# Correlation of serum lactate dehydrogenase (LDH) level with feto-maternal outcome in normal pregnancy and preeclamptic disorders

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**Manuscript submitted – 30th December 2021**
**Peer review completed – 12th March 2022**
**Accepted for Epub – 15th April 2023**



**Abstract:**

**Objectives:** To compare serum LDH level in normal and preeclamptic mothers in antenatal period and to study the correlation of maternal and perinatal outcome with this biomarker in normal and preeclamptic disorder. **Methods:** A prospective observational study was conducted in the department of obstetrics and gynaecology, Burdwan Medical College, Burdwan for a period of 18 months. Out of 200 pregnant women, 100 were normal pregnant women (control), 57 were mild preeclamptic and 43 had severe preeclampsia (n=100, study groups). Women with singleton pregnancy and cephalic presentation from 24 weeks onwards were enrolled in the study. Demographic and haematological parameters were recorded including the serum LDH levels of both the groups. The serum LDH level was measured in the second trimester at the time of admission and the mothers were followed-up till delivery to assess the maternal and perinatal outcome. **Results**: Higher level of LDH was observed in pregnant women with mild preeclampsia (553.54±183.33 IU/L) and severe preeclampsia (820.33±196.62 IU/L) as compared to normal pregnant women (196.18±55.96 IU/L). High LDH level had significant correlation with systolic and diastolic blood pressure ($p<0.001$). Maternal complications were found to be maximum in women with LDH level >800 IU/L. The perinatal mortality was38% in the study groups and had significant correlation with high serum LDH level of >800 IU/L. **Conclusion:** High serum LDH level correlates well with the poor maternal and perinatal outcome in normal and preeclamptic mothers, but the severity of the disease of preeclampsia is associated with the increased level of this enzyme.

**Keywords:** Lactate dehydrogenase, preeclampsia, maternal outcome, perinatal outcome, death, biomarker.

Pregnant mothers suffer from cardiovascular and metabolic changes from mid pregnancy onwards with increase in cardiac output by 40%, heart rate increases by 10 beats/min. Normal pregnancy is associated with fall in blood pressure due to decrease in systemic vascular resistance in second trimester. Preeclampsia, characterized by hypertension proteinuria and edema (classically) after 20 weeks of pregnancy is a multisystem disorder which complicates 5-8% of all pregnancies[1]. The etiology of preeclampsia is unknown. Evidences support that the endothelial cell dysfunction play an important role in the pathogenesis of preeclampsia [2]. Several biomarkers have been proposed to predict the severity of preeclampsia. Different markers of liver, kidney vascular growth factors (VEGF) and placental growth factors play an important role for prediction of preeclampsia [3]. Among the biochemical markers, lactate dehydrogenase (LDH) is conferred as a good marker associated with preeclampsia.

Modak R, Biswas DK, Talha A, Pal A. Correlation of serum lactate dehydrogenase (LDH) level with feto-maternal outcome in normal pregnancy and preeclamptic disorders. The New Indian Journal of OBGYN. 15th April 2023. Epub Ahead of Print.

LDH is an intracellular enzyme that converts lactic acid to pyruvic acid and elevated level indicates cellular death and leakage of enzyme from the cell [4]. Hypoxia in preeclampsia further enhances glycolysis and increases LDH activity. Studies have shown that LDH activity and gene expression are higher in placenta of preeclampsia than normal pregnancy. Hypoxia induces LDH isoenzyme activity in trophoblasts resulting in higher lactate production. LDH has 5 isomers but LDHA4 is most sensitive in preeclampsia affected placental hypoxia [5].

Preeclampsia and eclampsia constitute a major bulk in maternal complications like placental abruption, hepatic and renal failure and cardiovascular collapse [6]. High level of LDH reflects the severity of the disease, occurrence of complications and poor fetal and maternal outcome. So, the present study was undertaken with the objectives to compare the serum LDH level in normal pregnant women with preeclamptic mothers and to find out its correlation with the severity of the disease, maternal and fetal outcome.

