Original Research Article

Role of LDH (Lactate dehydrogenase) in preeclampsia – eclampsia as a prognostic marker: An observational study

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Abstract

Serum LDH is abnormal in a host of disorders, therefore the total serum LDH is highly sensitive but nonspecific test. In preeclampsia also LDH may be elevated and can indicate the prognosis for both mother and fetus. The present study was intended to assess the prognostic significance of the value of serum LDH as a marker of preeclampsia – eclampsia and its severity. Higher serum LDH levels were associated with increased incidence of maternal complications like abruption placenta, renal failure HELLP syndrome, cerebrovascular accidents etc. in the present study. There was an increase in maternal morbidity with increasing serum LDH levels. To conclude high serum LDH levels have significant association with severity of disease and maternal and fetal outcomes in patients of preeclampsia and eclampsia and can be considered as a supportive prognostic tool from early third trimester.

Key words

LDH, Preeclampsia, Prognosis.

Introduction

Preeclampsia is an idiopathic multisystem disorder that complicates 5-8% of all human pregnancies. It is a clinical diagnosis characterised by heterogeneous clinical and laboratory findings. The clinical findings manifest as maternal syndrome or fetal syndrome or both with subsequent increase in the perinatal and maternal morbidity and mortality [1-3].

LDH is an intracellular cytoplasmic enzyme. LDH enzymes are ubiquitous to all the major organ systems e.g. heart, kidney, muscle, leukocytes and erythrocytes. Cellular enzymes in the extracellular space although of no further

metabolic function in this space, 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. Serum LDH is abnormal in a host of disorders, therefore the total serum LDH is highly sensitive but nonspecific test. In order to optimize the diagnostic value, LDH isoenzymes can be measured. This can be further used as help in making decision, regarding the management strategies to improve the maternal and fetal outcome [4-7]. The present study was intended to assess the prognostic significance of the value of serum LDH as a marker of preeclampsia – eclampsia and its severity.

Aim and objectives

- To compare serum LDH levels in the normal pregnant women and in women with preeclampsia and eclampsia in ante-partum period.
- To study the correlation of maternal and perinatal outcomes with serum LDH levels.

Material and methods

A prospective comparative case control study was undertaken in the Department of Obstetrics and Gynecology and the Department of Biochemistry, King George Hospital, Visakhapatnam. In the present study, 150 pregnant women were included. 50 women who had normotensive pregnancies were matched for maternal age and gestational age with patients and were selected as control group. Another 100 women presented with clinical features of preeclampsia (50) and eclampsia (50) was selected as cases. They were sub classified into mild and severe preeclampsia depending upon the classification given by ACOG. Subjects were further divided according to the serum LDH levels into following groups : <600 IU/l, 600–800 IU/l and >800 IU/l.

Inclusion criteria

Singleton pregnancy, age 18 - 30 years, 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 (>28wk of gestation).

Exclusion criteria

Patients with history of liver disease, diabetes, renal failure, hemolytic anemias, stroke, coronary artery disease, chronic lung diseases, connective tissue disorders, disseminated intravascular coagulation and seizures, chronic hypertension, gestational diabetes, multiple pregnancy, smoking and alcoholism, hepatotoxic drugs were excluded.

Results

Total 150 patients were studied, of which 50 (33.3%) were normal pregnant women; remaining 100 (66.6%) cases included pregnancy with eclampsia and preeclampsia. Out of these 100 cases, 30 (20%) were mild preeclampsia, 20 (13.3%) were severe preeclampsia and 50 (33.3%) cases were of eclampsia. The maximum number of patients in control group as well as study group belonged to the age group of 21–25 years. When compared statistically, the age wise distribution in the subjects was almost similar to the control group. In the present study, majority were nullipara 106 (70.6%). (**Table – 1**)

Table - 1: Distribution of patients with age and parity.

