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Original Research Article

"A STUDY ON LDH BIOCHEMICAL MARKER, ITS CORRELATION WITH THE SEVERITY AND FETO MATERNAL OUTCOME IN PRE ECLAMPSIA AND ECLAMPSIA''

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ABSTRACT:

Background: In the course of glycolysis, the intracellular enzyme lactate dehydrogenase (LDH) transforms pyruvic acid into lactic acid. The main source of energy in the placenta is glycolysis. In PE, hypoxia further boosts glycolysis and raises LDH activity. Studies have revealed that PE placentas had more LDH activity and gene expression than placentas from healthy pregnancies.

OBJECTIVES:

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

Material & Methods: Study Design: Prospective hospital based cross – sectional study. **Study area:** study conducted in the Department of Obstetrics and Gynaecology in collaboration with the department of Biochemistry, Murshidabad Medical College, Berhampore, Murshidabad, West Bengal. **Study Period:** June 2021 - May 2022. **Study population:** Pregnant women in the third trimester were enrolled in the study. **Sample size**: study consisted a total of 100 cases and 100 controls. **Sampling Technique:** Simple Random sampling method. **Study tools and Data collection procedure:** The rest of the women were enrolled in the study and divided into the following groups

Group 1: Healthy normal pregnant women (controls)
Group 2: Patients of preeclampsia and eclampsia (cases). They were subdivided into two groups based on severity of preeclampsia

2a: Patients with non-severe preeclampsia
2b: Patients with severe pre-eclampsia

Results: In the control group, all had levels of LDH < 600 IU/L, the mean value of LDH being 395.16 ± 92.54 IU/L. Majority of the patients (77.4%) in the non-severe preeclampsia

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group had LDH levels < 600 IU/L, 6 (9.2%) patients had LDH in the range of 600-800 IU/L, 8(12.9%) patients had LDH in the range of > 800 IU/L. The mean LDH Level in the non-severe preeclampsia group is 513 ± 306.08.

CONCLUSION: A helpful biochemical indicator of the severity and occurrence of pre-eclampsia problems is lactic dehydrogenase. These issues may be avoided by identifying high-risk patients with increased levels of lactic dehydrogenase, closely monitoring them, and providing timely, appropriate care, which will reduce maternal and foetal morbidity and mortality.

Keywords: lactic dehydrogenase, preeclampsia, maternal and perinatal outcomes

INTRODUCTION:

Maternal tissues undergo significant morphological, physiological, and metabolic changes throughout pregnancy. At some point during pregnancy, these well planned modifications may go awry, leading to a number of feto-maternal problems. Hypertension (preeclampsia (PE)/gestational hypertension (GHTN), which can progress to eclampsia, is one of the most prevalent and feared consequences (E). They continue to be the main killers in emerging nations. Hypertension complicates 10% of all pregnancies. Even though the disease is not generally understood, PE & E account for nearly half of all occurrences globally and have been identified and documented for years.[1]

Despite decades of extensive investigation, it is still unclear how pregnancy causes or worsens hypertension [2]. The main characteristics are thought to be endothelial dysfunction and defective placentation. These anomalies have been associated with a number of causes, including genetic, racial, immunological, nutritional, increased insulin resistance, increased oxidative stress, hypoxia, and prostaglandin imbalance.

In the course of glycolysis, the intracellular enzyme lactate dehydrogenase (LDH) transforms pyruvic acid into lactic acid. The main source of energy in the placenta is glycolysis. In PE, hypoxia further boosts glycolysis and raises LDH activity. Studies have revealed that PE placentas had more LDH activity and gene expression than placentas from healthy pregnancies.[3-5]

The trophoblasts' increased LDH isoenzyme activity causes it to produce more lactate. LDH contains five isoforms, and LDHA4 is the one that responds to hypoxia the best when it is present in placentae with PE.[6] Elevated levels of LDH are indicative the cellular damage and dysfunction, so it can be used as a biochemical marker because it reflects the severity of the disease, occurrence of complications and fetal outcome. Its estimation would prove useful because these complications are preventable.

