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Research Article

Serum Lactate Dehydrogenase Levels: A Biochemical Marker of Adverse Pregnancy Outcome in Pre-eclampsia and Eclampsia

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Abstract:

Introduction: Pre-eclampsia and Eclampsia is one of the major causes of maternal mortality and morbidity. These conditions are largely preventable once detected, and are treatable. Defective placentation and endothelial dysfunction leading to endothelial cell injury are considered as the core features of preeclampsia. Lactate dehydrogenase (LDH) is an intracellular enzyme and is responsible for interconversion of Pyruvate and Lactate in the cell. Several studies report that serum LDH level increases with severity of preeclampsia and shows significant correlation with high blood pressure and poor maternal and perinatal outcomes. Studies have shown that LDH activity and gene expression are higher in placentas of pre-eclampsia than normal pregnancy. They serve as indicators suggestive of disturbance of cellular integrity induced by pathological conditions and is used to detect cell damage or cell death.

Objectives: To correlate level of LDH with severity and complications of preeclampsia and associated maternal and perinatal mortality and morbidity.

Material and Methods: An observational prospective study was conducted on 150 pregnant women in department of obstetrics and gynaecology, JNMCH AMU Aligarh U.P. Serum LDH was measured by continuous spectrophotometric method.

Results: Higher levels of LDH were found in women with preeclampsia and eclampsia as compared to normal pregnant women. Maternal complications and adverse perinatal outcome were maximum in women with LDH>800 IU/L.

Conclusion: LDH is an important prognostic marker of pregnancy induced hypertension. Elevated LDH levels may be considered as severe feature of preeclampsia.

Keywords: Pre-eclampsia, Eclampsia, Lactate dehydrogenase (LDH).

INTRODUCTION

Hypertensive disorders occur in about 6-8% of all pregnancies [1]. Pre-eclampsia and Eclampsia rank as one of the major cause of maternal mortality and morbidity [2]. Pre-eclampsia virtually affects all maternal organ systems including liver, kidneys, brain, clotting system and primarily the placenta [3, 4]. Lactate dehydrogenase (LDH) is an intracellular enzyme and is responsible for interconversion of Pyruvate and Lactate in the cell [5]. Elevated blood level of lactate dehydrogenase indicates cellular death followed by its leakage into the circulation [5]. In pre-eclampsia massive intracellular death occurs, so it is a very good marker to detect disease severity. Despite considerable research, exact cause of pre-eclampsia is still unclear [6]. Defective placentation and endothelial dysfunction are considered as the core features of pre-eclampsia [7]. Endothelial cell dysfunction can contribute to inappropriate vasoconstriction, platelet aggregation, activation of the coagulation system and ultimately decreased blood flow to organs. Recently, LDH level has been suggested as a potential marker to predict the severity of pre-eclampsia and an indicator for multi-organ involvement. Several studies report that serum LDH level increases with severity of pre-eclampsia and shows significant correlation with high blood pressure and poor maternal and

perinatal outcomes. But some researchers did not find significant difference of serum LDH level between pre-eclamptic women and healthy pregnant women [8, 9]. From the above studies, it has been observed that the result is conflicting. Therefore, the present study has been designed to assess the serum LDH level in pregnant women with pre-eclampsia.

MATERIALS AND METHODS

The prospective clinical study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry J.N.M.C.H, A.M.U. during 2017-2020. Total of 150 pregnant women were enrolled in this study. All women were provided with an informed written consent after they were fully instructed about the investigation. The study was approved by Institutional Ethics Committee, Faculty of Medicine, Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh. For this study, pre-eclamptic and eclampic women aged 18 to 35 years during third trimester (28-40 weeks) were included as study group. Women were divided into non-severe pre-eclamptic women (SBP >140 to <160mm Hg, DBP>90 to < 110mm Hg with or without proteinuria > 0.3gm/ 24 hrs), severe pre-eclamptic women (SBP>160mm Hg and/or DBP> 110mm Hg with significant proteinuria >5gm/24 hrs or >2+ on dipstick) and eclamptic women. For comparison, age matched healthy normotensive pregnant women in their third trimester (28-40 weeks) were included as control. The inclusion criteria includes singleton pregnancy, gestational age (28-40 weeks), known last date of menstrual period, history of regular menstruation, normotensive and pre-eclampsia women while exclusion criteria includes women with any medical disorders, known smoker, alcoholism and proteinuria before conception or before 20 weeks of gestation. Study and control population were also classified into 3 groups on the basis of serum LDH: Group I - serum LDH <600 IU/L, Group II - serum LDH 600-800 IU/L and Group III - serum LDH >800 IU/L.

