eclampsia was noted with serum LDH>800 IU/L. No maternal complications were present with serum LDH<600 IU/L (Figure 1).

## Discussion

In the study group, most of the women belonged to younger age group and were primigravidas comparable to the study done by Qublan et al., where the mean age group of preeclampsia was 26 years and those with severe preeclampsia was significantly younger with low parity. In women with serum LDH

levels >600 IU/systolic BP >160 mmHg and diastolic BP>110 mmHg were significantly higher in both studies (5).

In Qublan et al. study, mean LDH levels in women with mild preeclampsia was  $448 \pm 76$  IU/l and in with severe preeclampsia was  $674 \pm 69$  IU/l. Thus it demonstrated a significant association of serum LDH levels with severe preeclampsia ( $p<0.001$ ). In the study group, mild preeclamptic women, serum LDH levels were <600 IU/L and in severe preeclampsia, 20 (44.25%) had LDH levels <600 IU/l, 12(26%) LDH levels between 600 and 800 IU/l and 13 (28.8%) had levels >800 IU/l. Rukhsana Afroz et al. study also demonstrated that serum LDH level was significantly higher in preeclamptic women compared to normal pregnant women ( $p<0.001$ ). This value was significantly higher in women with severe preeclampsia than those with mild preeclampsia (7).

*Lactate dehydrogenase: indicator of preeclampsia*

TABLE 4 - ASSOCIATION OF SYSTOLIC AND DIASTOLIC BP WITH LDH LEVELS.

Groups	LDH levels (IU/L)			P value
	<600	600-800	>800	
Systolic BP (mm of Hg)				
140-160	40 (44.44%)	2 (2.2%)	3 (3.33%)	0.001 *
>160	13 (28.8%)	12 (26.6%)	20 (44.4%)	
Diastolic BP (mm of Hg)				
90-110	34 (37.77%)	6 (6.6%)	5 (5.55%)	0.001 *
>110	31 (34.44%)	6 (6.6%)	8 (8.8%)	

TABLE 5 - ASSOCIATION OF PERINATAL OUTCOME WITH LDH LEVELS.

Perinatal outcome	Serum LDH levels (IU/L)			P value
	< 600	600- 800	>800	
Fetal Growth restriction	19 (21.11%)	9 (10%)	12 (13.33)	0.001 *
Intra uterine fetal demise	2 (2.22%)	0	2 (2.22)	0.301
Preterm births	17 (18.88%)	9 (10%)	13 (14.44)	0.001 *
Low birth weights	19 (21.11%)	9 (10%)	12 (13.33%)	0.001 *
Low Apgar score	9 (10%)	8 (8.88%)	6 (6.66%)	0.022 *
Early neonatal deaths	0	0	1 (1.1%)	0.04 *

TABLE 6 - ASSOCIATION OF SERUM LDH LEVELS WITH SEVERITY OF DISEASE.

Severity of disease	Serum LDH levels (IU/L)			P value
	<600	600-800	>800	
Thrombocytopenia (Platelets <1,00,000)	7 (7.77%)	3 (3.33%)	7 (7.77%)	0.001*
Renal insufficiency (Serum creatinine >1.1)	27 (30%)	6 (6.66%)	10 (9%)	0.065
Serum urea >40	8 (8.88%)	5 (5.55%)	9 (10%)	0.001*

The association between low birth weights with increase in serum LDH levels was suggested by He et al. which was comparable to the present study (8).