Elevated levels of LDH have also been seen in cases of HELLP syndrome. Many authors have used elevated total LDH (usually more than 600 U/L) as a diagnostic criterion for hemolysis. Among all five isoforms, only two of them (LDH1 and LDH2) are released from ruptured red blood cells.[7]

Hence the present study was undertaken to study the usefulness of Lactic Dehydrogenase (LDH) as a marker of severity of preeclampsia and to study its correlation with the feto maternal outcomes in preeclampsia complicating pregnancy.

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OBJECTIVES:

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

Material & Methods:

Study Design: Prospective hospital based cross – sectional study.

Study area: study conducted in the Department of Obstetrics and Gynecology in collaboration with the department of Biochemistry, Murshidabad Medical College, Berhampore, Murshidabad, West Bengal.

Study Period: June 2021 - May 2022.

Study population: Pregnant women in the third trimester were enrolled in the study.

Sample size: study consisted a total of 100 cases and 100 controls.

Sampling Technique: Simple Random sampling method.

Inclusion Criteria: Pregnant women in the third trimester were enrolled in the study.

Exclusion Criteria:

1. Patients with chronic hypertension
2. Patients with preexisting diabetes mellitus
3. Patients with renal, liver, thyroid disorders
4. Patients with epilepsy

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

The rest of the women were enrolled in the study and divided into the following groups

Group 1: Healthy normal pregnant women (controls)

Group 2: Patients of preeclampsia and eclampsia (cases). They were subdivided into two groups based on severity of preeclampsia

2a: Patients with non-severe preeclampsia

2b: Patients with severe pre-eclampsia

Subjects were also divided according to the serum LDH levels into the following groups:-

1. <600 IU/L
2. 600 – 800 IU/L

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3. > 800 IU/L

All women were followed until delivery and early postpartum period and babies until early neonatal period. 2 cc of venous blood was drawn from the forearm into a plain tube without any reagent, irrespective of the state of fasting from all subjects included in the study. The blood drawn was allowed to stand for serum formation, later centrifuged for 5 minutes. The serum was separated and sent for the analysis of LDH levels.

Statistical Analysis: The data was collected, compiled and compared statistically by frequency distribution and percentage proportion. Quantitative data variables were expressed by using Descriptive statistics (Mean ± SD). Qualitative data variables were expressed by using frequency and Percentage (%). P values of <0.05 were considered statistically significant. Data analysis was performed by using SPSS Version 20. Independent sample t-test/ ANOVA/Paired t- test was used to assess statistical significance.

Observations & Results:

Table 1: Age wise and parity wise distribution of cases and controls

GROUP	**CONTROL**	**NON SEVERE PREECLAMPSIA**	**SEVERE PREECLAMPSIA**
NUMBER	100	62	38
MEAN AGE	22.66	23.3	23.6
MEAN PARITY	1.12	1.8	1.57
%PRIMIGRAVIDA	58	51.6	52.6
% MULTIGRAVIDA	42	48.3	47.3

The Maximum number of cases and controls belonged to the age group of 21 – 30 years. When compared statistically, the age wise distribution of the cases was almost similar to the controls ($P < 0.05$). The Control population comprised 42% primigravida women & 58% multigravida women, Mean parity: 1.12. The non-severe preeclampsia group comprised 51.6% primigravida women & 48.3% multigravida women, Mean parity : 1.8. The severe preeclampsia group comprised 52.6%primigravida women & 47.3% multigravida women. Mean parity 1.57.

