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Original Article

Serum Lactate Dehydrogenase Level Biomarkers for Severity and Outcome in Preeclampsia and Eclampsia

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ABSTRACT

Background: Hypertensive disorders of pregnancy are a major cause of maternal and perinatal morbidity and mortality. Among them, preeclampsia and eclampsia are associated with significant complications. Biochemical markers like serum Lactate Dehydrogenase (LDH) may help assess disease severity.
Objective: To compare serum LDH level in normotensive and hypertensive pregnant women and evaluate their correlation with disease severity and fetomaternal outcomes.
Materials and Methods: A comparative observational study was conducted in the Department of Obstetrics and Gynecology, in hospital associated with Medical College. Pregnant women were categorized into normotensive, preeclampsia, and eclampsia groups. Serum LDH and uric acid levels were measured and correlated with clinical severity and outcomes.
Results: Serum LDH level was significantly elevated in preeclampsia and eclampsia cases compared to normotensive women. Higher levels correlated with increased disease severity, adverse maternal complications, and poor perinatal outcomes.
Conclusion: Serum LDH is simple, cost-effective biomarker that can be used for early identification of severe preeclampsia and prediction of adverse outcomes.

Keywords: Preeclampsia, Eclampsia, LDH, Pregnancy Hypertension.

INTRODUCTION

Hypertension is a sign of an underlying pathology which may be preexisting or appears for the first time during pregnancy. American College of Obstetricians and Gynaecologists (2013, 2020)[1] describes four types of hypertensive disease: 1). Preeclampsia and eclampsia syndrome. 2). Chronic hypertension of any etiology. 3). Preeclampsia superimposed on chronic hypertension. 4). Gestational hypertension.

Hypertensive disorders complicate approximately 7–15% of pregnancies and are a leading cause of maternal and perinatal morbidity and mortality[2-12]. In the United States from 2011 to 2015, 7 percent of pregnancy related maternal deaths were caused by preeclampsia or eclampsia[13]. Preeclampsia is best described as a pregnancy-specific syndrome affects virtually every organ system, characterized by hypertension and often proteinuria after 20 weeks of gestation.

Eclampsia is the occurrence of generalized tonic clonic seizures in a pre eclamptic women that cannot be attributed to other causes. Eclampsia is an extremely severe form of preeclampsia. Early identification of severity of preeclampsia or eclampsia is crucial for timely intervention. Severe preeclampsia is frequently accompanied by hemolysis, which manifests as elevated serum lactate dehydrogenase levels and reduced haptoglobin levels[14]. Estimation of serum LDH level is a simple biochemical test, which quantitates the extent of cellular death and thereby the assessment of severity of preeclampsia and eclampsia.

So aim of this study is to compare serum LDH levels in normotensive pregnant women and in women with preeclampsia or eclampsia and to correlate serum LDH levels with severity of disease, maternal and perinatal outcome.

MATERIALS AND METHODS

This Observational comparative study was carried out among inpatients in the Department Of Obstetrics And Gynaecology at Hospital attached with Medical College from 12/10/2023 to 31/07/2024.

Inclusion Criteria: Women in age group of 18 – 35 year. Singleton and Multifetal pregnancy. Primigravida and multigravida. Normal (Vertex)and Abnormal presentation Willing for participation. Gestational age > 28 weeks.

Exclusion criteria: Women not willing for participation; Mothers with Hypertension < 28 weeks of gestation; Chronic Hypertension; Preexisting Diabetes Mellitus; Liver/Renal /Epilepsy/Thyroid/Cardiac/Coagulation/endocrinal disorders; Gestational diabetes mellitus; Leukemia; Hepatitis; Pancreatitis.

