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Original Research Article

Lactate dehydrogenase as a biochemical marker for prediction of maternal and perinatal outcomes in hypertensive disorders in pregnancy

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ABSTRACT

Background: Hypertensive disorder of pregnancy includes new onset hypertension in pregnancy that is gestational hypertension and already existing hypertension that is chronic hypertension and gestational hypertension sometimes worsened by preeclampsia. Preeclampsia can cause complications such as eclampsia, HELLP syndrome, renal failure, pulmonary edema, stroke, and left ventricular failure.

Aim: We aim to assess the predictive role of Lactate Dehydrogenase value in Hypertensive disorders in pregnancy.

Materials and Methods: After obtaining the informed consent, pregnant patients who were visiting Tertiary care centre and who were more than 28 weeks period of gestation were enrolled. Patients from both antenatal OPD clinics and from those who were presenting in emergency were included in this study. Serum levels of LDH were tested. Patients were monitored till delivery and 6 weeks following childbirth.

Results: The Mean serum levels of lactate dehydrogenase (LDH) in eclamptic group was 1495.000 ± 859.1230 , 804.569 ± 224.5519 in severely preeclamptic group and in mild preeclamptic group, mean LDH levels were 520.062 ± 110.3944 . The difference between both the groups was statistically significant (p < 0.001). Women with serum LDH levels > 800 IU/L and LDH levels between 601-800 IU/L, experienced considerably greater complications in preeclamptic-eclamptic group as compared to those with serum LDH levels < 600 IU/L.

Conclusion: The preeclamptic-eclamptic group of women had increased serum LDH levels. Greater LDH levels were linked to worse outcomes for mothers including placental abruption, hemolysis elevated liver enzymes low platelet count (HELLP syndrome), pulmonary edema and maternal death and they were also linked to fetal complications including intrauterine fetal death (IUFD), intrauterine growth restriction and neonatal intensive care unit (NICU) admission.

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1. Introduction

Worldwide, hypertensive disorder in pregnancy [HDP] is one of the leading cause of maternal and perinatal death. According to the World Health Organization (WHO), 19% of maternal deaths are caused by hypertension disorder in pregnancy. Hypertensive disorder of pregnancy includes new onset hypertension in pregnancy that is

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gestational hypertension and already existing hypertension that is chronic hypertension and gestational hypertension sometimes worsened by preeclampsia. Preeclampsia can cause complications such as eclampsia, HELLP syndrome, renal failure, pulmonary edema, stroke, and left ventricular failure. ² In the Eclampsia Registry (2013), the prevalence of preeclampsia was found to be 10.3%. ³ Hypertensive disorders are 4th most common cause of MMR. ⁴

Abnormal trophoblast invasion, immune dysfunction, parental incompatibility, and genetics are among the

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many mechanisms of preeclampsia. Preeclampsia is more common in young and nulliparous women whereas chronic hypertension with superimposed preeclampsia is more common in older women.⁵

Every body cell contains LDH, an essential enzyme that is highly concentrated in key organs such as the heart, liver, muscles, kidneys, lungs, and RBCS.⁶ Its primary role is to support the anaerobic metabolic pathway, which turns glucose into energy. Higher serum LDH levels are associated with number of clinical problems and tissue damage, making it a important marker for diagnosing and monitoring a variety of diseases, including preeclampsia.^{6,7}

Serum levels of LDH are to be significantly elevated in preeclamptic patients and a correlation is observed between heightened LDH levels and severity of condition. Therefore, the routine measuring of serum LDH levels can assist clinicians to estimate the progression and severity of preeclampsia and also assessing feto-maternal poor outcomes. ^{7,8}

2. Materials and Methods

This was a prospective study done in tertiary care c, after getting approval from the Institute Ethics Committee. The study was conducted from 01^{st} January, 2023 To 31^{st} March, 2024. The study included all antenatal women attending out-patient department (OPD) as well as emergency of tertiary care centre beyond 28 weeks gestation, willing to follow-up and give consent for the study. Patients were followed up till delivery and 6 weeks post-partum. Total 140 women were enrolled in the study after obtaining the written informed consent and obtaining clearance from ethical committee.