**Materials and methods**

The present study was conducted in the department of obstetrics and gynecology, Burdwan Medical College and Hospital, Burdwan over 18 months (January 2019 to June 2020). It was a prospective observational study conducted on 200 antenatal women attended in the labor room. Sample size was calculated by using the following formula: n=1Cp, power $d^2$; where n=number of subjects required in each group, d was the standard difference and Cp, power was the constant defined by the values chosen for the p value and power.

Inclusion criteria -

- Age 18-35 years
- Singleton pregnancy at 24-40 weeks
- Normal pregnancy
- Diagnosed cases of mild and severe preeclampsia

Exclusion criteria -

- Women, age <18 years and >35 years, chronic hypertension, epilepsy, thyroid disorders, preexisting renal, liver and connective tissue disorders, IUFD and fetal congenital anomalies.

Pregnant women were divided into two groups - Study group: Comprised of 100 pregnant women with mild preeclampsia (n=57) and severe preeclampsia (n=43) and they were further subdivided into three groups on the basis of LDH levels.

- 1.<600 IU/L
- 2. 600-800IU/L
- 3.>800 IU/L

Control groups: Comprised of 100 normotensive pregnant women.

The study was conducted after ethical clearance from the institutional ethics committee. All the subjects were enquired for detailed history taking including demographic profile, chief complaints, menstrual and obstetrical history, past and family history and were recorded in a specially designed case record proforma. General survey along with systemic and obstetrical examinations with special reference to BMI, edema, pallor, BP (mm of Hg) and gestational period in weeks were noted. Routine investigations like complete hemogram, LFT, kidney function tests were performed in all the groups. Seum LDH levels were also estimated in all subjects. Venous blood was taken from antecubital vein aseptically for serum LDH estimation. The sample was centrifuged and serum estimation of LDH level was done by autoanalyzer kinetic method in the department of biochemistry of the college. All the women were followed up till delivery and feto-maternal outcome was noted.

Statistical analysis was done by SPSS version 21.0. Categorical data between the two groups was compared by using chi-square/fisher exact test and quantitative data was compared by student t-test. P value of <0.05 was considered as significant. For multigroup comparison one way analysis of variance (ANOVA) was used.

**Results**

The profile of mothers in terms of age and parity were similar in preeclampsia and normotensive mothers. Mean gestational age among mild preeclampsia and severe preeclampsia groups were 37.09±1.60 weeks and 35.53±1.75

weeks respectively (table 1). Out of 100 preeclamptic women in the study groups, 57 mothers belonged to mild preeclampsia and 43 had severe preeclampsia. Majority of the women in our study population were in the age group of 21-25 years and 9.5% belonged to 31-35 years.

**Table 1: Distribution of patients in relation to age, parity and gestational age**

| Parameters | | Control (n=100) | Study group (n=100) | | P value | Significance |
|---|---|---|---|---|---|---|
| | | | Mild preeclampsia (n=57) | Severe preeclampsia (n=43) | | |
| Age (years) | Mean ±SD | 24.15±4.19 | 23.79±3.98 | 23.65±4.35 | 0.762 | NS |
| Gravida | Primi<br>Multi | 62(62)<br>38(38) | 35(61.40)<br>22(38.60) | 25(58.14)<br>18(41.86) | 0.9076 | NS |
| GA (weeks) | Mean ±SD | 37.50±1.49 | 37.09±1.60 | 35.53±1.75 | 0.000 | S |

GA – Gestational age; NS - Not significant; S – significant.