A detailed history and physical examination (general and systemic) including assessment of consciousness level and vitals were recorded. Both systolic and diastolic blood pressure was measured at the time of admission and also at 12 hours and 24 hours and 7 days following delivery. Serum LDH level were estimated by continuous spectrophotometric method. Normal serum lactate dehydrogenase level ranges from 230 to 460 IU/L. Hence, any significant difference in the serum Lactate Dehydrogenase levels of cases and controls was evaluated.

RESULTS

The demographic profile of women with pre-eclmapsia and the normotensive women was similar in terms of age, parity and socioeconomic status.

Table I: LDH Levels (Mean ± SD) in Study and Control Groups

	Mean ± SD LDH (IU/L)		
Study group		F- value	p- value
Normotensive (Control)	182.18 ± 148.23		
Non Severe Pre-eclampsia	419.49 ± 599.47		
		19.992	p <0.001
Severe Pre-eclampsia	517.96 ± 414.90		
Eclampsia	840.20 ± 442.70		

The Mean ± SD of LDH level was 182.18 ± 148.23 in control group, 419.49 ± 599.47 IU/L, 517.96 ± 414.90 in pre-eclampsia subgroups and 840.20 ± 442.70 IU/L in eclampsia. The difference in serum LDH level was highly significant (p < 0.001) as shown in Table I.

Out of 150 women, 116 had LDH level <600 IU/L, 13 women had LDH between 600-800 IU/L and 21 had LDH more than 800 IU/L. 72 out of 75 normotensive women had LDH <600 IU/L while 3 of them had LDH between 600-800 IU/L. In women with non-severe pre-eclampsia (n=24), 19 had LDH <600 IU/L, 2 had LDH 600-800 IU/L and rest 3 had LDH > 800 IU/L as depicted in Fig.1.

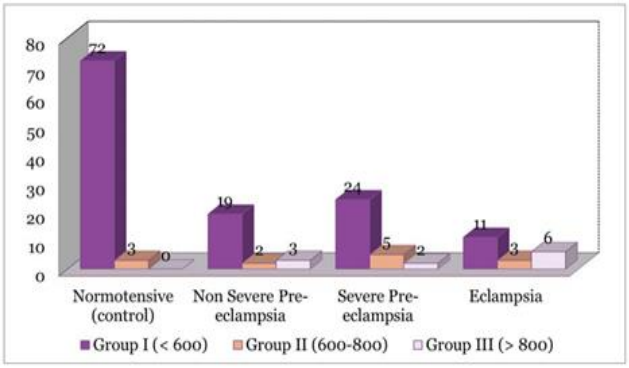

Fig-1: Distribution of study population according to LDH Levels (Mean+SD)

Table II: SBP and DBP (Mean ± SD) of different groups

Groups	SBP on admission (mm of Hg)	SBP at 12 hrs (mm of Hg)	SBP at 24 hrs (mm of Hg)
Group I	129.37 ± 22.29	125.23 ± 18.15	121.28 ± 18.85
Group II	145.84 ± 21.39	136.19 ± 35.66	131.52 ± 47.38
Group III	161.80 ± 16.36	141.23 ± 19.6	135.23 ± 11.59
	DBP on admission (mm of Hg)	**DBP at 12 hrs (mm of Hg)**	**DBP at 24 hrs (mm of Hg)**
Group I	82.85 ± 13.49	81.32 ± 11.58	78.95 ± 12.06
Group II	94.61 ± 15.67	89.04 ± 23.67	83.33 ± 30.66
Group III	100.00 ± 12.53	92.92 ± 12.18	86.46 ± 10.58

As shown in Table II women in Group I had SBP (Mean ± SD) on admission 129.37 ± 22.29 mm of Hg , 145.84 ± 21.39 mm of Hg in Group II and 161.80 ± 16.36 mm of Hg in Group III. The difference in SBP (Mean ± SD) on admission was highly significant ($p < 0.001$) among the three groups. Similarly, women in group I had SBP at 12 hours 125.23 ± 18.15 mm of Hg, 136.19 ± 35.66 mm of Hg in group II and 141.23 ± 19.6 mm of Hg in group III. The difference in SBP (Mean ± SD) at 12 hours was highly significant ($p < 0.001$). Women in group I had DBP at 12 hours 81.32 ± 11.58 mm of Hg, 89.04 ± 23.67 mm of Hg in group II and 92.92 ± 12.18 mm of Hg in group III. The difference in DBP (Mean ± SD) at 12 hours was highly significant ($p < 0.001$) among the three groups. Women in group I had SBP at 24 hours 121.28 ± 18.85 mm of Hg, 131.52 ± 47.38 mm of Hg in group II and 135.23 ± 11.59 mm of Hg in group III. The difference in SBP (Mean± SD) at 24 hours was highly significant ($p < 0.001$) among the three groups. Women in group I had DBP at 24 hours 78.95 ± 12.06 mm of Hg, 83.33±30.66 mm of Hg in group II and 86.46 ± 10.58 mm of Hg in group III. The difference in DBP (Mean ± SD) at 24 hours was highly significant ($p < 0.001$) among the three groups. Women in Group I had DBP (Mean ± SD) on admission 82.85 ± 13.49 mm of Hg , 94.61 ± 15.67 mm of Hg in Group II and 100.00 ± 12.53 mm of Hg in Group III. The difference in DBP (Mean ± SD) on admission among the three groups was highly significant ($p < 0.001$).