- 2.1. Inclusion criteria
 - 1. Singleton pregnancy
 - 2. After 28 weeks of gestation

2.2. Exclusion criteria

Patients with

- 1. Diabetes
- 2. Renal failure
- 3. Previous h/o Haemolytic anemia
- 4. Multiple pregnancy
- 5. Smoking and alcoholism
- 6. Liver disease
- 7. Hepatotoxic drug
- 8. Stroke, coronary artery disease
- 9. Chronic lung disease connective tissue disorders

Upon meeting the inclusion criteria, a thorough obstetric history and examination were conducted for each enrolled patient. Blood pressure (BP) was measured using an LED mercury sphygmomanometer, with readings taken either in the sitting or supine position. The zero level of the apparatus was aligned with the level of the heart, and BP was assessed in both arms. A cuff that fit snugly around the arm was used: a standard cuff was employed for arm circumferences of 33 cm or less, while a larger cuff (15×35 cm) was used for arm circumferences greater than 33 cm. The lower edge of the cuff was positioned 2.5 cm above the antecubital fossa. First, systolic blood pressure was measured at the brachial artery using the palpatory method. Subsequently, it was measured using the auscultatory method at Korotkoff phase I for systolic pressure and Korotkoff phase V (K5) for diastolic pressure. If K5 was absent, diastolic pressure was recorded at Korotkoff phase IV. Routine laboratory tests included a complete blood count, ABORh, VDRL, Anti-HIV, Anti-HCV, HBsAg, oral glucose tolerance test (OGTT), random blood sugar, and a complete urine analysis. Additional laboratory tests included liver function tests, renal function tests, serum uric acid, serum lactate dehydrogenase, peripheral blood film, prothrombin time index, and either an on-spot urinary protein-to-creatinine ratio or urine albumin measured by the dipstick method. Fundoscopy was recommended for all enrolled patients. Serum LDH test was done in all the patients using L TO P-IFCC method with a reference range of 120-246 U/L.

Statistical Analysis: The data was collected systematically and edited after collection. The data was then entered into computer and statistical analysis of the results was obtained by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22) (SPSSS Inc, Chicago, IL, USA). The results were presented in tables and graphs. Continuous variables were expressed as mean with standard deviation and categorical variables as count with percentage. Independent 't' test, One Way ANOVA and Pearson's correlation was used for data analysis in ICP and NON ICP patients.

1. Mean (average)
$$x = \frac{Total \ of \ the \ all \ values}{Number \ of \ values} \frac{\sum n}{n}$$

2. Chi square

$$X^2 = \sum \frac{(o-e)^2}{e}$$

Where

o = observed value

e = expected value

3. Standard deviation of observation (S.D) =

$$s = \sqrt{\frac{\sum (x - \bar{x})^2}{n - 1}}$$

Where

x = mean x

n= number of observation

4. d.f = (column-1) (row-1)

3. Results

140 women were enrolled in the study after submitting informed consent and taking into account the inclusion and exclusion criteria.

Table 1: Distribution of study groups

Study groups	No. of cases	% age
Mild pre eclampsia	81	57.9
Severe pre eclampsia	51	36.4
Eclampsia	8	5.7
Total	140	100.0

Distribution of study participants according to the Serum LDH levels and Correlation With Blood Pressure.

Table 2: Correlation of serum LDH levels with systolic blood pressure

LDH (IU/L)	No.	•	ic blood e(mmhg)
		Mean	SD
<600	74	143.86	10.800
601-800	40	152.40	14.551
>800	26	162.62	11.395
Total	140	149.79	13.980
p-value (ANOVA test)		0.	001

In our study, patients with serum LDH levels <600 IU/L, the mean systolic blood pressure was 143.86 mmHg. For patients with serum LDH levels between 601-800 IU/L, the mean systolic blood pressure was 152.40 mmHg. In patients with serum levels of LDH exceeding 800 IU/L, the mean systolic blood pressure was not provided, but the p-value obtained was significant, indicating a statistically significant association between serum LDH levels and systolic blood pressure.

