Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 04, 2023

ORIGINAL ARTICLE RESEARCH

Study of Serum Lactate Dehydrogenase in Pregnancy Induced Hypertension

Sangeeta B. Singh[1], Shikhaa Mahajan[2], S.P Singh[3], Farah Deeba Khan[4*], Asha Kumari[5], Yuthika Agrawal[6]

[1]Professor & Head, [2]Associate Professor, [4*] PG Resident, [5,6]Assistant Professor, Department of Biochemistry, Shaheed Hasan Khan Mewati GMC, Nuh, Haryana, India.
[3]Associate Professor, Department of Obstetrics and Gynaecology, Shaheed Hasan Khan Mewati GMC, Nuh, Haryana, India

***Corresponding Author: Dr. Farah Deeba Khan,** PG Resident, Department of Biochemistry, Shaheed Hasan Khan Mewati GMC, Nuh, Haryana, India.

Received: 20 March 2023 **Revised:** 17 April 2023 **Accepted:** 26 April 2023

ABSTRACT

Background: Hypertensive disorders in pregnancy are one of the common medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. Lactate dehydrogenase (LDH) is an enzyme that catalyses the oxidation of L lactate to pyruvate. LDH levels are increased in the scenario of damaged tissues, increased cell leakiness, hemolysis and cellular damage caused by pregnancy induced hypertension and its severity. **Objective:** To estimate and compare the levels of serum lactate dehydrogenase in pregnancy induced hypertension (PIH) cases and controls.

Materials and Methods: A hospital-based case control study was conducted in SHKM GMC Nuh Haryana between August 2021 to July 2022, on 90 cases of PIH (Mild preeclampsia, Severe preeclampsia and Eclampsia) and 90 controls aged 18-45 years females visiting the hospital, following inclusion and exclusion criteria and willing to participate. Samples were collected and analyzed for serum LDH by fully automated analyzer using spectrophotometry.

Results: Mean values of serum LDH levels in Eclampsia were (1365.17±275.22 U/L), severe preeclampsia was (791.13±93.96 U/L) and mild preeclampsia were (422.37±72.13 U/L), while in controls it was (193.71±34.12 U/L). On comparing statistically, a significant difference was observed between the groups with p value <0.001.

Conclusion: LDH levels can be used to assess the extent of cellular death and thereby the severity of disease so as to prevent progression of preeclampsia to eclampsia.

Keywords: Pre-eclampsia, Lactate Dehydrogenase

INTRODUCTION

Pregnancy Induced Hypertension is one of the common medical complications of pregnancy and contributes significantly to perinatal and maternal morbidity and mortality. It has been estimated that preeclampsia complicates 2-8% of pregnancies globally[1].

According to WHO incidence of preeclampsia in India is 2-15%. According to a study done in India, the prevalence of preeclampsia in Haryana is total 18.5% (Rural-16.6% and urban 23.7%).[2] Hypertensive disorders in pregnancy are responsible for 76,000 maternal and 50,0000 infants death each year worldwide. A WHO analysis of maternal deaths reveals that

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 04, 2023

hypertensive disorders in pregnancy are responsible for 16.1% maternal deaths in developed countries and a major contributor to maternal deaths in Asia 9.1% and Africa 9.1%.[3] Preeclampsia, a multisystem disorder of unknown etiology, is defined as maternal systolic blood pressure ≥140mmHg and diastolic blood pressure ≥ 90 mmHg on two occasions separated by at least 6 hours and proteinuria >300mg in a 24-hour period or qualitative >1+ after 20 weeks of gestation following the guidelines of ACOG (American College of obstetrics and gynecologists) 2002.

Preeclampsia without severe features (Mild Preeclampsia)-BP-Systolic ≥ 140 mmHg and Diastolic ≥ 90 mmHg, proteinuria 300mg 0r more per 24 hours. Preeclampsia with severe features (severe Preeclampsia)-BP-Systolic >160 mmHg and Diastolic 110mmhg, thrombocytopenia (Platelet count less than $100*10^9$/L), renal insufficiency, pulmonary edema, new onset of headache unresponsive to medication and visual disturbances. Eclampsia is defined by new onset of tonic- clonic, focal or multifocal seizures in the absence of other causative conditions such as epilepsy, cerebral arterial ischemia, infarction, intracranial hemorrhage or drug use.[4]

Literature shows that patients of pregnancy induced hypertension had a significant higher risk of developing chronic kidney diseases. Preeclampsia and eclampsia contribute to 75% of all causes of acute kidney injury in pregnancy.[5]