Table 2: Significance of the time of appearance of pedal edema among cases

Pedal Edema	No. of cases	Mean duration (days)	Range (days)
Prior to the onset of High BP recordings	52	25.6	1-60
Coincided with the onset of High BP	4		6-10
Superceded the onset of High BP	12	14	2-56

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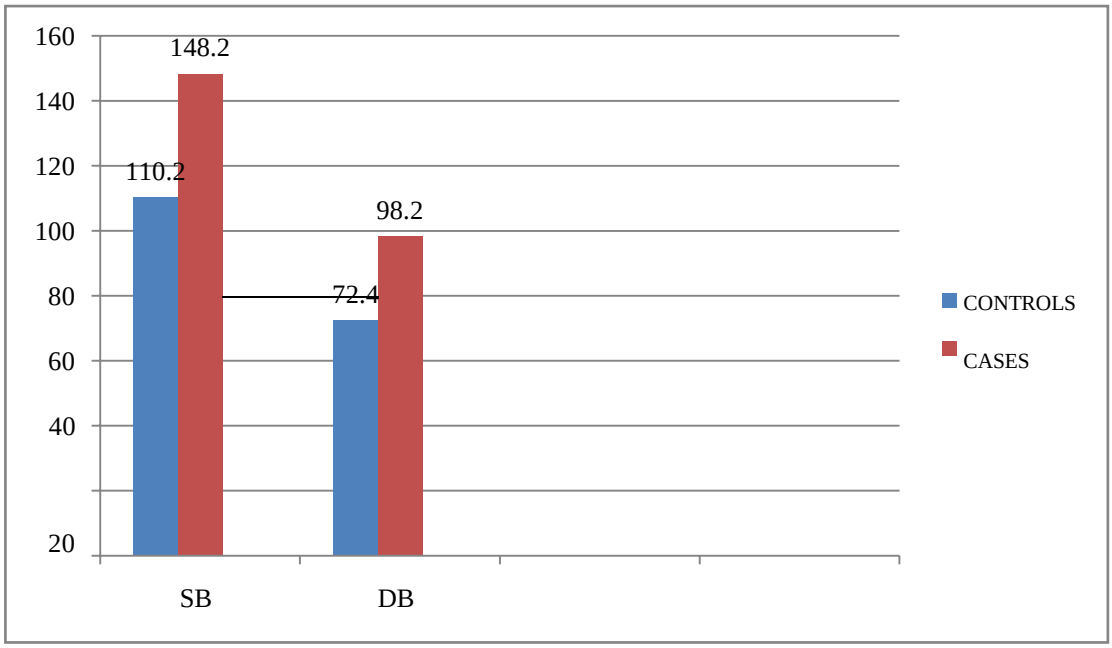
No pedal edema in the presence of High BP	4		

The Patients in the study group had H/O pedal edema for an average of 23.4 days prior to admission. Range (1d – 60 days).

Figure 1: Mean SBP and DBP among cases and controls

The mean SBP and DBP in controls and cases are 110.2 / 72.4, 148.2/98.2 respectively.



Among the cases, 10 had trace, 16 had 1+, 24 had 2+, 20 had 3+, 4 had 4+, albuminuria.

Table 3: Systolic and Diastolic BP with LDH levels in the study population

Groups	**LDH LEVEL (Mean)**	**LDH LEVEL SD**	**RANGE**
CONTROLS	395	92.54	228-550
NON SEVERE PREECLAMPSIA	513	306.08	180-1589
SEVERE PREECLAMPSIA	566.8	219.88	177-881

P value < 0.001 (Highly Significant)

Table 4: Association of SBP with LDH levels

GROUP SYSTOLIC BP (mm of Hg)	**<600 IU/I (n= 170)**	**600-800 IU/I (n=14)**	**>800 IU/I (n=16)**	**TOTAL (n = 200)**
90-140	116	2	4	122
140-160	36	4	4	44

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160 and above	18	8	8	34

P value < 0.001 (Highly Significant)

Table 5: Association of DBP with LDH levels

DBP (mm of Hg)	**<600 IU/I (n = 170)**	**600-800 IU/I (n = 14)**	**>800 IU/I (n = 16)**	**TOTAL (n = 200)**
60-90	102	0	2	104
90-110	50	10	10	70
110 and above	18	4	4	26

