Indian Journal of Obstetrics and Gynecology Research 2019;6(4):499–503

Content available at: iponlinejournal.com

Indian Journal of Obstetrics and Gynecology Research

Journal homepage: www.innovativepublication.com

Original Research Article

Evaluation of maternal and perinatal outcomes in preeclampsia and eclampsia in correlation with LDH

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ARTICLE INFO

Article history:
Received 21-08-2019
Accepted 28-08-2019
Available online xx xx xxxx

Keywords:
Maternal outcome
Perinatal outcome
Preeclampsia
Eclampsia
Lactate dehydrogenase

ABSTRACT

Introduction: Preeclampsia and eclampsia complicate 6-8% of pregnancies. It is a serious multisystem disorder specific to pregnancy and is a global problem leading to adverse maternal and perinatal complications. In the recent years monitoring of lactate dehydrogenase (LDH) levels is proposed as prognostic in predicting preeclampsia complications.

Materials and Methods: This prospective comparative study was conducted in the Department of Obstetrics and Gynaecology, Mysore Medical College and Research Institute. Total of 210 pregnant women were studied. They were divided into groups of mild preeclampsia (n=60), severe preeclampsia (n=60), eclampsia (n=30) and normotensive pregnant women (n=60) as control group. LDH levels were done in study group and correlated with maternal and perinatal complications.

Results: LDH levels were significantly elevated in patients with preeclampsia and eclampsi a (F -statistics value =43.4076, df = 3, P value < 0.001) when we compared to normotensive controls. High systolic and diastolic blood pressures correlated with high LDH ($P<0.001$). Maternal and also perinatal complications were significantly correlated with high LDH ($P<0.001$).

Conclusion: Serum LDH values significantly correlate with severity and clinical outcome of preeclampsia and eclampsia. Raised LDH levels suggest heightened risk developing maternal and perinatal complications. LDH can be offered as prognostic tool to predict preeclampsia and eclampsia complications.

1. Introduction

Hypertensive disorders of pregnancy are common and serious obstetric health hazard. They lead to various maternal and fetal complications. Preeclampsia - eclampsia are multisystem disorder complicating 5-15% of pregnancies in India.[1] Pre-eclampsia (PE) is one of the leading causes of maternal and fetal morbidity and mortality world wide.[2] Preeclampsia is a unique pregnancy-specific condition that is characterized by hypertension and proteinuria with onset after 20 weeks of gestation. The exact true etiology of preeclampsia is not clear and it is still regarded as disease of theories. There is significant evidence that abnormal trophoblastic invasion of placental blood vessels, altered endothelial cell function, oxidative stress with production of reactive oxygen species play an important role in the pathogenesis of preeclampsia.[3–5] Preeclampsia is still considered to be a major obstetric problem in pregnant women despite advancements in the field of medical sciences.[2]

LDH is an intracellular enzyme catalyses the interconversion of pyruvate and lactate. It converts pyruvate the final product of glycolysis to lactate in hypoxic situation. It is expressed extensively in body tissues such as blood vessels. It is released into circulation following cellular death and tissue injury. LDH is highly sensitive marker for tissue breakdown, but it is nonspecific as it also raised in multiple clinical disorders. Hence, to optimize diagnosis measurement of LDH isoenzymes can be suggested. As overall clinical utility, serum LDH levels reflect the extent of cellular death and thereby the severity of disease.[6,7] In the recently years, LDH level estimation has been

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https://doi.org/10.18231/j.ijogr.2019.108

suggested as potential markers to predict the severity of preeclampsia and subsequently as strong indicator for multiorgan involvement.[8] Preeclampsia produces potentially lethal complications including placental abruption, ARDS, hepatic failure, acute renal failure and cardiovascular collapse. The accurate detection of women at risk, early diagnosis, and appropriate management may help to reduce complications resulting in improved maternal and perinatal outcomes. The prediction of pre-eclampsia is necessary to prevent the complications, so it necessary to diagnose the disease at the earliest. The effects of LDH in pregnancy related complications like preeclampsia is now gaining attention.

The objectives of the present study are

1. Comparision of serum LDH levels in the normal pregnant women and in women with preeclampsia and eclampsia in their antepartum period
2. Study the correlation of maternal and perinatal outcomes with serum LDH levels.

2. Materials and Methods

It was a prospective comparative study conducted at Mysore Medical College and Research Institute department of obstetrics and gynaecology. This study was approved by Ethical Review Committee. In the study 210 pregnant women were included. Inclusion criteria were pregnant women in the age group of 18-35 years, singleton pregnancy, gestational age between 28-40 weeks and in study group blood pressure was normal in the initial 20weeks of gestation and there was no prior history of hypertension. Exclusion criteria were: privious history suggestive of pre-existing essential hypertension, diabetes mellitus, endocrine disorder, connective tissue disorder, epilepsy, hepaticdisorder disease, stroke, corononary artery disease, chronic renal disorder, chronic infections, multiple pregnancy.