The only consistently found pathological lesion in Preeclampsia is the renal lesion termed glomerular endotheliosis, which has been regarded as pathognomonic of the condition.[6]

Lactate Dehydrogenase is an enzyme that catalyzes the oxidation of L- lactate to pyruvate. It has a molecular weight of 134 k Da and is composed of four polypeptide chain of two types M and H and Five isoenzymes, LDH_1 and LDH_2 is found in heart, kidney and erythrocytes. LDH_3 in lung tissues, LDH_4 and LDH_5 are found in liver and skeletal muscle. Lactate Dehydrogenase levels are increased in the scenario of damaged tissues, increased cell leakiness, hemolysis and cell death, hence serum Lactate Dehydrogenase levels can be used to assess the extent of cellular death and thereby the severity of disease.[7]

Extensive review of literature has revealed that there are very few studies for levels of Lactate Dehydrogenase in pregnancy induced hypertension. Keeping in view the above facts the following study was planned.

Aim and Objective: To estimate and compare the levels of serum LDH in pregnancy induced hypertension cases and controls.

MATERIALS AND METHODS

Study Design: The present study was a case-control study, which was conducted in Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology, SHKM, Government Medical College, Nuh, Haryana.

Study period: 1 year

Study subjects: A total of 180 pregnant females were enrolled for this study of age 18 to 45 years (reproductive age group).

Grouping: Two groups were made

Group 1: Cases- Ninety diagnosed patients of pregnancy induced hypertension were selected out of which 30 was from each of the three groups: (a). Mild preeclampsia (Group A) (b). Severe preeclampsia (Group B) (c). Eclampsia (Group C) of age group 18-45 years, willing to participate in the study, single intrauterine pregnancy and with gestational age of 20 weeks or more were included in this study. Group 2: Controls–Ninety age and sex matched normotensive

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 04, 2023

pregnant women. Pregnant females not willing to participate in the study of age group <18 and >45 years, twin pregnancy, with gestational age less than 20 weeks and females with history of medical disorders like chronic hypertension, heart disease, acute and chronic kidney disease, thyroid disorders, liver disorders, gestational diabetes and gout were excluded from study.

Sample Collection: Five ml of venous blood sample was taken from antecubital vein under all aseptic conditions in plain vacutainers after informed consent. Sample was transported to laboratory immediately, centrifuged, serum was separated and analyzed. Serum was separated by centrifugation at 3000 revolutions per minute (RPM) for 5 minutes after clotting. Samples were analyzed for serum LDH by fully automated analyzer using spectrophotometry in which Lactate Dehydrogenase catalyzes the conversion of L-lactate to pyruvate, NAD is reduced to NADH in the process. The catalytic LDH activity has a direct correlation with the initial rate of NADH production. The rise in absorbance is measured photometrically to ascertain it.[8]

Ethical Consideration

The proposed study entitled "Study of serum Lactate Dehydrogenase in pregnancy induced hypertension", was conducted at the Department of Biochemistry, Shaheed Hasan Khan Mewati, Govt. Medical College, Nuh, Haryana, India after authorization by Institutional Ethics Committee approval no.EC/OA-13/2021dated 25.02.2021. Informed written consent was taken from all the subjects. No drugs were used in this study. No invasive/noninvasive procedures were done on the subjects. All the procedures used in the study do not carry any harmful effect on the patients. Thus, the present study is well within the ethical norms and ethically justified.

RESULTS

After analyzing the data following results were obtained.

Table 1: Distribution of cases (different groups) and Controls based on LDH levels

SN	LDH levels (135-225 U/L)	Group A (n=30)		Group B (n=30)		Group C (n=30)		Group 2 (n=90)	
		No.	%	No.	%	No.	%	No.	%
1	<135 U/L	0	0.0	0	0.0	0	0.0	8	8.9
2	135-225 U/L	0	0.0	0	0.0	0	0.0	72	80.0
3	>225 U/L	30	100.0	30	100.0	30	100.0	10	11.1
χ^2=144.000 (df=6); p<0.001									

Table 1. shows distribution of case (different groups) and controls where all the women in Group A, Group B and Group C had LDH levels ≥225 U/L, while a majority of women in Group 2 (80.0%) had LDH levels between 135 & 225 U/L, followed by >225 U/L and the remaining had <135 U/L. On comparing statistically, a significant difference was observed between the groups with p value <0.001.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 04, 2023