Groups		Number	Mean Age	Nullipara
I	Normotensive	50 (33.3%)	23.46 ± 3.29	36
II A	Mild preeclampsia	30 (20.0%)	23.80 ± 3.30	21
II B	Severe preeclampsia	20 (13.3%)	24.03 ± 3.99	11
III	Eclampsia	50 (33.3%)	24.50 ± 3.45	38

Out of total 115 cases with LDH levels <600 IU/l, 58 women had normal systolic BP, 28 women had systolic BP 140 to 160 mm of Hg and 29 women had systolic BP 160 mm Hg and above. Out of 24 patients with LDH levels between 600 and 800 IU/l, 5 women had systolic BP in the range of 140 to160 mm of Hg and 19 women had SBP >160 mm Hg. In the remaining 11 patients with LDH levels above 800 IU/l, 2 women had systolic BP in the range of 140 to 160 mm Hg and 9 women had systolic BP 160 mm Hg and above. On the other hand, out of total 115 cases with LDH levels <600 IU/l, 50 cases had normal diastolic BP, 45 cases had diastolic BP in the range of 90-110 mm of Hg and 20 cases had diastolic BP 110 mm Hg and above. Out of 24 patients with LDH levels between 600 and 800 IU/l, 15 women had diastolic BP in the range of 90-110 mm of Hg and 9 had diastolic BP 110 mm Hg or more. In the remaining 11 patients with LDH levels above 800 IU/l, 5 cases had diastolic BP in the range of 90-110 mm oh Hg and 6 had diastolic BP 110 mm Hg and above.

On statistical analysis it was found that high systolic and diastolic BP was associated with higher levels of serum LDH ($P < 0.001$). The mean LDH levels in the control group was 159.06 ± 41.93 IU/L, mild preeclampsia group was 323.30 ± 77.40 IU/L, severe preeclampsia group was 636.20 ± 132.29 IU/L and that of eclampsia was 649.32 ± 153.53 IU/L. The mean LDH levels are higher in severe preeclampsia group and eclampsia group. (**Table – 2**) On analyzing the above data it is clearly observed that there was significant rise in the LDH levels with increasing severity of the disease ($P < 0.001$).

Table - 2: Mean LDH levels in various groups.

Groups	**LDH (mean ± SD) IU/L**
Normotensive (n = 50)	159.06 ± 41.93
Mild preeclampsia (n = 30)	323.30 ±77.40
Severe preeclampsia (n =20)	636.20 ± 132.29
Eclampsia (n = 50)	649.32 ± 153.53

In the control arm all had levels of <600 IU/l, the mean value of LDH being 159.06 ± 41.93 IU/l. All the patients in mild preeclampsia group had levels <600 IU/l. Out of 20 cases of severe preeclampsia, 11 cases (55%) had LDH levels <600 IU/l, 7 cases (35%) had LDH levels between 600 and 800 IU/l and 2 cases (10%) had LDH levels above 800 IU/l. In eclampsia group, 9 (18%) had levels >800 IU/l. While 17 (34%) had levels between 600 and 800 IU/l and 24 (48%) had levels <600 IU/l.

Parameters of perinatal outcomes considered in the present study were mean gestational age at delivery, mean birth weights of newborn and APGAR scores at 1min and 5 min and are correlated with LDH levels. The mean gestational age at the time of delivery was 37.60 ± 2.76 weeks in cases with LDH levels <600 IU/l. It was less in patients with LDH level in between 600 and 800 IU/l, which was 36.71 ± 2.96 weeks and 36.27 ± 2.69weeks in patients with LDH >800 IU/l .

It was found that in cases with LDH levels <600 IU/l, the mean birth weight was 2.73 ± 6.38 kg in the group with LDH levels 600–800 IU/l, the mean birth weight was 2.54 ± 7.48 kg. The mean weight in the third group i.e., with LDH levels >800 IU/l was 2.28 ± 7.90 kg. This observation indicates that there is reduction in the average weight of babies with higher level of LDH. Association of systolic and diastolic BP with LDH levels in various groups was as per **Table – 3**.

The mean APGAR scores at 1 min and 5 min were found to be lower in cases with higher LDH levels.

When LDH levels were <600 IU/L (115 cases), 65 had an uneventful perinatal period. 37 had neonatal complications, while 8 early neonatal deaths were reported and there were no still births, and there were 5 intrauterine deaths. In the women with LDH levels in the range of 600–800 IU/l (24 cases), 12 cases had uneventful outcome, while 6 had neonatal complications and

3 had early neonatal death. In this group no still births and there were 3 intrauterine deaths. In the third group where LDH levels were markedly elevated (i.e., >800 IU/l) there were 11 cases out of which only 6 had uneventful outcome, whereas 2 had neonatal complications and 1 was early neonatal death. No still births were reported. And there were 2 intrauterine deaths.