P value < 0.001 (Highly Significant)

Table 6: Comparison of Perinatal outcome with LDH levels

PARAMETERS	**<600 IU/I**	**600-800 IU/I**	**>800 IU/I**
Mean gestational age (weeks)	37.7	33	36.2
Mean baby weight (gm)	2690	1530	2700
APGAR Score(5 Min)	8.5	4.4	7.5
OUTCOME			
Stillborn	12(7%)	6(43%)	2(12.5%)
Live born	158(93%)	8(57%)	14(88%)
NICU Admission	12(7%)	6(43%)	2(12.5%)
Neonatal Deaths	8(5%)	2(14%)	0
Perinatal Deaths	8(5%)	8(57%)	2(12.5%)

Table 7: Association of Maternal Complications with LDH

Complication	LDH < 600	LDH 600-800	LDH >800
Need for blood Transfusion	10(6%)	0	0
Acute kidney injury	4(2.3%)	2(14.2%)	0
Ascites	0	0	2(12.5%)
Sepsis	2(1.1%)	0	0
Antepartum Eclampsia	4(2.3%)	0	2(12.5%)

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Abruption	4(2.3%)	2(14.2%)	0

DISCUSSION:

Preeclampsia is a pregnancy specific condition that is characterized by hypertension and proteinuria occurring after 20 weeks of gestation and it complicates 5-8% of all pregnancies.[8] It carries substantial risks for both fetus and mother with a subsequent increase in the perinatal and maternal morbidity and mortality.

Lactate Dehyderogenase (LDH) is an intra cellular enzyme that convert lactic acid to pyruvic acid and elevated levels indicate cellular death and leakage of enzyme from the cell [9]. High level of LDH were found in association with severe preeclampsia in a limited number of studies [10,11]. As severe preeclampsia may lead to a numerous multisystem complication; it is hypothesized that elevated levels of LDH may reflect the severity of preeclampsia & the occurrence of complications.

The maximum number of patients in the control group as well as the study group belonged to the age group 21-30 years. When compared statistically, the age wise distribution in the subjects was almost similar to the control group ($p < 0.05$). The mean age of the controls was 22.6 ± 2.061 (19-30 years), cases was 23.6 ± 3.19 (18-32 years). Similar findings with regard to age was noted in study by S.P. Jaiswar et al [12] where majority of the case & control group population belonged to the age group of 21-30 years.

The control population comprised 42% primigravida women & 52% multigravida women with a mean parity of 1.12. The non-severe preeclampsia group comprised 51.6% primigravida women & 48.3% multigravida women with a mean parity of 1.8. The severe preeclampsia group compromised 52.6% primigravida women & 47.3% multigravida women with a mean parity of 1.57. A systemic review on the risk factors of preeclampsia by Duckitt et al showed that primigravid status is a risk factor for preeclampsia with a relative risk of 2.91. [13] The same is in concurrence with another study by young et al on risk factors of preeclampsia in developing countries. [14]

Pedal edema was a common accompaniment in the study group with preeclampsia (68 %). 68 (68%) out of 100 patients with preeclampsia had accompanying pedal edema. In 52 cases (76.47%) pedal edema preceded the onset of high BP recordings by an average of 25.6 days (1-60 days). In 4 cases (5.8%) pedal edema coincided and in 12 cases (17.64%) pedal edema succeeded the onset of high BP recordings by a mean of 14 days (2-56 days' range).