The pregnant women included for study were divided into two groups. The groups were matched demographically according to age and parity. Group I (Control group) with 60 normotensive pregnant women. Group II (Study Group) with 150 pregnant women with clinical features of Preeclampsia and Eclampsia. They were further subdivided into IIA - Mild Preeclampsia (n=60), IIB - Severe Preeclampsia (n=60) and IIC–eclampsia (n=30). Subjects were also divided according to the serum LDH levels into following 3 sub groups so as to find out the group with high risk of developing complication. The subgroups are those with LDH $<$600 IU/L, LDH 600-800 IU/L and LDH $>$800 IU/L.

The diagnosis of preeclampsia and eclampsia were made according to American College of Obstetrics and Gynecology (ACOG) criteria.[9] Patient's blood samples were collected for estimation of serum LDH by continuous spectrophotometric method.[10] All women in the study were admitted and followed up till delivery and early postpartum period. Also newborns were followed up till early neonatal period. For Statistical analysis SPSS software, version 22 was used. The results were expressed as mean $\pm$ SD. Difference in distribution of continuous variables like LDH, systolic BP, diastolic BP, gestational age (weeks) and birth weight (kg) was tested using ANOVA. Categorical variables like maternal complications, NICU admission, perinatal mortality were compared with LDH categories using Chi square test. Significance was interpreted at alpha error (P value) of 5% (0.05) that is P value $<$0.05.

3. Results

The baseline demographic characteristics of different study groups are shown in Table 1. In our study of the total patients 60 (28.5%) were normotensives and remaining 150 patients (71.5%) belonged to preeclampsia (PE), eclampsia group. Table 2 shows mean LDH levels compared between the groups. The mean LDH levels in the normotensives group I was 221.46$\pm$78.38 IU/L. In groups IIA LDH was 497.1$\pm$176.92 IU/L, group IIB was 692.26$\pm$355.11 IU/L and in group IIC was 856.12$\pm$492.29IU/L. The mean LDH levels are significantly higher in PE and eclampsia group when we compared to normotensive pregnant women ($p<0.001$). Again when we compared LDH levels in group II between PE, eclampsia groups there was significant proportionate rise in the LDH levels with increasing severity of the disease. Correlation of LDH values with severity of blood pressure is shown in Table 3. In control group and mild preeclampsia group all patients had serum LDH values $<$ 600IU/L. Severe preeclampsia and eclampsia showed trends towards higher blood pressure and higher LDH distribution. On analysis it was found that higher SBP and DBP correlated significantly with higher levels of serum LDH ($P < 0.001$).

Table 4 presents maternal outcome in relation to LDH levels. Maternal complications were found maximum when LDH values were above 800IU/L. HELLP syndrome was most common complication. Abruption was second most common complication. Both HELLP syndrome and abruption were significantly associated with high LDH levels ($p<0.001$). There were no maternal deaths in our study.

Perinatal outcomes are presented in Table 5. The observation supports that there is reduction in the average weight of babies with higher level of LDH ($P = 0.001$). Also with increasing severity of disease babies were delivered at earlier gestational age (P=0.006). The NICU admission rates ($P <0.001$) and perinatal deaths ($P <0.001$) were significantly more in babies whose mothers had elevated LDH levels.

Table 1: Baseline characteristics in different groups (n=210)

Parameters	Group I (n=60) Control	Group IIA(n=60) Mild preeclampsia	Group IIB (n=60) Severe preeclampsia	Group IIC (n=30) Eclampsia
Age (years) (mean ±SD)	23.52 ±2.68	23.25± 2.94	22.62 ± 3.1	21.16±2.56
Parity 0 (no.)	31	35	38	21

Table 2: Mean LDH levels in various groups

Parameter	Group I	Group IIA	Group IIB	Group IIC	F-statistics Value, df and P Value
LDH (IU/L) (mean ±SD)	221.46±78.38	497.1±176.92	692.26±355.11	856.12±492.29	F-statistics value= 43.4076 df = 3, Pvalue < 0.001

Table 3: Association of systolic and diastolic blood pressure (BP) with LDH levels

	LDH <600 IU/L	LDH 600-800 IU/L	LDH >800 IU/L	Statistics Value, df and P Value P value
Systolic BP (mmHg)				
90-<140	2 (2%)	-	-	
140-<160	65 (61.9%)	5 (18.5%)	4 (22.2%)	
>160	38 (36.1%)	22 (81.5%)	14 (77.8%)	Chi square Value= 24.38 df = 4 P-value < 0.001
Diastolic BP (mmHg)				
60-<90	2 (2%)	-	-	
90-<110	67 (63.8%)	7 (25.9%)	6 (33.3%)	
>110	36 (34.2%)	20 (74.1%)	12 (66.7%)	Chi square Value = 17.72 df = 4 P-value = .0013