Table 3: Correlation of serum LDH levels with diastolic blood pressure

LDH (IU/L)	No.	Diastolic blood pressure (mmhg)		
		Mean	SD	
<600	74	97.70	7.518	
601-800	40	104.35	7.908	
>800	26	110.69	6.424	
Total	140	102.01	8.956	
p-value (ANOVA test)		0.0	001	

In our study patients with serum LDH levels <600 IU/L, the mean diastolic blood pressure was 97.70 mmHg. For patients with serum LDH levels between 601-800 IU/L, the mean diastolic blood pressure was 104.35 mmHg. The mean diastolic blood pressure for patients with serum levels of LDH exceeding 800 IU/L was not provided, but the p-value

obtained indicated a significant association between serum LDH levels and diastolic blood pressure.

3.1. Distribution of study participants according to the serum LDH levels and correlation with maternal outcomes

Maternal outcome and LDH levels among study participants were cross-tabulated and analyzed, and it was found that the mean LDH level was 1303.600 ± 465.0186 IU in HELLP patients and 656.296 ± 322.7073 IU in non-HELLP patients. In patients experiencing abruption, the mean LDH level was 947.263 +/-403.6658 IU, while in those without abruption, it was 637.355 +/-320.5428 IU. In patients with maternal mortality, the mean level of LDH was 321; in those without maternal mortality, it was 661.158.The statistical analysis of the data shows a statistically significant correlation (p < 0.05) between the study groups' LDH levels, HELLP syndrome, abruption, and maternal death.

In our study, we observed that among patients with serum LDH levels below 600 IU/L, 15.79% had abruptio placenta while 58.68% did not have abruption. For those with serum LDH levels between 601-800 IU/L, 31.58% had abruptio placenta and 28.10% did not have abruption. In patients with serum LDH levels exceeding 800 IU/L, 52.63% had abruptio placenta and 13.22% did not have abruption. The mean LDH level was 947.263 \pm 403.6658 IU in patients with abruption and 637.355 \pm 320.5428 IU in patients without abruption. In our study, we found a significant correlation between serum LDH levels and the occurrence of abruptio placenta.

In our study, we observed that no patient with serum LDH levels below 600 IU/L had HELLP syndrome. Among those with serum LDH levels between 601-800 IU/L, 20% had HELLP syndrome, while 28.89% did not. For patients with serum LDH levels exceeding 800 IU/L, 80% had HELLP syndrome, and 16.30% did not. The mean LDH level in patients with HELLP syndrome was 1303.600 \pm 456.018 IU, significantly higher than the 656.296 \pm 322.703 IU observed in patients without HELLP. Our study found a significant correlation between heightened serum levels of LDH and the occurrence of HELLP syndrome.

In our study, we found that none of the patients with serum LDH levels below 600 IU/L experienced maternal mortality. Similarly, there were no cases of maternal mortality among patients with serum LDH levels between 601-800 IU/L. However, among patients with serum LDH levels exceeding 800 IU/L, 100% experienced maternal mortality, while 17.99% did not. The mean LDH level in patients with maternal mortality was 3217.000 ± 0.000 IU, significantly higher than the 661.158 ± 273.9175 IU observed in patients without maternal mortality. Our study demonstrated a significant correlation between heightened levels of serum LDH and the occurrence of maternal

Table 4: Correlation of serum LDH levels with Abruptio placenta

		Abruptio	Total				
LDH (IU/L)	No		Yes				
	No.	%age	No.	%age	No.	%age	
<600	71	58.68	3	15.79	74	52.86	
601-800	34	28.10	6	31.58	40	28.57	
>800	16	13.22	10	52.63	26	18.57	
Total	121	100.00	19	100.00	140	100.00	
Mean	637.355	5±320.542	947.263±403.665		679.414 ± 348.0668		

p-value (Independent t-test) 0.001

Table 5: Correlation of serum LDH levels with hellp syndrome

		HELLP S	Total			
LDH (IU/L)	No		Yes			
	No.	%age	No.	%age	No.	%age
<600	74	54.81	0	0.00	74	52.86
601-800	39	28.89	1	20.00	40	28.57
>800	22	16.30	4	80.00	26	18.57
Total	135	100.00	5	100.00	140	100.00
Mean	656.296	±322.703	1303.60	0±456.018	679.414	£348.0668
p-value (Independent t-test)			0.	001		