Based on NHBPEP Classification, The study had 4 separate groups, one being a normotensive control group with 120 women, and the rest three being cases with mild pre eclampsia, severe pre-eclampsia and eclampsia patients amounting to 40 in each group with help of Simple random sampling technique based on Blood Pressure as:

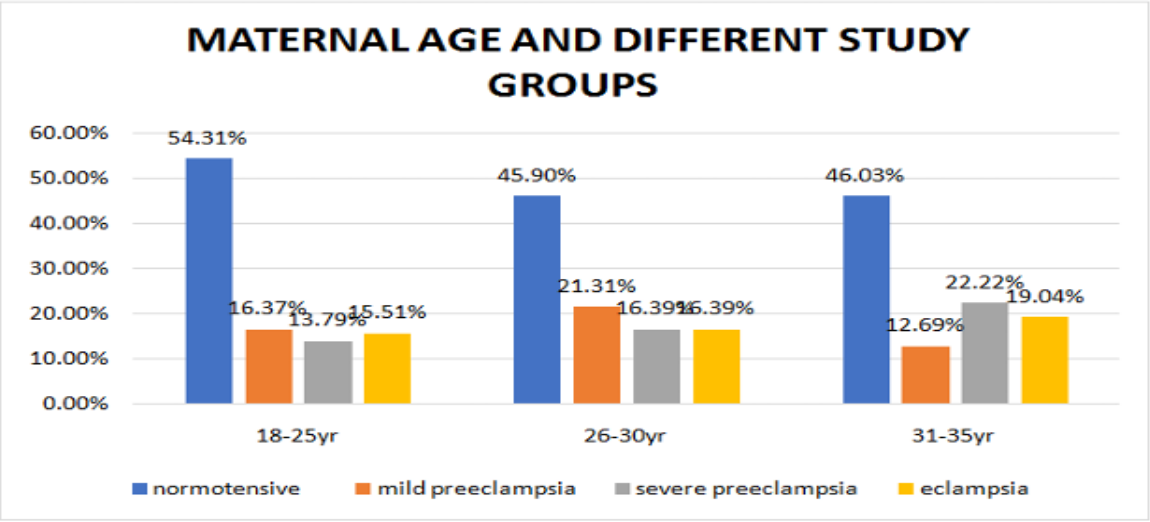
1. MILD PRE-ECLAMPSIA: Blood Pressure of ≥140/90 to +1
2. SEVERE PRE-ECLAMPSIA: Blood Pressure of ≥160/110 mmHg with or without urine albumin being positive.
3. ECLAMPSIA: Preeclamptic patients with 1 or more episode of Generalised Tonic Clonic Seizures.

Institutional Ethics Committee approval was obtained, and informed consent was taken from all participants. Patients were divided further according to serum LDH values as < 600, 600 – 800, > 800 IU/L. LDH values were compared with Maternal and Fetal outcomes and studied using appropriate statistical test. Patients were followed till delivery and early postpartum. Maternal complications like Abruption, HELLP, Eclampsia, Pulmonary edema, Intracranial haemorrhage, Maternal death and Fetal complications like low birth weight, Respiratory distress syndrome, HIE, Sepsis, neonatal death, IUD, IUGR were noted and correlated with serum LDH and Uric acid values. Statistical Analysis was done through SPSS v20.0 software. The results were compared based on chi-square test and one proportion z test and differences were considered as significant if p value is < 0.05.

RESULTS

A total of 240 Antenatal women attending OPD / Labour ward in medical college from October 2023 to April 2024 were included in the study. In our study out of 116 patients belongs to the age group 18-25yr in which 63 [54.31%] patients were normotensives, 19 [16.37%] were mild pre eclampsia patients, 16 [13.79%] were severe pre-eclampsia patients and 18 [15.51%] were eclampsia patients. Out of 61 patients with age group 26-30yr, 28 [45.90%] were normotensive, 13 [21.31%] were mild pre-eclampsia patients, 10 [16.39%] were severe pre-eclampsia patients and 10 [16.39%] were eclampsia patients. Out of 63 patients with age 31-35yr, 29 [46.03%] patients were normotensive, 8 [12.9%] were mild pre-eclampsia patients, 14 [22.22%] were severe pre-eclampsia patients and 12 [19.04%] were eclampsia patients.