There was significant association of low birth weight and increasing LDH levels ( $P < 0.019$ ) which was due to higher incidence of premature deliveries. Jyoti

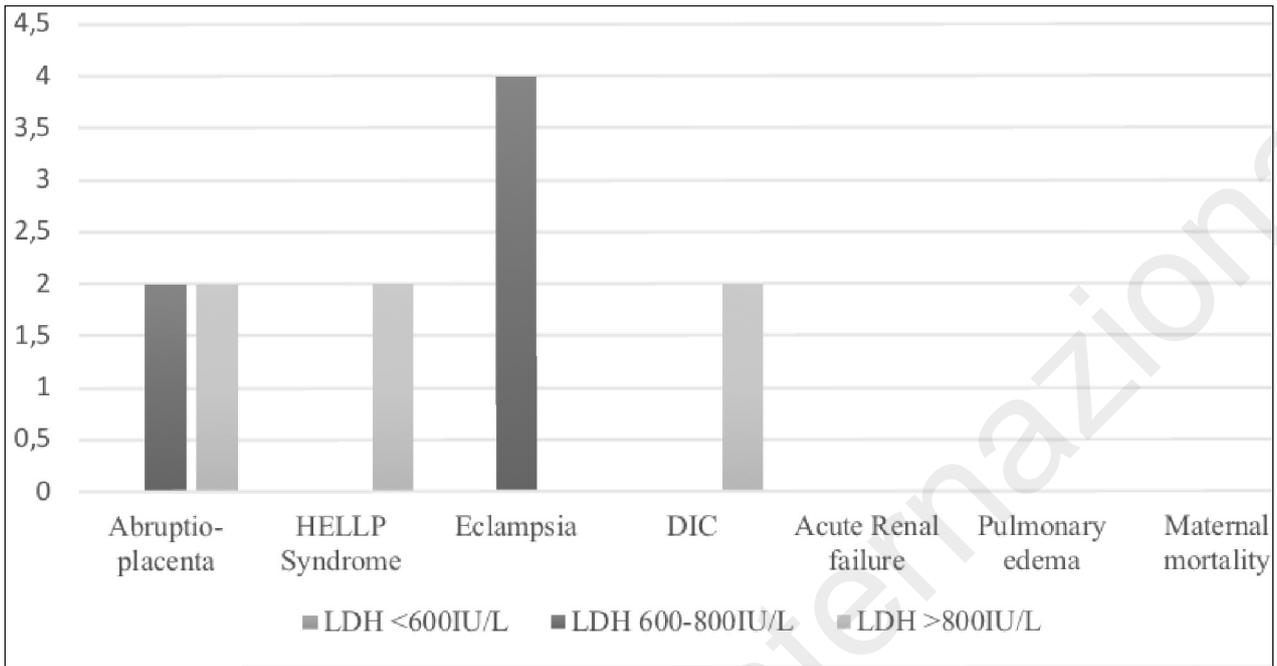


Figure 1 - Correlation between maternal complications and serum LDH levels.

Hak et al. study demonstrated that low birth weight and low Apgar scores were significantly higher in women with raised LDH levels (9).

Severely pre-eclamptic women with LDH levels of more than 800 IU/l resulted in a significant increase in complications in terms of eclampsia, abruptio-placenta, HELLP syndrome and DIC compared to women who had lower serum LDH levels. Similar results were observed in Qublan et al. study (5). A higher levels of serum LDH (1,100 IU/l) were shown to have a high predictive value for significant maternal morbidity in a study conducted by Martin et al. (10). Catanzerite et al. observed that women with elevated levels of LDH manifested HELLP syndrome and were at a higher risk for developing maternal mortality (11). Sarkar et al. also concluded in their study, main cause of preeclampsia is due to elevated levels of serum LDH which indicates the tissue damage is related to endothelial vascular damage (12).

In a study done by Umasatyasri et al., the mean gestational age during parturition was 37.60±2.76 weeks in LDH levels <600 IU/l, 36.71±2.96 weeks when LDH levels between 600-800 IU/l and

36.27±2.69 wks in LDH >800 IU/l which was comparable to the present study (13).

## Conclusion

Serum Lactate dehydrogenase levels can be used as an indicator for the prediction of severity in women with preeclampsia. Hence monitoring of serum LDH levels in high risk pregnant woman may help in early diagnosis of preeclampsia and eclampsia and early intervention may also help in preventing maternal and perinatal morbidity and mortality.

## Declarations

### Funding

None.

### Conflict of interest

None declared.

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