Table 6: Correlation of serum LDH levels with maternal mortality

		Maternal 1	Total				
LDH (IU/L)	No		Yes				
	No.	%age	No.	%age	No.	%age	
<600	74	53.24	0	0.00	74	52.86	
601-800	40	28.78	0	0.00	40	28.57	
>800	25	17.99	1	100.00	26	18.57	
Total	139	100.00	1	100.00	140	100.00	
Mean	661.158±273.9175		3217.0	00 ± 0.000	679.414±348.0668		

p-value (Independent t-test) 0.001

mortality.

3.2. Distribution of study participants according to the serum LDH levels and correlation with perinatal outcomes

In our study, we observed that among patients with serum LDH levels below 600 IU/L, 21.62% had intrauterine growth restriction (IUGR), while 64.08% did not. For those with serum LDH levels between 601-800 IU/L, 29.73% had IUGR, and 28.16% did not. Among patients with LDH levels exceeding 800 IU/L, 48.65% had IUGR, and 7.77% did not. Our findings indicate a significant correlation between heightened levels of serum LDH and the occurrence of IUGR.

In our study, we observed that among patients with serum LDH levels below 600 IU/L, 33.33% had IUD, while 53.73% did not. For those with serum LDH levels between 601-800 IU/L, 16.67% had IUD, and 29.10% did not. Among patients with LDH levels exceeding 800 IU/L, 50% had IUD, and 17.16% did not. Our findings indicate a

significant correlation between heightened levels of serum LDH and the occurrence of IUD.

4. Discussion

In our study, patients with serum levels of LDH below 600 IU/L mean SBP was 143 mmhg and DBP was 97, LDH levels between 601-800 mean SBP was 152 mmhg and mean DBP was 104 mmhg and in patients with serum LDH levels exceeding 800 ,mean SBP was 160 mmhg and DBP was 110 mmhg. There was significant association with raised LDH levels with high blood pressure.

Gupta et al. 9 conducted a study in 2019, majority of the patients with serum levels of LDH below 600, SBP was </=140mmhg and DBP was </= 90 mmhg, in patients with LDH levels between 601-800 SBP was 140-<160 mmhg and DBP was 90-<110 mmhg and in patients with LDH levels >800, SBP was >160 mmhg and DBP was >110 mmhg. In this study also, there was significant association with heightened levels of serum LDH with high blood pressure.

Table 7: Correlation between serum LDH levels and IUGR

		IUC	Total				
LDH (IU/L)	No		Yes				
	No.	%age	No.	%age	No.	%age	
<600	66	64.08	8	21.62	74	52.86	
601-800	29	28.16	11	29.73	40	28.57	
>800	8	7.77	18	48.65	26	18.57	
Total	103	100.00	37	100.00	140	100.00	
Mean	603.301	±243.7660	891.297	891.297±486.5150		679.414±348.0668	

p-value (Independent t-test) 0.001

Table 8: Correlation between serum LDH levels and IUD

		IU	Total				
LDH (IU/L)	No		Yes				
	No.	%age	No.	%age	No.	%age	
<600	72	53.73	2	33.33	74	52.86	
601-800	39	29.10	1	16.67	40	28.57	
>800	23	17.16	3	50.00	26	18.57	
Total	134	100.00	6	100.00	140	100.00	
Mean	646.664±245.9982		1410.833±1042.8652		679.414±348.0668		

p-value (Independent t-test) 0.001

4.1. Serum LDH levels in preeclamptic-eclamptic pregnant women group

In the present study, LDH levels greater than 800 IU/L were found in 75% of patients in the eclampsia group (6 patients), 37.25% of patients in the severe preeclampsia group (19 patients), and 1.23% of patients in the mild preeclampsia group (1 patient). Additionally, LDH levels between 601 and 800 IU/L were noted in 43.14% of patients with severe preeclampsia (22 patients), 25% of patients with eclampsia (2 patients) and 19.75% of patients with mildly preeclampsia (16 patients). The mean serum LDH levels were 1495.000±859.1230 IU/L in the eclampsia group, 804.569±224.5519 IU/L in the severe preeclamptic group, and 520.062±110.3944 IU/L in the mild preeclampsia group.