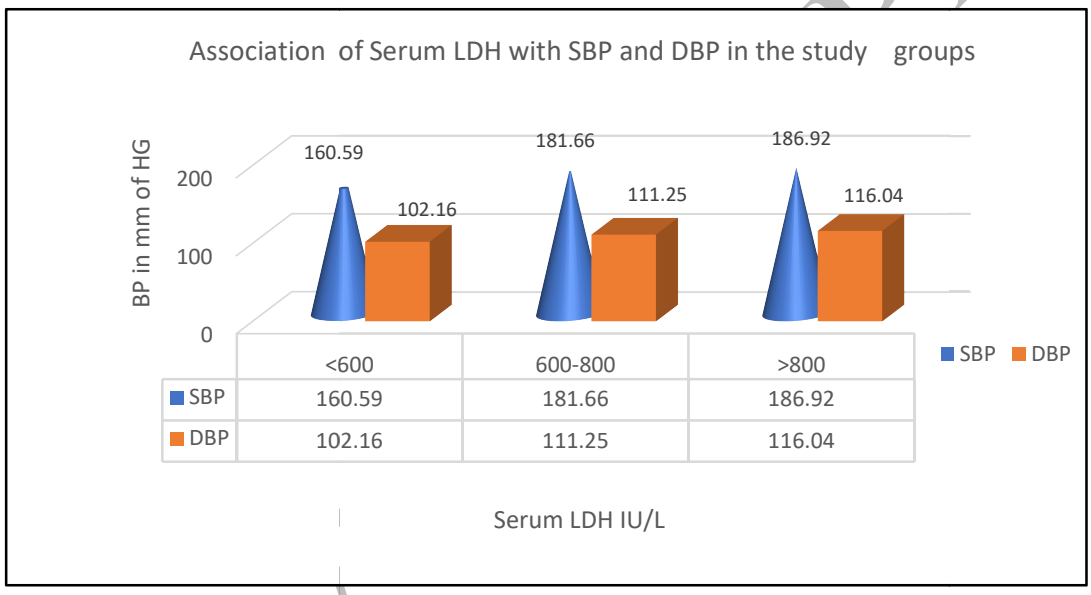


**Figure 1: Distribution of SBP and DBP with serum LDH level in study groups**

Figure 1 depicts that levels of serum LDH with systolic and diastolic blood pressure. SBP and DBP increases significantly with the rise of serum LDH level ($p < 0.05$).

**Table 2: Distribution of serum LDH level in the study and control group**

| Parameters | Study group; n=100 | | | Control group n=100 | Chi-sqare test | P value |
|---|---|---|---|---|---|---|
| LDH group (IU/L) | Mild Preeclampsia (n=57) n(%) | Severe Preeclampsia (n=43) n(%) | Total preeclampsia (n=100) | | | |
| <600 | 42(73.68) | 2(4.65) | 44 | 85 | 37.003 | 0.000 |
| 600-800 | 12(21.06) | 20(46.51) | 32 | 10 | | |
| >800 | 3(5.26) | 21(48.84) | 24 | 5 | | |

Table 2 shows the distribution of preeclamptic and normotensive mothers according to LDH level. Twenty four percent of mother had LDH >800 IU/L in preeclampsia groups, whereas it was 5% in normal pregnant mother (p=0.000).

| **Table 3: Mean LDH level in both the study and control groups** | | | |
|---|---|---|---|
| **Study group LDH level (IU/L) Mean±SD** | | **Control group LDH level(IU/L) Mean±SD** | **P value** |
| **Mild preeclampsia** | **Severe preeclampsia** | | |
| 553.54±183.33 | 820.33±196.62 | 196.18±55.96 | 0.000(S) |
| S - Significant | | | |

Table 3 shows that the mean LDH level was significantly higher in women with preeclampsia than normotensive pregnancies.

| **Table 4: Association of maternal outcome with serum LDH level in the study group** | | | | | | |
|---|---|---|---|---|---|---|
| **Maternal outcome** | **Serum LDH level (IU/L)** | | | **Total n=100** | **P value** | **Significance** |
| | **<600 n=44** | **600-800 n=32** | **>800 n=24** | | | |
| Eclampsia | 0 | 5(15.63) | 8(33.33) | 13(13) | 0.000421 | S |
| Abruptio placentae | 2(4.55) | 3(9.38) | 3(12.5) | 8(8) | 0.482882 | NS |
| ARF | 0 | 3(9.38) | 4(16.67) | 7(7) | 0.029688 | S |
| Death | 0 | 0 | 2(8.33) | 2(2) | 0.039506 | S |
| MODS | 1(2.27) | 1(3.13) | 4(16.67) | 6(6) | 0.048781 | S |
| PRES | 0 | 0 | 1(4.17) | 1(1) | 0.20203 | NS |
| ARF - acute renal failure; MODS - multi organ dysfunction syndrome; PRES - posterior reversible encephalopathy syndrome; NS - not significant; S – significant. | | | | | | |