When the LDH levels were < 600 IU/L, there were two cases of postpartum hemorrhage and one case of abruption placenta. In the second group where LDH levels were 600–800 IU/l one case of pulmonary edema and 5 cases of postpartum hemorrhage were noted. In the third group i.e., with marked elevations of serum LDH levels (>800 IU/l), complications were observed in 6 cases. Two cases of abruption placentae, one case of pulmonary edema and three cases of postpartum hemorrhage were observed. (**Table – 4**) There was statistically significant increase in maternal complications with increasing LDH levels ($P < 0.001$).

Table - 3: Association of systolic and diastolic BP with LDH levels in various groups.

	LDH <600 IU/L	**LDH 600-800 IU/L**	**LDH >800 IU/L**
Systolic blood pressure			
90 - <140 mm Hg	58 (50.4%)	-	-
140 - <160 mm Hg	28 (24.3%)	5 (20.8%)	2 (18.1%)
>160 mm Hg	29 (25.2%)	19 (79.1%)	9 (81.8%)
Diastolic blood pressure			
60 - <90 mm Hg	50 (43.4%)	-	-
90 - <110 mm Hg	45 (39.1%)	15 (62.5%)	5 (45.5%)
>110 mm Hg	20 (17.3%)	9 (37.5%)	6 (54.5%)

Table - 4: Comparison of perinatal outcome with LDH levels.

Parameters	**LDH <600IU/L**	**LDH 600 – 800IU/L**	**LDH >800IU/L**
Mean gestational age	37.60 ± 2.76 wks	36.71 ± 2.96 wks	36.27 ± 2.69wks
Mean birth weight	2.73 ± 6.38 kg	2.54 ± 7.48 kg	2.28 ± 7.90 kg
APGAR 1 min	7.32 ±1.65	5.57 ± 2.95	5.27 ± 3.13
APGAR 5 min	8.73 ± 1.62	7.33 ± 3.63	6.91 ± 3.83
Outcome			
Alive and well	65 (56.5%)	12 (50%)	6 (54.5%)
Neonatal complications	37 (32.1%)	6 (12.5%)	2 (18.1%)
Neonatal deaths	8 (6.1%)	3 (25%)	1 (9%)
Intra uterine deaths	5 (4.3%)	3 (12.5%)	2 (18.1%)

Discussion

Preeclampsia is considered as an idiopathic multisystem disorder that is specific to human pregnancy. The prevention of severe preeclampsia and eclampsia has become the main problem of toxemia of pregnancy. In order to prevent it, we must diagnose the disease at its earliest beginnings. The triad of high blood pressure, oedema and albuminuria is neither specific nor sensitive enough; therefore the search is on for a reliable marker. In the present study, LDH has been evaluated as a biochemical marker for preeclampsia and eclampsia.

In the present study majority of the patients belonged to younger age group and were nulliparous. This finding was also observed by Qublan HS, et al. [7], where the mean age of

normal controls was 30 years and those with severe preeclampsia was significantly younger with low parity.

On analyzing the data in the present study it is clearly observed that there is significant rise in the LDH levels with increasing severity of the disease ($P < 0.001$ – statistically significant).

Qublan HS, et al. [7] found in their study that the mean LDH levels in normal controls was 299 ± 79 IU/l, in patients with mild preeclampsia was 348 ± 76 IU/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 ($P < 0.001$).

Systolic and diastolic BP was significantly higher in patients with higher serum LDH levels ($P < 0.001$) in both studies.

In another study by Jaiswar S.P, et al. [5], the control arm had mean LDH levels of 278.3 ± 119.2 IU/l (normotensives). In mild preeclampsia group it was 400.45 + 145.21 IU/l, in severe preeclampsia group it was 646.95 ± 401.64 IU/l and eclampsia group was 1648.10 ± 1992.29 IU/l. Jaiswer SP, et al. [5] also demonstrated a significant rise in the LDH levels with increasing severity of the disease ($P < 0.001$). In the present study, the LDH levels were significantly raised with the severity of the disease ($P < 0.001$) and this was in accordance with the above studies.

In a cross sectional study published in 2012; taking 30 women with preeclampsia (group I), 30 with gestational hypertension (group II), 30 with normal pregnancy (group III) and 30 age matched healthy non-pregnant women (controls). A serum level of LDH was measured using commercially available kits. It was seen that the mean serum LDH was 26% higher in group I when compared with group II and 135% higher when compared with group III. The mean serum LDH was 86% higher in group II when compared with group III.