In the control group, all had levels of LDH < 600 IU/L, the mean value of LDH being 395.16 ± 92.54 IU/L. Majority of the patients (77.4%) in the non-severe preeclampsia group had LDH levels < 600 IU/L, 6 (9.2%) patients had LDH in the range of 600-800 IU/L, 8(12.9%) patients had LDH in the range of > 800 IU/L. The mean LDH Level in the non-severe preeclampsia group is 513 ± 306.08. Out of 38 cases of severe preeclampsia, 22 (57.8%) patients had levels less than 600 IU/L, 4 cases (10.5%) had levels between 600-800 IU/L, 10 (26.3%) patients had levels > 800 IU/L. The mean LDH in the severe preeclampsia group is 566.8 ± 219.8 ($p < 0.001$) – Highly significant. On analyzing the above data, it is clearly observed that there is significant rise in the LDH levels with increasing severity of the disease ($P < 0.001$). Similar findings were reported by S.P. Jaiswar et al [12]. In their study, all in the control arm had LDH levels < 600 IU/L, the mean value of LDH was 278.3 ± 119.2 IU/C.

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most of the patients in the non-severe preeclampsia group had LDH levels< 600 IU/L, only 2 patients (5.7%) had LDH level between 600-800 IU/L. The mean LDH level in this group was 400.45 ± 145.21 IU/L. In the severe preeclampsia group, 58% had LDH levels < 600 IU/L ,13.9% had LDH between 600-800 IU/L ,27.7% had LDH levels above 800 IU/L. The mean LDH level in this group was 646.95 ± 401.64 IU/L (P < 0.001).

Another study by JyotiHak et al [15] reported similar findings. The mean LDH in the control group was 179.1 ± 23.13, non-severe preeclampsia group was 394.23 ± 119.23 and the severe preeclampsia group was 740.60 ± 142.24 (P < 0.001).

It was found that in cases with LDH levels < 600 IU/L the mean birth weight was 2.7kgs, in the group with LDH levels 600-800 IU/L the mean baby weight was 1.53 kg and in the group with LDH > 800 IU/L the mean birth weight was 2.7kg. The mean APGAR score at 5 minutes in the group with LDH <600 IU/L is 8.5, 600-800 IU/L is 4.4, > 800IU/L is 7.5. When LDH levels were <600 IU/L 158 (93%) of the babies are live born, 12(7%) were still born, 12(7%) had NICU admission, 8(4.7%) died in the neonatal period.

The overall PNMR (perinatal mortality) was 4.7%. In the group with LDH between 600-800 IU/L, 8 (57%) were born alive, 6(43%) were still born 4(28%) had NICU admission, 2 (14%) had neonatal death. The overall PNMR in this group is 57%. In the group with LDH > 800, 14 (87.5%) were born alive, 2(12.5%) were still born, 2(12.5%) were admitted in NICU. There were no neonatal deaths in this group. The overall PNMR is 12.5%. The correlation between serum LDH levels and the perinatal outcomes is not found to be significant statistically (correlation coefficient = 0.06).

Study by Jaiswal et al [12] showed that in the group with LDH < 600,84% had uneventful perinatal period, 20% had neonatal complication ,9% neonatal deaths, 7% still births with a PNMR of 16%, This is much higher compared to the PNMR of the present study.

But studies by Qublan et al [16] reported no significant difference between the different subgroups of severe preeclampsia according to the levels of LDH in terms of Birth weight & mode of delivery, but patients who had LDH > 600IU/L showed a significant increase in the incidence of perinatal death (P<0.001).

When compared to the control group, the study group had significantly higher rate of maternal complications. Study by S.P. Jaiswar et al[12] showed that when LDH was <600 IU/L there were no maternal complications. When LDH was between 600 - 800 IU/L, the following complications were noted abruption placenta (7.7%), cerebro vascular accident (7.7%), when LDH was greater than 800 IU/L the following complications were noted, Abruptio placenta

,HELLP syndrome with renal failure, metabolic encephalopathy, pulmonary embolism, pulmonary embolism, pulmonary edema, renal failure, CVA. Overall complication rate was 22.2%.