In a study conducted by Eleti et al. 10 in 2023, it was found that serum levels of LDH exceeding 800 IU/L were significantly more in the eclamptic group (60% or 9 patients), in the severely preeclampsia group (40% or n=16 patients), and the mildly preeclamptic group (10% or n=6 patients), with none in the normotensive group (p < 0.0001). Similarly, LDH levels between 600 and 800 IU/L were significantly higher in the severe preeclampsia group (37.5% or 15 patients), the eclampsia group (33.33% or 5 patients), and the mild preeclampsia group (21.66% or 13 patients) compared to the normotensive group (1.73% or 2 patients) (p < 0.0001). The mean serum LDH levels in eclamptic group was 1515.86 \pm 754.13 IU/L, 932.20 \pm 448.28 IU/L in the severely preeclampsia group, and 580.56 \pm 213.21 IU/L in the mildly preeclampsia group.

In a study by Jaiswar et al. 11 in 2011, it was observed that most patients with mildly preeclampsia had LDH levels below 600 IU/L, with a mean value of 278.3 \pm 119.2 IU/L. Only two(n=2) patients (5.7%) had serum levels of LDH between 600 and 800 IU/L, with a mean LDH level of 400.45 ± 145.21 IU/L. Among the 36 cases of severe preeclampsia, 58.3% (21 cases) had serum levels of LDH below 600 IU/L, 13.9% (5 cases) had levels between 600 and 800 IU/L, and 27.7% (10 cases) had levels more than 800 IU/L, with a mean LDH level of 646.95 \pm 401.64 IU/L. In the eclampsia group, 69.4% (25 patients) had levels above 800 IU/L, 19.4% (7 patients) had levels of serum LDH between 600 and 800 IU/L, and 11.1% (4 patients) had levels of LDH below 600 IU/L, with a mean LDH level of 1648.10 ± 1992.29 IU/L. The data clearly indicate a significant raise in serum LDH levels with the complication of disease (P<0.001).

4.2. Serum LDH and maternal complications

In our study, we observed that Among patients with serum levels of LDH below 600 IU/L, there were 3 (15.79%) cases of abruptio, no cases of HELLP syndrome and no maternal mortality. In the group with serum LDH levels between 601 and 800 IU/L, there were 6 (31.58%) cases of abruptio, 1(20%) case of HELLP syndrome, and no maternal mortality. For patients with LDH levels exceeding 800 IU/L, there were 10(52.63%) cases of abruptio, 4 (80%) cases of HELLP syndrome, and 1(100%) maternal mortality.

The findings of our study align with those of Jaiswar et al. 11 who reported that only one case of abruptio

placenta occurred in patients with serum levels of LDH between 600-800 IU/L. In contrast, among those with LDH levels exceeding 800 IU/L, there were eight cases of abruptio placenta, HELLP syndrome and pulmonary edema. Similar to our study, their study also demonstrated a statistically significant correlation of raised incidence of maternal complications with higher serum levels of LDH (p < 0.001).

Mary et al. 12 similarly found a raised incidence of maternal complications with increasing serum levels of LDH. In their study, 94.3% of patients with serum levels of LDH greater than 800 IU/L developed complications, including eclampsia (38.8%), abruptio placenta (22.2%), HELLP syndrome (11.1%).In comparison, 13.6% of patients with LDH levels between 600-800 IU/L experienced complications such as eclampsia (6.8%) and abruptio placenta (3.4%), with these findings also being statistically significant. High serum levels of LDH were strongly correlated with significant impairments in renal and liver function.