Table 4: Correlation of maternal outcome with LDH levels in study group

	LDH <600IU/L	LDH 600-800 IU/L	LDH >800 IU/L	Statistics Value, df and P Value
Abruption	1 (0.9%)	2 (7.4%)	6 (33.3%)	Chi square Value = 28.68 df = 2 P-value < 0.001
HELLP syndrome	0	3 (11.1%)	8 (44.4%)	Chi square Value = 45.36 df = 2 P-value < 0.001
DIC	0	0	2(11.1%)	NS
Renal failure	0	0	1 (5.5%)	NS
Pulmonary edema	0	0	1 (5.5%)	NS

(NS – not significant)

Table 5: Correlation of perinatal outcome with LDH levels in study group

	LDH <600 IU/L	**LDH 600-800 IU/L**	**LDH >800IU/L**	**Statistics Value, df and P Value**
Mean gestational age (weeks)	37.2±2.85	36.51±1.65	35.1 ±2.12	F-statistics value= 5.2613 df = 2 P –value =0.0062
Mean birth weight (kg)	2.8±0.31	244±0.54	1.96±0.38	F-statistics value= 44.3496 df = 2 P –value < 0.001
Still birth	0	0	1 (5.5%)	NS
NICU admission	16 (15.2%)	8 (29.6%)	11 (61.1%)	Chi square Value = 18.81 df = 2 P-value < 0.001
Perinatal mortality	1 (0.9%)	2 (7.4%)	4 (22.2%)	Chi square Value = 16.18 df = 2 P-value < 0.001

NICU – Neonatal intensive care unit

4. Discussion

In our study we observed the elevation of LDH levels significantly in preeclampsia and eclampsia cases than control group (P< 0.001). Qublan HS, et al[7] confirmed in their study that the mean LDH levels in normal controls was 299 ± 79 IU/l, in women with mild preeclampsia was 3 48 ± 76 IU/l and women with severe preecla mpsia was 774 ± 69.61 IU/l. Hence they demonstrated a significant association of LDH levels with severe preeclampsia (P < 0.001). Similar results with elevation in LDH in preeclampsia, eclampsia were observed in studies conducted by Jaiswar et al, Umasatyasri et al, Qulban et al, Sarkar et al and Sarmah et al.[11–14] SBP and DBP were significantly higher in women with higher serum LDH levels (P < 0.001) in the above studies.[7,11–14] We also observed direct association of elevated serum LDH with increasing SBP and DBP in our study population (P<0.001).

Complications of PE and eclampsia affect both mother and fetus. According to Qublan et al[7] and Sarkar et al[13] the multi organ dysfunction in preeclampsia which is caused by vascular endothelial damage, including maternal liver, lungs, kidney, neuronal system, coagulation pathway system will leads to excessive LDH leakage due to cellular dysfunction, which may lead to the occurence of preeclampsia and present with elevated serum LDH.[7,13] This explains association of preeclampsia complications with high serum LDH levels.

Jaiswar SP et al[11] observed that there was significant increase in maternal morbidity with elevated serum LDH levels >800 IU/L which was a significant rise (P = 0.006). They concluded LDH levels have significant association in various maternal and fetal outcomes in patients of preeclampsia and eclampsia.

Umasatyasri et al[12] and Andrews L et al[15] also observed increase in maternal complications with increasing serum LDH levels. They observed that higher serum LDH levels would lead to increased incidence of maternal complications like abruption, renal failure, HELLP syndrome, pulmonary edema etc. In our present study also we observed increased incidence of maternal complications when LDH was elevated. HELLP syndrome and abruption were more in the present study population significantly (P <0.001).

Several studies have shown significant increase in perinatal complications with increasing levels of LDH.[7,11–15] Jaiswar SP et al[11] and Andrew et al[15] confirmed association of low birth weight of infants with elevation in serum LDH levels. Chronic placental hypoperfusion leads to fetal growth restriction. Our study also showed decrease in mean birth weight of newborns with elevated serum LDH levels (P<0.001). This is different to Umasatyasri et al[12] and Qublan HS, et al[7] who did not find any significant correlation. Increased neonatal complications, perinatal deaths were observed in many other studies.[7,11–13,15] In the present study also similar results were observed showing statistically significant increase in NICU admissions and perinatal mortality with higher LDH values but there was no significant rise in still birth. It is evident that monitoring LDH levels helps in predicting severity of preeclampsia and eclampsia. Elevated LDH levels correlate with poorer maternal and perinatal outcome.

5. Conclusion

Serum LDH values significantly correlate with severity and clinical outcome of preeclampsia and eclampsia. Raised LDH levels suggest heightened risk developing maternal

and perinatal complications. LDH is a reasonably less expensive easily available investigation. LDH estimation should be used to predict prognosis of preeclampsia and eclampsia. Thus, prompt early diagnosis, treatment at higher centre, early prediction of complications may alleviate complication rates of preeclampsia-eclampsia.

6. Acknowledgments

We acknowledge our work to professors in the department for guidance

7. Conflict of interest

Nil

8. Source of funding

Nil

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Cite this article: Dev SV, Hemalatha CR. Evaluation of maternal and perinatal outcomes in preeclampsia and eclampsia in correlation with LDH. *Indian J Obstet Gynecol Res* 2019;6(4):499-503.