Out of 120 normotensive patients, 117 [97.5%] had serum LDH <600 I/U, 3 [2.5%] had serum LDH 600-800I/U no one had serum LDH >800IU/L. Out of 40 mild pre-eclampsia patients, 37 [92.5%] had serum LDH <600 I/U , 3 [7.5%] had serum LDH 600-800I/U and no patient had serum LDH >800 I/U. Out of 40 severe pre-eclampsia patients, 10 [25%] had serum LDH <600 I/U, 14 [35%] had serum LDH 600-800I/U and 16 [40%] had serum LDH >800 I/U. Out of 40 eclampsia patients, 9 [22.5%] had serum LDH <600 I/U, 12 [30%] had serum LDH 600-800I/U and 19 [47.5%] patient had serum LDH >800 I/U, and the p value was < 0.0001, which indicates significant association between serum LDH and severity of preeclampsia and eclampsia.



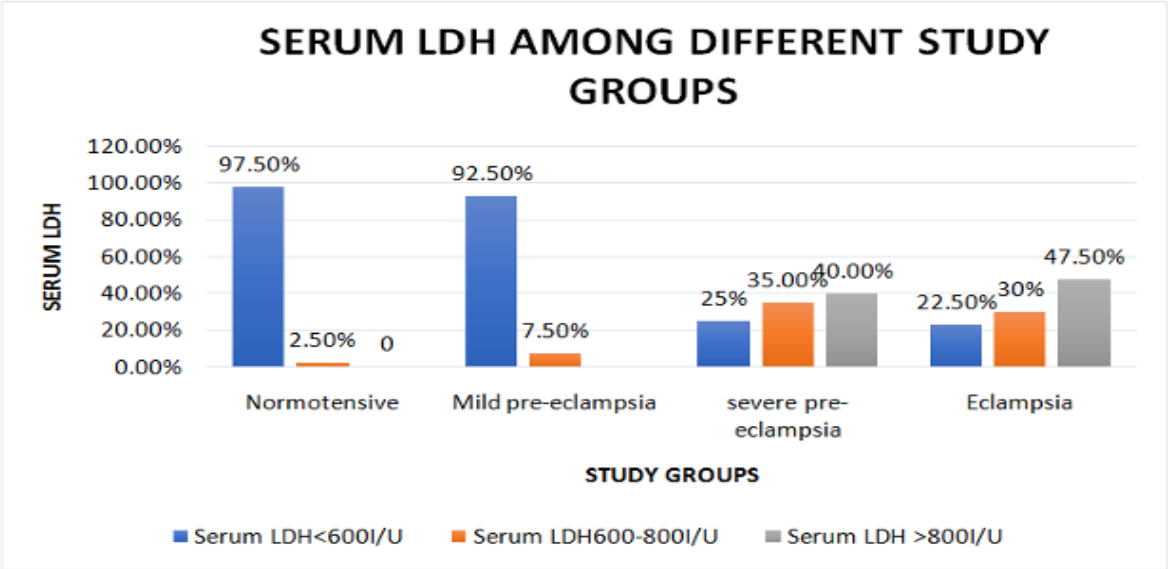


Table 1: Association Between Serum LDH And Systolic Blood Pressure

Systolic blood Pressure	Serum LDH <600	Serum LDH 600 – 800	Serum LDH >800	P value
90 – 139 mmHg [120]	117 [97.5%]	3 [2.5%]	0	<0.0001
140 – 159 mmHg [52]	44 84.6%]	8 [15.38%]	0	
>159 mmHg [68]	12 [17.64%]	21 [30.38%]	35 [51.47%]	
Total [240]	**173 [72.08%]**	**32 [13.33%]**	**35 [14.58%]**	

Out of 120 patients with systolic BP of 90-139mmHg 117 [97.5%] had serum LDH <600 I/U, 3 [2.5%] had serum LDH 600-800I/U. Out of 52 patients with systolic BP of 140-159mmHg 44 [84.6%] had serum LDH <600 I/U, 8 [15.38%] had serum LDH 600-800I/U. Out of 68 patients with systolic BP of 90-139mmHg 12 [17.64%] had serum LDH < 600 I/U, 21 [30.88%] had serum LDH 600-800I/U, and 31 [51.47%] had serum LDH >800 I/U and the p value was < 0.0001, which indicates significant association between serum LDH and systolic blood pressure.

