Original Article

Correlation of lactate dehydrogenase to cardiovascular risk in preeclampsia

Sunil Kumar Jena, Sangram Keshori Sahoo[1], Biswabhusan Mohanty[2]

Departments of Physiology and [1]Obstetrics and Gynecology, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur, [2]Department of Anatomy, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India

Abstract

Background and Aim: Preeclampsia is a type of pregnancy-induced hypertension, which results in severe hazardous conditions for maternal, fetal, and neonatal life. Altered biomarkers profile has been reported in preeclamptic patients. However, the association of altered vascular biomarkers with the increased cardiovascular (CV) risk in preeclamptic patients has not been studied. Thus, the aim of this study was to associate lactate dehydrogenase (LDH) to rate pressure product (RPP), an indicator of CV risk in preeclamptic patients.

Methods: Basal CV and serum biomarkers such as LDH, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) parameters were recorded in 60 subjects divided into controls (n = 30) and preeclamptic patient (n = 30) groups. Association of these biomarkers to RPP was performed by Pearson's correlation analysis.

Results: Systolic blood pressure, diastolic blood pressure, RPP, heart rate, LDH, AST, and ALT were found to be significantly increased in preeclamptic women compared to control group. There was a positive correlation between RPP and LDH in preeclampsia cases.

Conclusion: Increased serum LDH in preeclamptic women are linked to RPP, an index of myocardial work stress. Therefore, increased LDH and RPP might predispose preeclamptic women to future morbidities.

Key words: Alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, preeclampsia, rate pressure product

Received: 8th September, 2015; *Revised:* 29th October, 2015; *Accepted:* 15th November, 2015

INTRODUCTION

Preeclampsia and other pregnancy-induced hypertensive disorders are the major cause of maternal, fetal, and neonatal morbidity as well as mortality. Preeclampsia is an important disorder of pregnancy that may lead to potentially severe consequences for both mother and child.[1] It affects about 5–10% of all pregnancies throughout the world and is a vital factor for maternal, fetal, and neonatal morbidity as well as mortality.[2] Preeclampsia is a syndrome which affects almost all maternal organs and it is thought to result from an abnormal placenta, the removal of which ends the disease in most cases.[3] Preeclampsia produces potentially lethal complications including placental abruption, disseminated intravascular coagulation, hepatic failure, acute renal failure, and cardiovascular (CV) collapse. Pathogenesis of preeclampsia is not clearly understood; however, endothelial dysfunction has been considered to play a central role in the pathogenesis of preeclampsia.[4] Some researchers have suggested that hypoxia of placenta may play another important role in the pathogenesis of preeclampsia.[5] Dysfunction of endothelial cells can contribute to vasoconstriction and

Access this article online	
Quick Response Code:	Website: www.ijcep.org
	DOI: 10.4103/2348-8093.175400

Address for correspondence: Dr. Sunil Kumar Jena, Department of Physiology, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur - 768 017, Odisha, India.
E-mail: drsunil80@gmail.com

How to cite this article: Jena SK, Sahoo SK, Mohanty B. Correlation of lactate dehydrogenase to cardiovascular risk in preeclampsia. Int J Clin Exp Physiol 2015;2:224-7.

platelet aggregation, which may lead to atherosclerosis and hypertension.[6] Lactate dehydrogenase (LDH) is an intracellular enzyme widely distributed in many tissues and mostly found in heart, liver, kidney, blood cells, etc. In conditions where tissue damage occurs, serum LDH level increase and its estimation provides some information of such damage.[7] The analysis of a combination of biochemical markers particularly markers related to vascular dysfunction such as increased uric acid, LDH, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) concentration in serum may be helpful to prevent the consequence of preeclampsia in the near future.[8] Though several studies have reported altered biochemical markers in preeclamptic women, the association of these biomarkers to the CV risk has not been studied. Increased rate pressure product (RPP), an index of myocardial work stress, has been documented to be an indicator of CV risk. Therefore, the present study aim to assess the association of these biomarkers to RPP in preeclamptic women.

MATERIALS AND METHODS

This study was conducted in the Department of Physiology with the help of the Department of Obstetrics and Gynecology, Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR), Burla, Sambalpur, Odisha, after getting approval by the Institutional Ethical Committee VIMSAR, Burla. The study period was carried out from January 2015 to August 2015. A total of 60 subjects were recruited, out of which 30 were case and 30 were control. Thirty normal pregnant women of more than 20 weeks of gestation with normal blood pressure and normal urine protein were taken as control. Similarly, 30 preeclamptic women of more than 20 weeks of gestation with systolic blood pressure (SBP) more than 140 mmHg, diastolic blood pressure (DBP) more than 90 mmHg, and protein concentration more than 0.3 g (1+)/24 h were taken as case. Both the case and control groups were selected from the outpatient department and inpatient department of Obstetrics and Gynecology, Department of VIMSAR, Burla. Pregnant women with a previous history of hypertension, having urinary tract infection, liver disease, diabetes mellitus, heart disease, musculoskeletal disease, and hemolytic disease were excluded from the study. A written consent was taken from each subject and with all aseptic measures 3 ml of blood was drawn from the medial cubital vein of each subject in fasting state and sent for the estimation of serum LDH, AST, and ALT level in pathology laboratory. These parameters were estimated in pathology laboratory by autoanalyser. Data regarding the age, gestational age, blood pressure, heart rate (HR), and urine protein were taken from the patients' record. RPP, a determinant of myocardial oxygen consumption and work load, was calculated using the formula: RPP = (basal HR × SBP) $\times 10^{-2}$.

