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High serum lactate dehydrogenase levels as a prognostic marker for morbid perinatal outcome in pre eclampsia

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Abstract

Introduction: Hypertension during pregnancy is an important causative factor of perinatal and maternal morbidity and mortality globally. There are several biochemical markers like ALP, AST, ALT, LDH, Uric acid to ascertain the severity of disease. The aim of our study was to determine the effectiveness of lactate dehydrogenase as a prognostic marker in assessing the sequelae of preeclampsia.

Materials and Methods: This analysis was conducted at RMMCH in the Department of OB-GYN for a period of 2 years (2016-2018). It was a prospective case control study. A total of 60 antenatal mothers were included in the study, of which 30 were healthy pregnant females and 30 were pre eclamptics.

Results: The mean values of serum LDH levels were found to be high in preeclamptics compared to normotensives which was significant statistically (p value of < 0.001). Adverse perinatal effects were seen in females with raised LDH levels (p value of < 0.005).

Conclusion: Serum LDH can be utilized as a prognostic marker to ascertain the severity of preeclampsia and it can also be used as a marker to predict the perinatal and maternal outcome.

Keywords: Pre Eclampsia, Serum Lactate Dehydrogenase, Prognosis, Sequelae

Introduction

Hypertensive disorders represent the most prevalent medical complication of pregnancy affecting 7-15% of antenatal women and contribute to one quarter of all admissions¹. According to WHO systematic review on maternal mortality worldwide, hypertensive disease remains the foremost cause of direct maternal mortality along with the triad of hemorrhage and infection.

Preeclampsia is a disorder affecting all the organ systems and is specific to pregnancy and puerperium, which manifests by commencement of hypertension and proteinuria >20 weeks gestation and resolves by 12 wks postpartum. The incidence of preeclampsia is 2-8% and is an important cause of perinatal and maternal mortality and morbidity. Defects in placentation and endothelial cell dysfunction are commonly understood pathophysiology of preeclampsia although the exact cause is still unclear²⁻³. Endothelial cell dysfunction can contribute to inappropriate vasoconstriction, platelet aggregation, activation of the coagulation system and ultimately decreased blood flow to organs^{4,5}.

Preeclampsia is greatly associated with restriction of fetal growth in utero, reduced birth weight, spontaneous or iatrogenic premature delivery, hyaline membrane disease and more admissions to NICU.

Placental abruption, eclampsia, disseminated intravascular coagulation, intracranial hemorrhage, heart failure, hepatic failure and renal failure are the lethal maternal complications.

Early screening of hypertension during pregnancy and preeclampsia may reduce perinatal and maternal complications.

Lactate Dehydrogenase is an intracellular cytoplasmic enzyme required for interconversion of lactate to pyruvate during hypoxic states. There are five iso enzymes of LDH-LDH1, LDH2, LDH3, LDH4 and LDH5, LDH2 is predominant in serum.

LDH is the earliest marker detected in blood during oxidative stress and hypoxia. Hypoxia in preeclampsia increases glycolysis and raises LDH. Quantitative measurement of serum LDH values reflects the range of cellular death and its association with various complications indicating its severity.

Serum LDH levels can also be helpful in decision making for the betterment of perinatal and maternal outcome. The analysis of compilation of biomarkers, particularly markers related to vascular dysfunction like LDH and uric acid, may help in predicting and preventing complications in preeclampsia.

Aims and objectives

To establish the relationship of maternal serum LDH levels with perinatal outcome in preeclampsia.

To observe the serum LDH levels in normal antenatal mothers and in preeclamptic mothers and to analyse its association with blood pressure in pregnant women.

Materials and methods

A Prospective case control study was carried out in the Department of Ob-Gyn, Rajah Muthiah Medical College, and Chidambaram. This study included 60 patients in total, out of which 30 were normal antenatal mothers who served as controls and 30 were pre eclamptics.