Table 4 shows the outcome of preeclamptic women in association with LDH levels. Maximum maternal complications were noted with serum LDH level >800 IU/L. Eclampsia was the most common complication (33.33%) with LDH level of >800 IU/L. Abruption was found in 13% of cases and only 2 maternal deaths were noted in women with LDH level of >800 IU/L. MODS (multi organ dysfunction syndrome) was found in17% of cases with high LDH levels of >800 IU/L.

| **Table 5: Perinatal outcome according to LDH levels in the study groups** | | | | | | |
|---|---|---|---|---|---|---|
| **Parameters** | **Serum LDH** | | | **Total n=100** | **P value** | **Significance** |
| | **<600 IU/L n=44** | **600-800 IU/L,n=32** | **>800 IU/L,n=24** | | | |
| Mean gestational age | 37.02±1.41 | 36.09±2.01 | 35.75±1.98 | - | 0.010 | S |
| Mean BW(Kg) | 2.61±0.44 | 2.37±0.50 | 2.12±0.41 | - | 0.000 | S |
| Prematurity | 5(11.36) | 10(31.25) | 11(45.83) | 26(26) | 0.00590 | S |
| Birth asphyxia | 3(6.82) | 4(12.5) | 4(16.67) | 11(11) | 0.43896 | NS |
| IUGR | 9(20.45) | 5(15.63) | 7(29.17) | 21(21) | 0.46533 | NS |
| NICU admission | 7(15.91) | 12(37.5) | 12(50) | 31(31) | 0.00925 | S |
| Perinatal death | 4(9.09) | 6(18.75) | 9(37.5) | 219(19) | 0.01703 | S |
| NS - not significant; S - significant; IUGR - intrauterine growth restriction; NICU - neonatal intensive care unit. | | | | | | |

Table 5 shows the perinatal outcome according to LDH levels in the study groups. There is significant association with prematurity, LBW, perinatal death and NICU admission with serum LDH levels.

Table 6 shows significant association of serum LDH level with PPH and placental abruption with the control groups. Higher level of LDH had higher incidence of preterm baby, birth asphyxia and IUGR babies.

| **Table 6: Association of serum LDH and maternal and foetal outcome in the control groups** | | | | | | |
|---|---|---|---|---|---|---|
| **Parameters** | **Serum LDH (IU/L)** | | | **Total n=100** | **Chi-square test** | **P value** |
| **Maternal outcome** | **<600 n=85** | **600-800 n=10** | **>800 n=5** | | | |
| PPH | 3(3.53) | 0 | 2(40) | 5(5) | 13.808 | 0.001003(S) |
| Placental abruption | 2(2.35) | 1(10) | 2(40) | 5(5) | 14.675 | 0.0006507(S) |
| **Perinatal outcome** | | | | | | |
| Preterm | 10(11.76) | 2(20) | 2(40) | 14(14) | 3.4591 | 0.177367 |
| Birth asphyxia | 7(8.23) | 1(10) | 1(20) | 9(9) | 0.811607 | 0.666441 |
| IUGR | 6(7,06) | 3(30) | 2(40) | 11(11) | 9.33125 | 0.009413(S) |
| PPH – postpartum haemorrhage; IUGR - intrauterine growth restriction; S - significant | | | | | | |

**Discussion**

Preeclampsia is considered as an idiopathic multisystem disorder. The prevention is necessary to minimize its complications. So, the disease must be diagnosed at the earliest. In the present study, serum LDH level has been evaluated as a biomarker of preeclampsia.