Maximum number of vaginal delivery 71 (61.20%) occurred in Group I in which LDH level is <600 IU/L compared to Group II and Group III. Women who had LDH level >800 IU/L showed increase in the rate of caesarean section 13 (61.90%) out of 21 as observed in Table II. There was no significant difference between the different subgroups of severe pre-eclampsia and eclampsia according to the levels of LDH ($p > 0.05$) as depicted in Fig.2

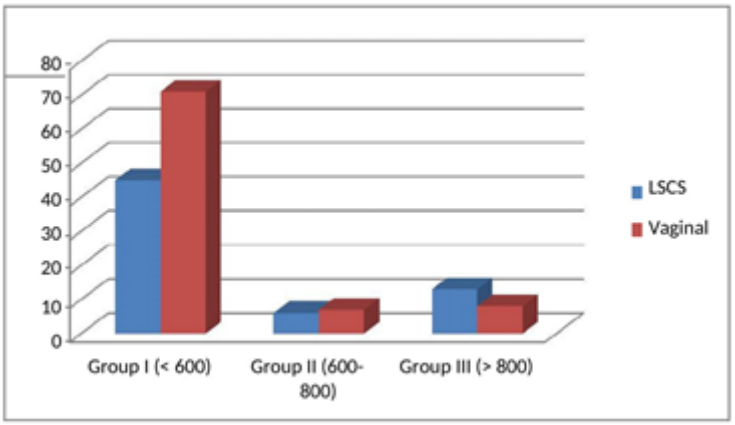

Fig-2: Mode of delivery

Table-III: Maternal Complications

Groups	DIC	Abruption	AKI	Eclampsia	HELLP	Pulmonary Edema	PRES	PPH	Maternal Death	Repeated Convulsions
GroupI	0	3	2	0	2	9	0	0	0	0
GroupII	0	1	0	0	0	1	0	1	0	1
GroupIII	1	2	0	2	2	8	1	0	5	0
Total	1	6	2	2	4	18	1	1	5	1

Table III shows that Group III women with LDH level > 800 IU/L showed increase in terms of eclampsia, abruption placenta, pulmonary oedema, HELLP syndrome, acute kidney disease and disseminated intravascular coagulation compared to women who had lower levels of LDH <600 IU/L and 600-800 IU/L. Pulmonary oedema was the commonest complication among all groups followed by abruption placentae & HELLP syndrome. All the women who had mortality in our study population belonged to group III (LDH level more than 800 IU/L). Women who had LDH level >800 IU/L showed highly significant increase in the incidence of intensive care unit (ICU) admission (p<0.001) compared to women who had lower levels of LDH <600 and <600-800 IU/L as shown in Fig. 3.

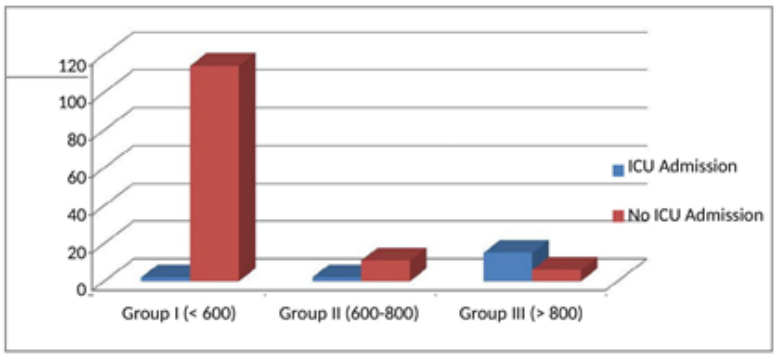

Fig-3: Maternal ICU Admission

Table-IV: Neonatal Outcome

	Group I	Group II	Group III	F-Value	P- Value
Mean birth weight(kg)	2.48 ± 0.61	2.26 ± 0.38	2.25 ± 0.47	1.633	p > 0.05
Apgar Score (1min)	5.94 ± 1.26	5.23 ± 1.48	3.66 ± 2.72	19.236	p <0.001
Apgar Score(5 mins)	7.24 ± 1.39	6.84 ± 1.46	4.42 ± 3.09	23.346	p <0.001
Intrauterine Death (IUD)	1	1	6	--	--
NICU Admission	9	3	12	--	--
Perinatal Mortality	3	0	2	--	--