All antenatal mothers between 18 and 35 years age group as per the inclusion and exclusion criteria attending our OG-OPD were enlisted in our study. All the data was collected and summarized in tables which was analysed statistically using SSPS-21 software applying student's t-test, chi-square test and pearson

correlation coefficient. P-value < 0.05 was considered significant.

Inclusion Criteria

All antenatal mothers >28 weeks GA was divided into 2 groups:

Group I: healthy normal antenatal mothers (controls)

Group II: preeclamptic mothers (subjects)

Two groups were analysed according to age, parity, maternal weight, routes of delivery, perinatal and maternal outcomes.

Exclusion Criteria

Antenatal mothers with essential hypertension or hypertension before 20 weeks, pre existing diabetes, gestational diabetes, renal disease, liver disease, thyroid disorder, epilepsy, patients with UTI.

Results

Table 1: Comparison of baseline variables between two groups

Variables	Group	N	Mean	Std. Deviation	t value	P value
AGE	I	30	23.97	2.988	0.800	0.427 (NS)
	II	30	24.77	4.591		
BMI	I	30	23.923	1.7015	3.089	0.003 (S)
	II	30	25.440	2.0827		

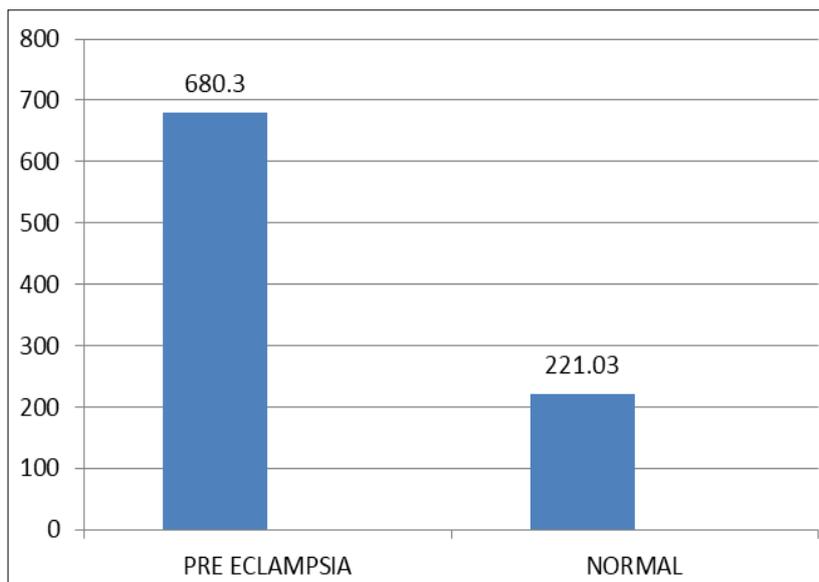
The maximum number of patients in both the groups belonged to 21-30 years, and no significant difference in the age distribution was observed between the two groups.

The mean body mass index in preeclamptics was

25.440±2.0827, higher than in normal antenatal mothers having a mean of 23.923±1.7015, which was considered statistically significant with p value of <0.003. Hence, increased BMI might be a predisposing factor in preeclampsia.

Table 2: Comparison of serum LDH values between the two groups

SR LDH	Group	N	Mean	Std. Deviation	t value	P value
	I	30	221.03	66.390	10.101	<0.001 (S)
	II	30	680.30	240.023		