Another study by Qublan et al[16] noted a similar trend of increase in maternal complications with increase in serum LDH concentrations. In their study, no maternal complications were noted when LDH was <600 IU/L. 1 out of 21 cases developed eclampsia in the group with LDH between 600-800 IU/L, 12 out of 13 patients i.e. 92.3% developed complications (eclampsia – 2, Abruption – 1, Intracranial hemorrhage – 1, HELLP syndrome – 2, AK1-1, Pulmonary edema – 1, DIC – 1).

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CONCLUSION:

A helpful biochemical indicator of the severity and occurrence of pre-eclampsia problems is lactic dehydrogenase. These issues may be avoided by identifying high-risk patients with increased levels of lactic dehydrogenase, closely monitoring them, and providing timely, appropriate care, which will reduce maternal and foetal morbidity and mortality.

REFERENCES:

1. Craici I, Wagner S, Garovic VD. Pre-eclampsia and future cardiovascular risk: formal risk factor or failed stress test? Ther Adv Cardiovasc Dis. 2008;2(4):249–259.

2. Cunningham FC, Leveno KJ, Bloom SL, et al. Williams obstetrics. 23. New York: McGraw-Hill; 2010. p. 706.

3. Tsoi SCM, Zheng J, Xu F, et al. Differential expression of lactate dehydrogenase isozymes (LDH) in human placenta with high expression of LDH-A4 isozyme in the endothelial cells of pre-eclampsia villi. Placenta. 2001;22(317):22.

4. Kay HH, Zhu S, Tsoi S. Hypoxia and lactate production in trophoblast cells. Placenta. 2007;28(8-9):854–860.

5. Burd LI, Simmons MA, Makowski EL, et al. Placental production and foetal utilization of lactate and pyruvate. Nature. 1975; 254:710–711.

6. Bougneres PF, Rocchiccioli F, Nurjhan N, et al. Stable isotope determination of plasma lactate conversion into glucose in fasting infants. Am J Physiol. 1995;268: E652–E800.

7. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynaecol. 2004;103(5):1–981.

8. Lain KY, Roberts JM: Contemporary concepts of the pathogenesis and management of preeclampsia. JAMA, 2002; 287: 3183–86.

9. Krefetz RG: Enzymes. Clinical Chemistry, 4th ed. Lippincott Williams and Wikins; Philadelphia 2000; 196–98.

10. Beyer C: Lactate dehydrogenase isoenzymes in serum of patients with preeclampsia/eclampsia complicated by the HELLP syndrome. ClinChimActa, 1991; 202: 119–20.

11. Makkonen M, Penttila IM, Castren O: Serum lactic dehydrogenase and isoenzymes during pregnancy and labor. ActaObstetGynecolScand, 1980; 59: 97–102.

12. s.p. Jaiwar, Amit Gupta, RekhaSachan, S.N.Natu, Mohan Shaili. Lactic Dehydrogenase: A Biochemical Marker for preeclampsia – Eclampsia. The Journal of Obstetrics.and Gynaecology of India 2011; 61 (6): 645-648.

13. Duckitt K, Harrington D. Risk Factors for preeclampsia at antenatal booking: systemic review of controlled studies. BMJ 2005; 330: 565.

14. Young BC, Levine RJ, Karumanchi SA. Pathogenesis of preeclampsia.Annu Rev Patnol.2010 : 5 : 173 – 92.

15. JyotiHak, Nayar – Un-Nisa, Swarn Gupta, LDH Levels in Pregnancy and its Association with Severity of the Disease and Fetomaternal outcome in Preeclampsia and Eclampsia. JK Science. 2015: 17 (3); 110-113.

16. QublanHs, Ammarin V, Bataineh O, Al-Shraidehz, Tahat Y, Awanleh I, Kheisat B, Nussaiv B, Amarin 20. Lactic dehydrogenase as a biochemical marker of adverse pregnancy outcome in severe pre – eclampsia. Med SciMonit . 2005 Aug; 11 (8): (R393-7.