As shown in Table IV the mean birth weight was comparatively lower in group III as compared to group I. However, the difference was not statistically significant (p>0.05). The Apgar score at birth (p < 0.001) and at 5 minutes of birth (p< 0.001) was found to be significantly low in patients with higher LDH levels. Maximum number of intrauterine deaths 6 out of 8 (60%) were from group III with LDH>800 IU/L. Fetal outcome was also poor in group with LDH>800 IU/L with maximum number of Neonatal ICU admission (57.14%) compared to group II (23.07%) and group I (7.75%). Perinatal mortality rate was highest in group III. Meconium aspiration syndrome was the most common complication (6.66%) requiring NICU admission among all groups followed by prematurity (6%), intrauterine growth retardation (5.33%) and respiratory distress (4%).In group I most common neonatal complication was prematurity (5.17%) followed by IUGR (4.31%). Group III had highest number of NICU admission with 6 (28.57%) having meconium aspiration and 5 (23.8%) neonates admitted for respiratory distress.

DISCUSSION

Pre-eclampsia are multisystem disorders and lead to a lot of cellular death [10]. The mechanism behind elevation of blood pressure or aggravation of hypertension still remains an enigma despite considerable research for many decades, thus remaining one among the most significant and unsolved problems in obstetrics. Several studies have been carried out till date to understand the pathophysiological basis of this disease. But still the exact pathophysiology of this disease is not known. Lactate Dehydrogenase (LDH) is mainly an intracellular enzyme and its levels can be used to assess the extent of cellular injury and thereby the severity of disease. Early detection of women at higher risk and optimal management requires establishment of diagnosis, close observation for signs and premonitory findings and delivery at the optimal time considering both maternal and fetal well-being.

In present study, the mean age, parity and socioeconomic status in the control and pre-eclampsia groups were comparable and the difference was not statistically significant.

A significant rise in the LDH levels in preeclampsia patients as compared to control group was observed. The progressively increased LDH level in pre-eclampsia indicates progression of

cellular injury with severity of this disorder. Various studies also demonstrated a significant rise in the LDH levels with increasing severity of the disease [11-13].

Majority of eclamptic women had LDH >800 IU/L in our study. Our results were similar to Gupta A *et al.* who also observed that there was significant increase in number of women with severe pre-eclampsia with higher LDH level [13].

The systolic blood pressure (SBP) and diastolic blood pressure (DBP) was significantly higher with higher serum LDH levels. These results correlate with the studies conducted by Umasatyashri *et al*. Bhave NV *et al*. and Mallika A *et al*. [14-16].

There was no significant difference in mode of delivery between the different subgroups of severe pre-eclampsia and eclampsia according to the levels of LDH this is in contrary to Gupta A *et al*. in which authors found that with increasing LDH values, rate of cesarean delivery increases significantly[13].

Maternal complications were more in women with LDH>800 IU/L compared to women who had lower levels of LDH <600 IU/L and 600-800IU/L. Our result shows pulmonary oedema was the most common complication observed among all the subgroups followed by placental abruption. Abruption was the most common complication observed among all the subgroups followed by eclampsia in the study conducted by Gupta *et al*. [13]. In present study statistically increased incidence rate of ICU transfer on comparing the three subgroups of women with LDH levels <600, 600-800 and >800 IU/l. The results were in harmony with the various studies [12, 13].

In the present study the difference was not statistically significant in the mean birth weight of study and control groups while the mean Apgar score at birth and at five minutes of birth was found to be lower in group III compared to group I and group II. Overall Fetal outcome was also poor in group with LDH>800 with maximum number of Neonatal ICU admissions compared to group II and group I. Perinatal mortality rate was also highest in group III. The occurrence of neonatal complications, stillbirths and perinatal deaths were significantly higher in mothers who had increased serum levels of LDH [11, 14]. In study by V P Mary *et al*. perinatal death was seen in 77.7% women with LDH more than 800 IU/L, 20.6% with LDH 600-800 IU/L and 6.25% in women with LDH <600 IU/L which is statistically very significant [17].

CONCLUSION

Serum Lactate dehydrogenase (LDH) levels were found to be significantly increased in women with pre-eclampsia and eclampsia in comparison to normal pregnant women. Maternal complications were associated with higher LDH levels in severe pre-eclampsia and eclampsia. Thus, it is useful biochemical marker as it reflects the severity of the disease and the occurrence of the complications of pre-eclampsia and eclampsia. Thus, we conclude from this study, that screening of all pregnant women with Pre-eclampsia and eclampsia with LDH levels should be made mandatory as a part of antenatal care.

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Ethical approval

The study was approved by the Institutional Ethics Committee

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