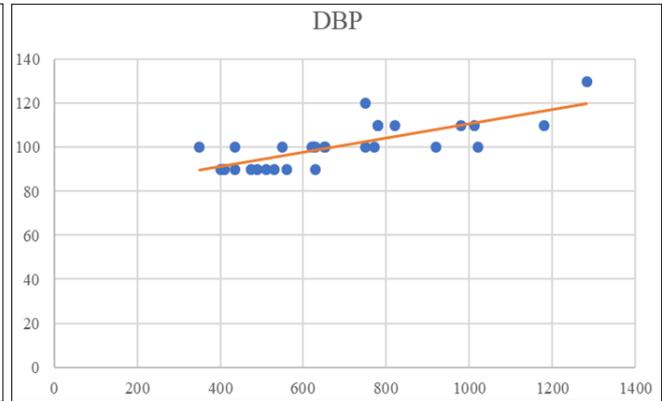
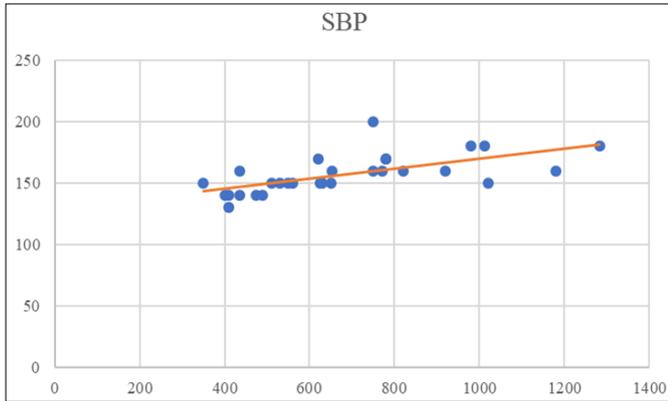
The mean serum LDH values in pre eclamptics was 680.30±240.023 compared to normal antenatal mothers whose mean was 221.03±66.390, which was significant statistically. This comparison points out that there is a notable difference between the two groups.

The mean systolic BP in pre eclampsia patients was 156.67±15.162mmhg compared to a mean of 108.67±6.814 mmhg in normal antenatal mothers. The mean diastolic Blood pressure in pre eclampsia was 100.33±9.994 mmhg whereas a mean of 73.00±6.513 mmhg was seen in normotensives.

Table 3: Correlation between serum LDH and systolic and diastolic BP

Group	Variables	r*	P-value
Cases	Sr.LDH	1	
	Systolic BP	0.646	<0.05
	Diastolic BP	0.772	<0.05
Controls	Sr.LDH	1	
	Systolic BP	-0.097	>0.05
	Diastolic BP	-0.161	>0.05

*Pearson correlation was applied.



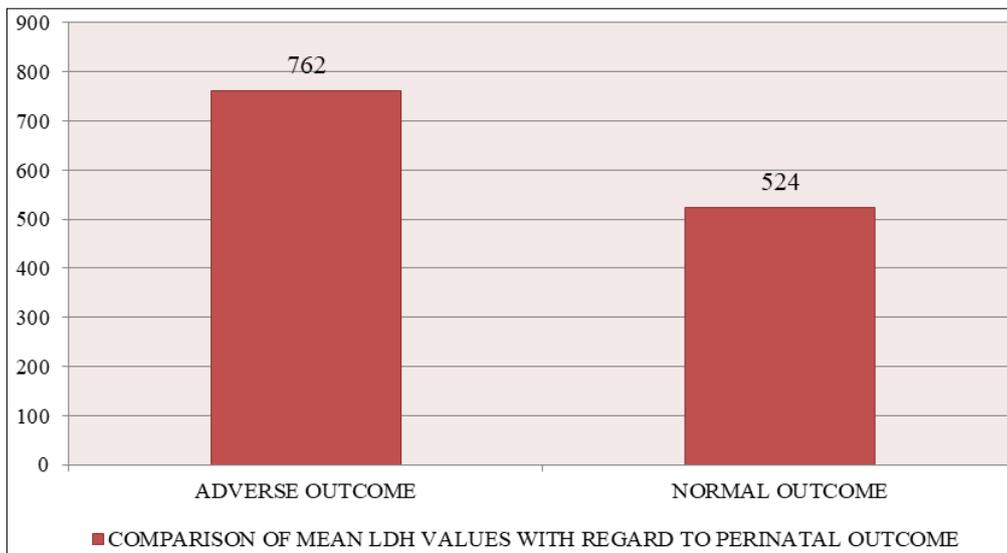
The above table infer that serum LDH had a significant positive correlation with high SBP and DBP that is statistically significant.