Out of 120 patients with Diastolic BP of 60-89mmHg 117 [97.5%] had Serum LDH <600 I/U, 3 [2.5%] had Serum LDH 600-800 I/U. Out of 48 patients with Diastolic BP of 90-109mmHg 41 [85.41%] had Serum LDH <600 I/U, 7 [14.58%] had Serum LDH 600-800 I/U. Out of 72 patients with Diastolic BP of >109mmHg 15[20.83%] had Serum LDH of < 600 I/U, 22 [30.55%] had Serum LDH of 600-800 I/U and 35 [48.61%] had Serum LDH > 800 I/U and the p value was <0.0001 which indicates significant association between serum LDH and systolic blood pressure.

Table 2: Association Between Serum LDH And Diastolic Blood Pressure

Diastolic blood Pressure	Serum LDH <600 IU/L	Serum LDH 600-800 IU/L	Serum LDH > 800IU/L	P value
60-89 mmHg [120]	117 [97.5%]	3 [2.5%]	0	<0.0001
90-109 mmHg [48]	41 [85.41%]	7 [14%]	0	
>109 mmHg [72]	15 [20.83%]	22 [30.55%]	35 [48.61%]	
Total [240]	**173 [72.08%]**	**32 [13.33%]**	**35 [14.58%]**	

In our study total 87 different maternal complications [Table 3] were noted and of which 9[10.34%] complications were seen with serum LDH < 600IU/L, 18[20.68%] complications were seen with serum LDH 600-800IU/L and 60[68.96%] complications were seen with serum LDH > 800IU/L. Total 20 patients had abruption, of which 2 [10%] had serum LDH 600-800IU/L and 18 [90%] had serum LDH > 800IU/L. 11 patients had HELLP Syndrome, of which 2 [18.18%] patients had serum LDH 600-800IU/L and 9 [81.81%] had serum LDH >800IU/L. 40 patients had eclampsia and of which 9 [22.50%] had serum LDH < 600IU/L, 12 [30%] had serum LDH 600-800IU/L and 19 [47.50%] had serum LDH >800IU/L. Total 5 patients had acute renal failure, of which 1 [20%] patient had serum LDH 600-800IU/L and 4 [80%] had serum LDH >800IU/L. 4 [100%] patients had pulmonary edema and all had serum LDH >800IU/L. 7 patients had postpartum hemorrhage and of which 1 [14.28%]

Table 3: Association Between Serum LDH And Maternal Complications

Maternal Complications	Patients with LDH<600 IU/L	Patients with LDH 600-800 IU/L	Patients with LDH >800 IU/L	P value

Abruption [20]	0 [0]	2 [10%]	18 [90%]	<0.034
HELLP Syndrome [11]	0 [0]	2 [18.18%]	9 [81.81%]	
Eclampsia [40]	9 [22.5%]	12 [30%]	19 [47.5%]	
Acute renal failure [5]	0 [0%]	1 [20%]	4 [80%]	
Pulmonary edema [4]	0 [0%]	0 [0%]	4 [100%]	
Postpartum haemorrhage [7]	0 [0%]	1 [14.28%]	6 [85.71%]	
Total [87]	**9 [10.34%]**	**18 [20.68%]**	**60 [68.96%]**	

Table 4: Association Between Serum LDH And Fetal Complications

Fetal Complications	Patients with LDH <600IU/L	Patients with LDH 600-800IU/L	Patients with LDH >800IU/L	P value
Low birth weight [55]	14 [25.45%]	18 [32.72%]	23[41.81%]	<0.027
Respiratory distress Syndrome [14]	1 [7.14%]	3 [21.42%]	10 [71.42%]	
HIE [17]	2 [11.76%]	7 [41.17%]	8 [47.05%]	
Sepsis [12]	1 [8.33%]	1 [8.33%]	10 [83.33%]	
Neonatal Death [13]	1 [7.69%]	2 [15.38%]	10 [76.92%]	
Intrauterine growth restriction [16]	1 [6.25%]	1 [6.25%]	14 [87.5%]	
Intrauterine fetal death [9]	0	2 [22.22%]	7 [77.77%]	
Total [136]	20 [14.70%]	34 [25%]	82 [60.29%]	

Patients had serum LDH 600-800 IU/L and 6 [85.71%] had serum LDH >800IU/L and the p value was <0.034, which indicates significant association between serum LDH and occurrence of different maternal complications.