The present study is concerned with mean age of controls, preeclampsia and eclampsia were 24.15±4.19 years, 23.79±3.98 years, 23.65±4.35 years respectively. Young age and primigravida are well-known predisposing factors for preeclampsia and eclampsia [4,7, 8]. In our study, maximum patients in the study groups were found in the gestational age between 37.09 weeks to 35.53 weeks. Rachkonda et al noted that majority of the patients (43%) in case group had gestational age between 34-36.6 weeks and this is mainly due to early termination of preeclampsia [9]. In our study the mean value of LDH in mild preeclampsia and severe preeclampsia was 553.54 IU/L and 820.33 IU/L respectively where as in the control group it was only 196.18 IU/L($p<0.001$). Qublan HS et al in their study also demonstrated a significant association of serum LDH levels with severe preeclampsia ($p<0.001$)[4]. In another study by Umasatyasri et al, mean LDH in the control group was 156.06 ±41.93IU/L (normotensives), but in mild preeclampsia, severe preeclampsia, and eclampsia group it was 323.30±77.40 IU/L ,636.20±139.29 IU/L and 649.32±153.53 IU/L respectively [10]. The principal cause of preeclampsia is due to elevated level of serum LDH level and gamma glutamyl transferase (GGT) which indicates the tissue damage and is related to vascular damage [11]. Sonagra et al noted high positive correlation of higher serum LDH level in case group than normotensive control groups[12]. The present study revealed that 26% of mild preeclampsia and 95% of severe preeclamptic mother had LDH level of >600 IU/L whereas Hemalatha et al found 89.8% of preeclampsia and 99.9 % of eclampsia had LDH level of >600 IU/L[13].

In our study it was observed that both systolic and diastolic blood pressures were higher in women with higher LDH levels. This result correlates well with the other studies [10, 14,15].

High serum levels of LDH were associated with increased incidence of maternal complications like abruptio placentae, renal failure, MODS when compared with women of low LDH values. Jaiswar et al observed that there was a significant increase in maternal morbidity with increasing serum LDH levels ($p<0.001$)[14]. Maternal mortality occurred in two women in our study where serum LDH values were 880 IU/L and 1020 IU/L respectively. This signifies strong association of LDH values with adverse maternal outcome. Qublan et al, Demir et al and Andrew et al in their studiesfound similar results [4,8,16].

In our study not only the maternal mortality, but the fetal outcome was poor in patients having higher serum LDH levels. Ninety two percent of babies had birth weight below 2.5 kg at LDH level of >800IU/L. Qublan et al [4] did not find any correlation of babies' birth weight with serum LDH level, but Dave et al and Hemalatha et al found inverse relationship between birth weight and serum LDH level[17,13]. Bera S et al showed that LDH is a good parameter to predict severity of PIH and adverse fetal outcome[18]. In our study prenatal morbidity and mortality was increased in women with higher LDH values. Perinatal death was 38% in the study group with LDH level of >800 IU/L in the present study. Significant increase in the incidence of perinatal mortality was also observed by Qublan et al in patients with increasing level of serum LDH ($p<0.001$) [4].

Perinatal morbidity and mortality were increased significantly in patients with higher LDH levels of >800 IU/L which suggest chronic hypoxia due to hypoperfusion and placental insufficiency as a result of endothelial dysfunction.

**Conclusion**

Serum lactate dehydrogenase level was significantly higher in preeclamptic mothers, which correlates well with the severity of the disease. Poor maternal outcome with fetal morbidity and mortality were associated with high serum LDH level in preeclampsia. It also serves as a significant independent marker in predicting feto-maternal outcome in normotensive pregnancies. So, serum LDH level monitoring with proper management of pregnancy may prevent pregnancy complications and improve the feto-maternal morbidity and mortality in pregnancies with risk factors.

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**Conflict of interest:** None. **Disclaimer:** Nil.