Statistical analysis of data

LDH, AST, and ALT level of case and control group were analyzed by unpaired *t*-test. Correlation of RPP with LDH, AST, and ALT was performed using Pearson correlation analysis. Statistical analysis was done by using statistical software SPSS 16 version IBM Corporation. For generation of tables and graphs, Microsoft Word and Excel were used, respectively.

RESULTS

Table 1 depicts the variation of data collected from the record of subjects. From this study, it was observed that the mean age of case group was 28 ± 3.57 years whereas the mean age of control group was 27 ± 5.73 years. The mean gestational age of case group was 34 ± 5.14 weeks whereas that of control group was 30 ± 5.42 weeks. Mean SBP of case group was 166 mmHg with standard deviation (SD) of 12.8 and that of control group was 128 mmHg with SD 5.3. The mean difference of SBP between case and control group was 38 mmHg and this variation in SBP between these two groups was significant at $P < 0.001$. Mean DBP of case group was 107 mmHg with SD of 12.5 and that of control group was 82 mmHg with SD of 3.8. The mean difference of DBP between case and control group was 25 mmHg and this variation in DBP between case and control groups was significant at $P < 0.001$. Mean HR of case group was 97/min with SD of 1.97 and that of control group was 77/min with SD of 4.51. The mean difference of HR between case and control group was 20/min and significant at $P < 0.001$. Mean RPP of case group was 161.55 mm of Hg/min with SD of 12.6 and that of control group was 99.36 mmHg/min with SD of 6.96. The variation of RPP between case and control group was significant at $P < 0.001$.

Table 2 depicts the variation in serum LDH, AST, and ALT between case and control group. Mean LDH of case was

Table 1: Comparison of data collected from patient record

Parameters	Mean±SD (*n*=30)		*P*
	Case	Control	
Age (years)	28±3.57	27±5.73	0.502
GA (weeks)	34±5.14	30±5.42	0.008
SBP (mmHg)	166±12.8	128±5.3	0.000
DBP (mmHg)	107±12.5	82±3.8	0.000
HR (/min)	97±1.97	77±4.51	0.000
RPP (mmHg/min)	161.55±12.6	99.36±6.96	0.000

Values are expressed in mean±SD. Statistical analysis done by unpaired *t*-test. $P<0.05$ was considered to be significant. GA: Gestational age, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, RPP: Rate pressure product, SD: Standard deviation

649 IU/L with SD of 102.9 whereas in control mean was 235 IU/L with SD of 26.3. This variation of LDH between case and control group was significant at $P < 0.001$. Mean AST of case group was 62.7 IU/L with SD of 17.4 whereas in control group mean was 29.7 IU/L with SD of 4.2. This variation of AST between case and control group was significant at $P < 0.001$. Mean ALT of case group was 50.2 IU/L with SD of 20.9; similarly, mean ALT in control group was 31.8 IU/L with SD of 5.3. This variation found here was significant at $P < 0.001$.

Table 3 depicts the correlation of RPP with LDH, AST, and ALT. This correlation was analyzed by Pearson correlation. Correlation coefficient (r) between RPP and LDH was 0.494 [Figure 1], between RPP and AST was 0.232 [Figure 2] and between RPP and ALT was 0.296 [Figure 3]. Only correlation between RPP and LDH shows significance at $P < 0.01$. However, the correlation of RPP with AST and ALT was not significant.