Total 136 different type of fetal complications [Table 4] were noted and of which 20 [14.70%] complications were seen with serum LDH < 600IU/L group, 34[25%] complications were seen with serum LDH 600-800IU/L group and 82[60.29%] complications were seen with serum LDH >800IU/L group. In this study 55 patients gave birth to low birth weight babies of which 14 [25.45%] had serum LDH <600IU/L, 18 [32.72%] had serum LDH 600-800IU/L and 23 [41.81%] had serum LDH >800IU/L. 14 babies had respiratory distress syndrome out of which 1 [7.14%] had serum LDH < 600IU/L, 3 [21.42%] had serum LDH 600-800IU/L and 10 [71.42%] had serum LDH >800IU/L. 17 babies had HIE, of which 2 [11.76%] had serum LDH < 600IU/L, 7 [41.17%] had serum LDH 600-800IU/L and 8 [47.05%] had serum LDH >800IU/L. 12 babies had sepsis, of which 1 [8.33%] had serum LDH <600IU/L, 1 [8.33%] had serum LDH 600-800IU/L and 10 [83.83%] had serum LDH > 800IU/L. 13 patients had neonatal death, of which 1 [7.69%] patient had serum LDH <600IU/L, 2 [15.38%] had serum LDH 600-800IU/L and 10 [76.92%] had serum LDH > 800IU/L. 16 patients had intra uterine growth restriction as a complication, of which 1 [6.25%] had serum LDH < 600IU/L, 1 [6.25%] had serum LDH 600-800IU/L and 14 [87.5%] had serum LDH >800IU/L. 9 patients had intra uterine fetal death, of which 2 [22.22%] had serum LDH 600-800IU/L and 7 [77.77%] had serum LDH >800IU/L and the p value was < 0.027, which indicates significant association between serum LDH and different fetal complications as mentioned above.

DISCUSSION

Preeclampsia is not only a simple gestational hypertension with proteinuria. It is a pregnancy-specific syndrome which involves multi-organs of body, if it is not treated properly, it may progresses to eclampsia, requiring immediate termination of pregnancy. While the degree of hypertension is a clinically important guide for predicting the severity of preeclampsia, certain biochemical markers aid in determining the severity, prognosis and management. We did a study to demonstrate relationship in the severity of hypertensive disorders with serum LDH level.

In the present study majority of the patients belonged to younger age group [18-25yrs] but the P value was not significant [p=0.63]. The same observation was noted in the study conducted by Rizwana Habib et al[15], in which 60% in the study group and 57% in the control group were in the age group of 25-29 years. Mean age in the study group was 26.2±2.8 years and in the control group was 26.0±2.9 years. Renu at al[16] conducted a study, where the mean age of subjects in the study group was 25.75±4.54 years and in the control group was a 25.30±4.01 year, which was statistically non-significant. In age group 18-25yrs 16.37% subjects were having mild pre eclampsia, 13.79% were having severe pre-eclampsia and 15.51% were having eclampsia where as In age group 31-35yr, 12.9% were having mild pre-eclampsia , 22.22% were having severe pre-eclampsia and 19.04% were having eclampsia. These results show severity of pre- eclampsia increases with age. Out of 120 normotensive patients, majority [97.5%] had serum LDH <600 I/U and no one had serum LDH >800IU/L. Out of 40 mild pre-eclampsia patients, 92.5%[37] had serum LDH <600 I/U and no patient had serum LDH >800 I/U. Out of 40 severe pre-eclampsia patients, 25%[10] had serum LDH <600 I/U, 35%[14] had serum LDH 600-800I/U and 40%[16] had serum LDH >800 I/U. Out of 40 eclampsia patients, 22.5%[9] had serum LDH <600 I/U, 30%[12] had serum LDH