Table 2: Comparison of LDH cases (different groups) and Controls based on LDH levels

	Group A (n=30)		Group B (n=30)		Group C (n=30)		Group 2 (n=90)		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	p
LDH (U/L)	422.37	72.13	791.13	93.96	1365.17	275.22	193.71	34.12	725.871	<0.001
	Median (Range)		Median (Range)		Median (Range)		Median (Range)			
	416.0 (302.0-578.0)		812.0 (608.0-902.0)		1367.0 (924.0-1830.0)		200.0 (109.0-252.0)			

Table 2. descriptive analysis of serum LDH levels among cases (different groups) and controls which depicts that it was highest in women in Group C (1365.17±275.22 U/L), followed by Group B (791.13±93.96 U/L) and Group A (422.37±72.13 U/L), while LDH level was least in Group 2 (193.71±34.12 U/L). On comparing statistically, a significant difference was observed between the groups with p value <0.001.

Table 3: Comparison of LDH with respect to Control Group (Dunnet Test).

Parameter	Group (Cases) vs. Controls	Mean Difference	SE	p	95% Confidence Interval	
					Lower Bound	Upper Bound
LDH	Group A	228.656	26.146	<0.001	165.88	291.43
	Group B	597.422	26.146	<0.001	534.65	660.19
	Group C	1171.456	26.146	<0.001	1108.68	1234.23

Table 3: Shows comparison of LDH levels of cases with respect to control group, mean difference was highest among Group C, then Group B followed by Group A. The difference between the groups were highly significant with p value <0.001.

Table 4: Intergroup comparison of LDH (Tuckey HSD)

Parameter			Mean Difference	SE	P	95% Confidence Interval	
						Lower Bound	Upper Bound
LDH	Group A	Group B	-368.767	32.022	<0.001	-451.82	-285.71
		Group C	-942.800	32.022	<0.001	-1025.86	-859.74
		Group 2	228.656	26.146	<0.001	160.84	296.47
	Group B	Group C	-574.033	32.022	<0.001	-657.09	-490.98
		Group 2	597.422	26.146	<0.001	529.61	665.24
	Group C	Group 2	1171.456	26.146	<0.001	1103.64	1239.27

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 04, 2023

Table 4. shows intergroup comparison between cases (Group A, Group B, Group C and control Group 2) there is statistically significant difference in serum LDH levels with p value <0.001.

DISCUSSION

Lactate Dehydrogenase (LDH), a predominantly intracellular cytoplasmic enzyme of anaerobic glycolysis, is released to the general circulation during cell death and may be increased in preeclampsia due to vigorous glycolysis and chronic anoxemia as a result of placental ischemia. [9] This study is in accordance with study done by Fazal et al [10] where he found levels of LDH increases with increasing severity of the disease such as in MPE -473U/L, SPE-648 U/Land E-1535U/L where as in controls 533U/L. with p value <0.001.

Similar to our results, mean LDH level was 257.24 U/L in normotensive patients as compared to 417.84 U/L in patients with pre-eclampsia & 565.51 in patients with eclampsia with (p< 0.01) was observed by V.V Kulkarni et al [11] LDH leakage & elevated levels in serum due to cellular dysfunction. These results are also supported by HS Qublan.[12]

Lactate Dehydrogenase (LDH) is an intracellular enzyme that converts lactic acid to pyruvic acid & elevated levels indicate leakage & cellular death of enzyme from the cell. The results from our study showed that the levels of serum LDH were significantly higher in pre-eclamptic/ eclamptic women as compared to normal pregnant women is in accordance with the results observed by several other studies. Aziz R et al[13] in a study observed mean serum LDH concentration significantly higher in pre-eclamptic patients compared to normal pregnant women. (348.34+/- 59.17 vs 255.92+/- 43.26, p< 0.01).

The study concluded that LDH may be increased due to liver damage. This endothelial vascular damage is the main cause in the occurrence of pre-eclampsia. Higher levels of LDH are very useful marker to identify occurrence of pre-eclampsia. Similar to our results, results were observed by Andrews L et al[14] with significant rise in the LDH levels with increasing severity of the disease, normotensive (172.37 +/- 28.09), mild preeclampsia (356.33+/- 24.47), severe pre-eclampsia (609.91+/- 136.92) & eclampsia (854.05 +/-247.45) (p < 0.001).