Various parameters of perinatal outcomes in respect to LDH levels have been studied. There was no significant decrease in mean gestational age with increase in serum LDH levels in the present study ($p = 0.128$ - no statistical significance)

In Jaiswar S.P., et al. [5] study, the mean gestational age in the similar groups was 36.92 ± 3.44 weeks (<600 IU/l), 34.77 ± 3.11 weeks (600 and 800 IU/l) and 35.25 ± 3.23 weeks (LDH >800 IU/l) respectively.

There is reduction in the average weight of babies with higher level of LDH but not statistically significant ($p = 0.926$). This indicates increase in preterm deliveries in patients with higher LDH levels in the present study.

The association of low birth weight of infants with increase in serum LDH levels was suggested by He S, et al. [4] in their study. This was in contrary to Qublan HS, et al. [7] who did not find any significant association. In the present study it was not significant ($p >0.05$)

According to Jaiswar SP, et al. [5] study, there were significant low birth weight babies in women with higher LDH levels. ($P = 0.019$)

The mean Apgar scores were significantly reduced at 1 min and 5 min, in the present study, showing mild to severe depression of the newborn baby with increasing LDH levels. ($p <0.01$ – statistically significant)

The occurrence of neonatal complications ($p = 0.33$) and perinatal deaths ($p = 0.79$) were higher in mothers who had increased serum levels of LDH but not statistically significant in the present study. ($p >0.05$)

Increase in the incidence of perinatal deaths was observed by Qublan HS, et al. [7] in patients with increasing levels of serum LDH levels ($P < 0.001$). According to Jaiswar SP, et al. [5] study, significant increase in neonatal complications ($P = 0.003$), still births ($P < 0.001$)

and perinatal deaths ($P = 0.003$) was noted. Their study concluded that LDH levels were significantly elevated in women with preeclampsia and eclampsia and higher LDH levels had significant correlation with severity of the disease as well as poor maternal and perinatal outcome. In the present study, there was an increase in maternal complications with increasing LDH levels which was statistically significant ($p < 0.05$)

Severely pre-eclamptic women with LDH levels of >800 IU/l showed a significant increase in complications in terms of abruption placenta, postpartum hemorrhage and various other complications compared to women who had lower serum LDH levels, in the study of Qublan HS, et al. [7]. A high serum level of LDH (>1,400 IU/l) were shown to have a high predictive value for significant maternal morbidity in a study conducted by Martin JN Jr, et al. [6]; Catanzerite VA, et al. [1] reported a subgroup of patients who had elevated levels of LDH manifested with hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome and were at a high risk for developing maternal mortality. Demir SC, et al. [2] 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 [3].

Higher serum LDH levels were associated with increased incidence of maternal complications like abruption placenta, renal failure HELLP syndrome, cerebrovascular accidents etc. in the present study. There was an increase in maternal morbidity with increasing serum LDH levels.

Conclusion

To conclude high serum LDH levels have significant association with severity of disease and maternal and fetal outcomes in patients of preeclampsia and eclampsia and can be considered as a supportive prognostic tool from early third trimester.

References

1. Catanzerite VA, Steinberg SM, Mosley CA, et al. Severe preeclampsia with fulminant and extreme elevation of aspartate aminotransferase and lactate dehydrogenase levels. Am J Perinatol., 1995; 12: 310–313.
2. Demir SC, Evruke C, Ozgunen FT, et al. Factors that influence morbidity, and mortality in severe preeclampsia, eclampsia and HELLP syndrome. Saudi Med J., 2006; 27: 1015–1018.
3. Hall DR, Odendaal HJ, Kirsten GF, et al. Expectant management of early onset, severe preeclampsia perinatal outcome. BJOG, 2000; 107: 1258–1264.
4. He S, Bremme K, Kallner A, et al. Increased concentrations of lactate dehydrogenase in pregnancy with preeclampsia; a predictor for birth of small for gestational age infants. Gynecol Obstet Invest., 1995; 39: 234–238.
5. Jaiswar S.P., Gupta Amrit, Sachan Rekha, Natu S.N, Shaili Mohan. Lactic Dehydrogenase: A biochemical marker for preeclampsia-eclampsia. JOGI, 2011; 61(6): 645-648.
6. Martin JN Jr, May WL, Magann EF, et al. Early risk assessment of severe preeclampsia: Admission battery of symptoms and laboratory tests to predict likelihood of subsequent significant maternal morbidity. Am J Obstet Gynecol., 1999; 180: 1407–1414.
7. Qublan HS, Amarun V, Bateinen O, et al. LDH as biochemical marker of adverse pregnancy outcome in severe preeclampsia. Med Sci Monit., 2005; 11: 393–397.