600-800I/U and 47.5%[19] patient had serum LDH >800 I/U, and the p value was < 0.0001, which indicates significant association between serum LDH and severity of preeclampsia and eclampsia, same was observed in study conducted by K Omkara Murthy et al[17], in which they found the mean LDH levels were 286.75±100.68, 555.85±133.44 and 711.88±119.05 respectively in normotensive, mild preeclampsia and severe preeclampsia respectively and it was statistically significant. In group (Table 1) with systolic BP of 90-139mmHg 97.5% [117] had serum LDH <600 I/U, 2.5%[3] had serum LDH 600-800I/U none of them had serum LDH more than 800 I/U . In group with systolic BP of 140-159mmHg 84.6% [44] had serum LDH <600 I/U, 15.38% [8] had serum LDH 600-800I/U, none of them had serum LDH more than 800 I/U. In group with systolic BP of >159mmHg 17.64%[12] had serum LDH < 600 I/U, 30.88%[21] had serum LDH 600-800I/U, and 51.47%[31] had serum LDH >800 I/U and the p value was < 0.0001, which indicates significant association between serum LDH and systolic blood pressure. The same results were seen in studies conducted by Qublan HS et al[18] and Vinitha PM et al[19].

In our study total 87 different complications (Table 3) were noted and out of which only 9 [10.34%] complications were noted with serum LDH < 600IU/L, 18[20.68%] complications were seen with serum LDH 600-800 IU/L and 60 [68.96%] complications were seen with serum LDH > 800IU/L, details of maternal complications enlisted in table 3.

In a study conducted by Vinitha Padmini Mary et al[19], severely pre eclamptic women with LDH >800 IU/l showed significant increase in maternal complications as compared with women who had lower levels ($p<0.001$). Jaiswar et al[20] conducted a study where no maternal complications were seen when the LDH levels were in the normal range, but In the second group where LDH levels were moderately elevated (600–800 IU/l) one case of abruption placentae (7.7%) and another case of cerebrovascular accident (7.7%) was noted. In the third group i.e., with marked elevations of serum LDH levels (800 IU/l), complications were observed in 8 (22.2%) cases. One case each of abruption placentae, HELLP syndrome with RF, metabolic encephalopathy, pulmonary embolism, pulmonary edema and renal failure and two cases of cerebrovascular accident were present.

In this study total 136 different type of fetal complications (Table 4) were noted and of which 20 [14.70%] complications were seen with serum LDH 800 IU/L group. In my study 55 patients gave birth to low birth weight babies of which 14 [25.45%] had serum LDH >800 IU/L. 14 babies had respiratory distress syndrome of which 1 [7.14%] had serum LDH >800 IU/L. 17 babies had HIE, of which 2 [11.76%] had serum LDH > 800 IU/L. 12 babies had sepsis, of which 1 [8.33%] had serum LDH> 800 IU/L. 13 patients had neonatal death, of which 1 [7.69%] patient had serum LDH > 800 IU/L. 16 patients had intra uterine growth restriction as a complication, of which 1 [6.25%] had serum LDH >800 IU/L. 9 patients had intra uterine fetal death, of which 2 [22.22%] had serum LDH 600- 800 IU/L and 7 [77.77%] had serum LDH >800 IU/L and the p value was <0.027, which indicates significant association between serum LDH and different fetal complications as mentioned above.

According to study conducted by Hussein S. Qublan et al[18], Intrauterine fetal death was seen in 4.8% of cases, intrauterine growth restriction in 33.9%, and prematurity in 77.9%. Neonatal death occurred in 59 of the 62 (95.2%). Respiratory distress syndrome was responsible for 64.4% of deaths, followed by sepsis (16.9%), intraventricular hemorrhage (8.5), necrotizing enterocolitis (6.8), and congenital anomalies (3.4%).

CONCLUSION

Serum LDH is a valuable, inexpensive, and easily accessible biomarker. This study demonstrates that serum LDH level increase significantly with the severity of hypertensive disorders in pregnancy. LDH elevation reflects cellular damage and hemolysis, which are prominent in severe preeclampsia and HELLP syndrome. These findings are consistent with previous studies showing that biochemical markers can help predict adverse maternal and fetal outcomes.

Limitations of study: Single-centre study; Sample size limitations; Need for multicentric validation.

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