The percentage of lower segment cesarean sections were higher in pre eclamptic women (57.9%), whereas vaginal deliveries were more (63.63%) in normal pregnant mothers, which was significant statistically (p value of < 0.017) indicating that there were more number of operative deliveries in pre eclamptic women.

Table 4: Comparison of type of delivery between the two groups

	Group I		Group Ii	
	N	%	N	%
Vaginal	14	63.63	8	36.37
LSCS	16	42.10	22	57.9

Neonatal Outcome



Among 30 preeclamptic women studied, 21 patients had morbid perinatal sequelae including fetal growth restriction in utero, intrauterine death, sick babies requiring NICU admissions and perinatal deaths. 9 preeclamptic mothers had good neonatal outcomes. The mean serum LDH values when adverse sequelae occurred was 762.6 IU/L and the mean serum LDH value in which normal sequelae was noted was 524.67 IU/L. Mean birth weight of neonates were reduced in preeclamptic mothers owing to increased LDH values (2.013±0.503 kgs) when compared to healthy antenatal mothers (2.775±0.430 kgs), proving that there exists a significant positive correlation

between BW and LDH values. The mean GA at delivery when compared between two groups showed that there occurred reduction in gestational age in preeclamptics (252.73±17.805 days), compared to normal women (267.20±11.164days), which might be either due to spontaneous or iatrogenic preterm delivery. The mean apgar scores were decreased significantly at 1 min and 5mins in our current study indicating mild to severe neonatal depression with increasing values of LDH(p value <0.001).

Discussion

Researches have proved that in preeclampsia, the progressive endothelial cell dysfunction in maternal vascular system, induced by toxins from hypoxic placenta causes vasoconstriction of blood vessels affecting all the organs including liver. The resulting hypoperfusion, induced ischaemic injury to the liver cells and other organs causing more release of LDH from the cells to peripheral circulation. In the current study, raised serum LDH level in preeclamptic mothers than controls is linked to the above mentioned facts. Moreover, the increasing LDH levels in severe preeclampsia points towards progression to cellular death with severity of this disorder.

In our current study, the mean age among normotensives and pre eclampsia were 23.97 ± 2.988 and 24.77 ± 4.591 respectively, but it was not statistically significant. Qublan *et al.*, Ali *et al.* and Demier *et al.* [6] also reported similar data in their studies [7, 8-9].

In a study by Dave *et al.* [9] 84.3 % pre eclampsia and 97.03 % of eclamptics had LDH values >600 IU/L, compared to this study where 60 % of preeclamptics and 100% of eclamptics had LDH values >600 IU/L.

The values of systolic and diastolic BP were higher in patients with increasing LDH levels, which is similar to a study by Ali *et al.* [10] and Demeir *et al.*

The mean GA at delivery in mothers with LDH values >800 IU/L was 32.7 ± 7.94 weeks in this study, similar analysis by Jaiswar *et al.* had a mean of 35.25 ± 3.23 weeks.

The mean BW of neonates was reduced in mothers with raised LDH values. 73.2% of babies weighed <2.5 kgs and 27.8% of babies weighed >2.5 kgs. Similar result was found in Dare *et al.* study and Jaiswar *et al.* [7] study where reduced birth weight had association with levels of raised LDH, whereas Qublan *et al.* study showed no significant association between BW and LDH levels. This shows that there is a higher rate of preterm deliveries, low birth weight and IUGR babies in mothers with raised LDH levels.

There was also reduction in the mean apgar scores seen at 1 min and 5 mins in preeclamptics with raised LDH values.

Conclusion

From the above results, we can conclude that high serum LDH level is linked with severity of preeclampsia. Therefore, quantification of serum LDH levels in preeclamptic mothers might be useful for better management of patients to reduce the perinatal and maternal morbidity and mortality. Serum LDH is a simple, easily available biochemical test that can be carried out in all antenatal mothers with gestational hypertension. With raised LDH values, decision regarding management and prevention of complications can reduce the global burden in pre eclampsia [11].

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