In a study done by Agrawal P et al[15], they observed mean value of serum LDH in control group as 391.4 +/- 10.9 IU/L, in mild pre-eclampsia as 531.5+/- 24.5 IU/L, in severe preeclampsia as 922.1 +/- 515.5 IU/L and in eclampsia 1497.6+/- 602.1 IU/L. The difference in serum LDH level was highly significant (p < 0.01). Findings in our study are in agreement with many previous studies like N.V. Bhave et al, S.P Jaiswar et al and He S, K Bremm, A Kallner which show high serum LDH levels correlate well with the severity of the disease and out comes in patients of preeclampsia.[16,17,18]

CONCLUSION

Serum LDH levels were significantly high in PIH and the levels increased with the severity of the disease, indicating increased cellular turnover due to cellular death and ischemia. Hence, LDH may be a prime candidate marker of ischemia and tissue damage associated with the severity of PIH.

REFERENCES

1. coronary Steeger EA, Von Dadelszen P, Duvekot JJ, Pijnenbor. Preeclampsia. Lancet 2010; 376:631-44.
2. Malik A, Jee B, Gupta SK. Preeclampsia. Disease biology and burden its management strategies with reference to India. Pregnancy Hypertension 2018; 15:23-31.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 04, 2023

3. Say L, Chou D, Gemmill A, Tuncalp O, Moller AB, Daniels J et al. Global causes of maternal death: A WHO systematic analysis. Lancet Glob Health 2014; 2:323-33.
4. Gestational Hypertension and Preeclampsia. ACOG Practice Bulletein. American College of Obstetricians and Gynecologists. Obstet Gynecol 2020; 135:237-60.
5. Prakash J, Ganiger VC. Acute kidney Injury in pregnancy specific disorders. Indian J of Nephrol 2017; 27:258-70.
6. Raghupathy R. Cytokines as key players in pathophysiology of preeclampsia. Med Princ Pract 2013; 22:8-19.
7. Jialal I, Sokoll LJ. Clinical utility of lactate dehydrogenase: a historical perspective. Am J Clin Pathol 2015;143(2):158-9
8. Heiden CV, Bais R, Gerhardt W. Approved recommendation on IFCC methods for the measurement of catalytic concentration of enzymes. Part 8. IFCC method for Lactate Dehydrogenase. Eur J Clin Chem Clin Biochem 1994; 32:639-55.
9. Makkonen M, Penttila IM, Castren O. Serum lactic acid dehydrogenase and isoenzymes during pregnancy and labour. Acta Obstet Gynecol Scand. 1980;59(2):97–102.
10. Saleem F R, Chandru S, Biswas M.Evaluation of total LDH and its isoenzymes as markers in preeclampsia.J Med Biochem 2020;39:392-98.
11. Kulkarni V V, Shaikh B. To Study Levels of LDH in Normal Pregnancy, Pre-Eclampsia & Eclampsia. J. Evolution Med. Dent. Sci 2019; 8:2769-78.
12. Qublan HS, Ammarin V, Bataineh O. Lactic Dehydrogenase as a biochemical marker of adverse pregnancy outcome in severe pre-eclampsia. Med Sci Monit 2005;11(8):393-7.
13. Aziz R, Mahboob T. Relation between preeclampsia and cardiac enzymes. ARYA Atheroscler 2008;4(1):29-32.
14. Andrews L, Patel N. Correlation of serum Lactate Dehydrogenase and pregnancy induced hypertension with its adverse outcomes. International Journal of Research in Medical Sciences 2016;4(5):1347-50.
15. Agrawal P, Rajoria L, Vyas J. Serum LDH in preeclampsia and eclampsia and maternal outcomes. Sch J App Med Sci 2016; 4:2052-5.
16. Bhave NV, Shah PK. A correlation of Lactate Dehydrogenase enzyme levels in pregnancy induced hypertensive disorders with severity of disease, maternal and perinatal outcomes. International Journal of Reproduction. 2017;6(10):4302–8.
17. Jaiswar SP, Gupta A, Sachan R, Natu SN, Shaili M. Lactic Dehydrogenase: A Biochemical Markers for Preeclampsia-Eclampsia. The Journal of Obstetrics and Gynecology of India 2011; 61(6): 645–8.
18. He S, Bremme K, Kallner A, Blomblock M. Increased Concentrations of Lactate Dehydrogenase in Pregnancy with Preeclampsia: A Predictor for birth of Small-for Gestational-Age Infants. Gynecological and Obstetric Investigation 1995; 39: 234–8.