Prajapati and Maitra et al. ¹³ also documented a raised incidence of maternal adverse outcomes with rising serum levels of LDH. In their study, among patients with LDH levels greater than 800 IU/L, 36.3% developed eclampsia, 12.12% experienced abruptio placenta, 62.5% had HELLP syndrome, 24.24% required maternal ICU admission, and 3.03% resulted in maternal death. The majority (62.5%) of cases with LDH levels greater than 800 IU/L had complications (p < 0.001). In the same study, for LDH levels between 600-800 IU/L, maternal complications included HELLP syndrome (8.33%), abruptio placenta (4.1%), pulmonary edema (4.1%), and maternal ICU admission (4.16%). For LDH levels below 600 IU/L, complications included HELLP syndrome (2.02%), eclampsia (5.05%) and abruptio placenta (2.02%).

4.3. Perinatal outcome

In our study, 7.84% of patients with severe preeclampsia experienced intrauterine demise, while 25% of patients with eclampsia had intrauterine demise. P-value is significant.

Panda et al. ¹⁴ conducted the study reported that 60 cases, accounting for 14.9%, resulted in perinatal mortality. This rate was significantly higher among women with eclampsia and severe preeclampsia, with a p-value of less than 0.0001, indicating strong statistical significance. Moreover, perinatal mortality was more prevalent in cases of eclampsia compared to severe preeclampsia, also with a p-value of less than 0.0001.

4.4. Serum LDH levels and its correlation with perinatal outcomes

In our study, In patients with LDH levels below $600\,$ IU/L, there were 8~(21.62%) cases of intrauterine growth

restriction (IUGR), 2(33.33%) cases of intrauterine death (IUD). For patients with LDH levels between 601-800 IU/L, there were 11(29.73%) cases of IUGR, 1 (16.67%) case of IUD, 13(37.14%) NICU admissions. In patients with serum levels of LDH exceeding 800 IU/L, there were 18 (48.65%)cases of IUGR, 3 (50%)cases of IUD, 20(57.14%) NICU admissions, The p-value is significant for all outcomes.

Eleti et al. ¹⁰ conducted a study in 2023 observed the outcomes in patients with varying LDH levels. They found that among patients with serum levels of LDH below 600 IU/L, , 13 (26%) had intrauterine growth restriction (IUGR), and none had intrauterine death (IUD). In patients with serum levels of LDH between 600 and 800 IU/L, 17 (60.7%) experienced IUGR, and 1 (3.57%) had an IUD. Among those with LDH levels greater than 800 IU/L, 11 (50%) had IUGR, and 3 (13.6%) had an IUD.

According to Gupta et al., 9 in 2019, low birth weight occurred in 21(39.6%), with LDH levels below 600 IU/L. In patients with LDH levels between 600-800 IU/L, 18(66%) had low birth weight. In patients with LDH levels above 800 IU/L,17(85%) had low birth weight.

Lavanya et al. ¹⁵ in 2021 reported that 4(7.8%) intrauterine growth restriction (IUGR),1(2%) had intrauterine fetal demise in patients with LDH levels below 600 IU/L.1(3.4%) intrauterine growth restriction (IUGR),none of the patient had intrauterine fetal demise in patients with LDH levels between 600-800 IU/L.3(15%) had IUGR with LDH levels above 800 IU/L.

5. Conclusion

The conclusion is that a crucial biochemical marker that indicates the severity of pre-eclampsia and eclampsia is lactate dehydrogenase. Women belonging to the preeclamptic-eclamptic group had greater serum LDH levels. Elevated levels of liver disease-related hemolysis (LDH) were linked to worse outcomes for mothers, including placental abruption, hemolysis, elevated liver enzymes, low platelet count (HELLP), and maternal death. Fetal complications, such as intrauterine fetal death (IUFD) and Intrauterine growth restriction (IUGR) were also be associated with higher serum levels of LDH. Raised LDH levels are also indicative of organ damage, as seen by elevated urine albumin in preeclamptic and eclamptic individuals. Increased levels of serum LDH should be detected and should prompt tight monitoring, scheduled delivery, and quick management to reduce the risk of major bad outcomes for both the mother and the fetus, as well as potential reductions in morbidity and mortality for both.

6. Source of Funding

None.

7. Conflict of Interest

None.

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