DISCUSSION

This study had demonstrated that LDH, AST, and ALT of preeclamptic women was higher than the normal pregnant women and these variations were statistically significant. Different studies stated that elevated level of serum LDH and AST indicates tissue damage as well as endothelial vascular dysfunction which are the main cause of the occurrence of preeclampsia.[7,9] Researchers also thought that preeclampsia to be an idiopathic multisystem disorder which is specific to human pregnancy.[10] Several potential biochemical markers have been proposed to predict the severity of preeclampsia.[11,12] LDH is an intracellular enzyme that converts lactic acid to pyruvic acid inside the cell. Elevated LDH in serum indicates that there is tissue damage and leakage of enzyme from cell.[13]

Preeclampsia is a multisystem dysfunction caused by vascular endothelial damage, damage to maternal liver, kidney, lungs, blood cell damage, and coagulation system dysfunction, and all these events leads to increase serum LDH level,[7] which is in agreement with the findings of the

Table 2: Comparison of mean serum level of lactate dehydrogenase, aspartate aminotransferase, and alanine

Parameters	Mean±SD (*n*=30)		*P*
	Case	Control	
LDH (IU/L)	649±102.9	235±26.3	0.000
AST (IU/L)	62.2±17.4	29.7±4.2	0.000
ALT (IU/L)	52.6±20.9	31.8±5.3	0.000

Values are expressed in mean±SD. Statistical analysis was done by unpaired *t*-test. *P*<0.05 was considered to be significant. LDH: Lactate dehydrogenase, AST: Aspartate aminotransferase, ALT: Alanine, SD: Standard deviation

Table 3: Correlation between rate pressure product and serological parameters

Parameter	Parameter	Pearson correlation coefficient (*r*)	*P*
RPP	LDH	0.494	0.006
RPP	AST	0.232	0.218
RPP	ALT	0.296	0.112

Statistical test was done by Pearson correlation coefficient (*r*). *P*<0.05 was considered to be significant. LDH: Lactate dehydrogenase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, RPP: Rate pressure product

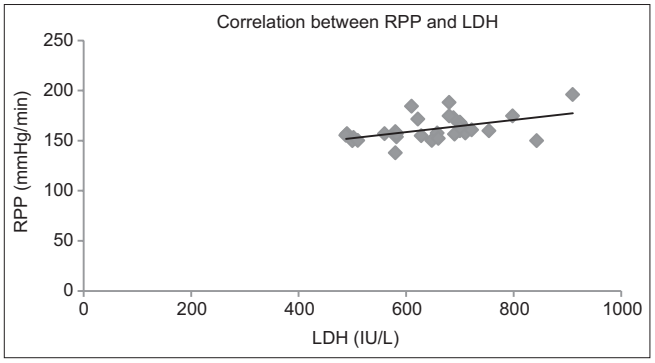

Figure 1: Correlation between rate pressure product and lactate dehydrogenase. Pearson correlation coefficient = 0.494, $P = 0.006$ (significant at $P < 0.01$)

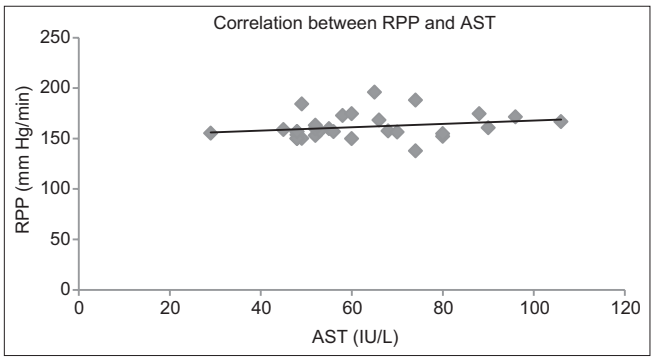

Figure 2: Correlation between rate pressure product and aspartate aminotransferase. Pearson correlation coefficient = 0.232, $P = 0.218$ (not significant)

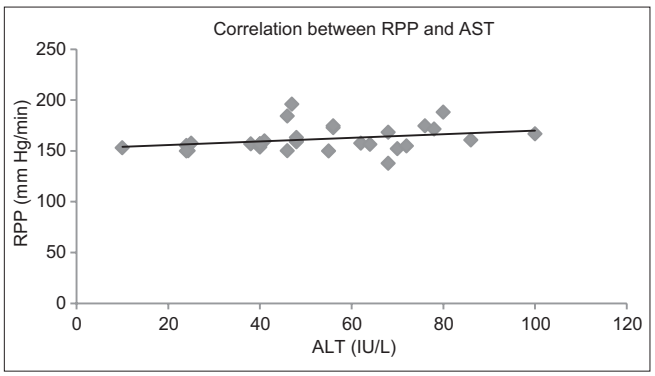

Figure 3: Correlation between rate pressure product and alanine aminotransferase. Pearson correlation coefficient = 0.296, $P = 0.112$ (not significant)

present study. AST is also another intracellular enzyme which is elevated in conditions where the tissue abundant in this enzyme is damaged, i.e., liver. In this study, AST and ALT levels were increased which is indicative of liver damage in these patients. The findings of the present study are in concordance with the findings of the other reports.[7,14,15]

RPP, the indicator of myocardial work load and stress, was significantly less in control group, compared to case group. Thus, preeclampsia subjects with increased RPP were more prone to CV risk than normal pregnant women.[16] This, in turn, is supported by the decreased HR in normal pregnant women, as decrease in HR has been reported to reduce CV risk.[16] RPP is a valuable indicator of the oxygen requirement in the heart in a given condition.[17] It reflects the internal myocardial work performed by the beating heart whereas the performance of the external myocardial work is represented by the stages of exercise.[17,18] A muscular organ heart needs steady supply of oxygen and nutrients for its regular functioning. If these supplies are deficient, there are all chances of heart failure to occur.[17]

In the present study, LDH was found to be significantly correlated with RPP in preeclamptic patients. The probable mechanism could be that the myocardium is working more in pregnancy induced hypertension patients, which might result in increased myocardial work stress. LDH is a biochemical expression of cardiac work status, reflecting the metabolic stress of the ventricular muscle cell. However, assessment of myocardial metabolism should be done and the link of degree of metabolism to LDH and RPP should be established.

Limitations of the study

The profiles of inflammatory and metabolic markers have not been assessed in the present study, which could have further validated the link of LDH to RPP in preeclamptic women.

CONCLUSION

Increased serum LDH in preeclamptic women might be linked to RPP, an index of myocardial work stress and an established CV risk factor. Findings of the present study also suggest that the LDH could be the biochemical expression of myocardial work stress. Therefore, increased LDH and RPP might predispose preeclamptic women to future CV-related morbidities.

Acknowledgments

It is our immense pleasure to acknowledge the subjects those who were agreed to participate in this valuable study, without whom it was not completed. Because of their consent, we the authors were successful to get some information regarding the LDH owing to preeclampsia. Authors are also thankful to senior teachers for their warm inspiration in this research work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Cnossen JS, Vollebregt KC, de Vrieze N, ter Riet G, Mol BW, Franx A, *et al*. Accuracy of mean arterial pressure and blood pressure measurements in predicting pre-eclampsia: Systematic review and meta-analysis. BMJ 2008;336:1117-20.
2. Schmidt M, Kimmig R. Pathophysiology of preeclampsia. Gynakol Geburtshilfliche Rundsch 2007;47:199-204.
3. Jan AK, Jamil M. Management of pre-eclampsia and eclampsia. JPMI 2000;14:7-19.
4. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: Current concepts. Am J Obstet Gynecol 1998;179:1359-75.
5. Kay HH, Zhu S, Tsoi S. Hypoxia and lactate production in trophoblast cells. Placenta 2007;28:854-60.
6. Pasaoglu H, Bulduk G, Ogüs E, Pasaoglu A, Onalan G. Nitric oxide, lipid peroxides, and uric acid levels in pre-eclampsia and eclampsia. Tohoku J Exp Med 2004;202:87-92.
7. Qublan HS, Amanin V, Bataineh O, Shraideh ZA, Tahat Y, Awamieh I, *et al*. Lactic dehydrogenase as a biochemical marker of adverse pregnancy outcome in severe preeclampsia. Med Sci Monit 2005;11:393-7.
8. Matsubara K, Matsubara Y, Masaharu IT. The utility of vascular dysfunction studies in the prediction and prevention of preeclampsia: A historical review. Vasc Dis Prev 2009;6:163-9.
9. Purnima Dey S, Jonal S. Evaluation of serum LDH and gamma glutamyl transferase in preeclamptic pregnancy in third trimester. Int J Res Med Sci 2013;1:365-8.
10. Norwitz ER, Hsu CD, Repke JT. Acute complications of preeclampsia. Clin Obstet Gynecol 2002;45:308-29.
11. Lopez-Jaramillo P, Casas JP, Serrano N. Preeclampsia: From epidemiology observation to molecular mechanisms. Braz J Med Biol Res 2001;34:1227-35.
12. Page NM. The endocrinology of pre-eclampsia. Clin Endocrinol (Oxf) 2002;57:413-23.
13. Krefetz RG. Enzymes. Clinical Chemistry. 4th ed. Philadelphia: Lippincott Williams and Wikins; 2000. p. 196-8.
14. Malarewicz A, Gruszka O, Szymkiewicz J, Rogala J. The usefulness of routine laboratory tests in the evaluation of sudden threat of pregnant woman and fetus in pre-eclampsia. Ginekol Pol 2006;77:276-84.
15. Bayhan G, Atamer Y, Atamer A, Yokus B, Baylan Y. Significance of changes in lipid peroxides and antioxidant enzyme activities in pregnant women with preeclampsia and eclampsia. Clin Exp Obstet Gynecol 2000;27:142-6.
16. White WB. Heart rate and the rate-pressure product as determinants of cardiovascular risk in patients with hypertension. Am J Hypertens 1999;12(2 Pt 2):50S-5S.
17. Selwyn AP, Braunwald E. Ischemic heart disease. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's Principles of Internal Medicine. 13th ed. New York: McGraw-Hill, Inc.; 1994. p. 1081-2.
18. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 15th ed. New York: McGraw Hill; 2001. p. 1402.