International Journal of Sciences & Applied Research

www.ijsar.in

Lactic acid dehydrogenase and uric acid as prognostic markers for hypertensive disorders of pregnancy

Lata Rajoria, Nenkar Sonia*, Chitra Gidwani

Department of Obstetrics and Gynecology, SMS Medical College,Jaipur, India.

Corresponding author: *Dr. Nenkar Sonia, Mahila chikitsalya PG hostel room no.26, Sanganeri gate, Jaipur, India.

Abstract

Background: Hypertensive disorders of pregnancy are one of the most common medical disorders in pregnancy with a 5-15% incidence rate in India. These are multisystem disorders and lead to a lot of cellular death. LDH is an intracellular enzyme and its level is increased in these women due to cellular death. Hyperuricemia is found to be one of the earliest laboratory manifestations of preeclampsia. It is likely to be resulted from reduced UA clearance from reduced glomerular filtration rate (GFR) and reduced tubular secretion. Its increased levels suggest serious impending damage to kidney functions. So, serum LDH levels and Uric acid can be used to assess the extent of cellular death and thereby the severity of disease.

Objectives: This study was done to compare serum levels of lactate dehydrogenase (LDH) and uric acid (UA) among women with HDP and normal pregnant women and its significance as prognostic markers in Hypertensive disorders of pregnancy.

Materials and methods: This study was a comparative observational study conducted among 140 Antenatal women in third trimester attending Antenatal OPD/Labour ward at SMS Medical College during January to December 2017. Serum levels of LDH and UA were measured using commercially available kits. Statistical analysis was done.

Observation and results: In our study, Serum levels of LDH and UA were significantly increased in women with HDP compared with controls. LDH & UA were significantly high in preeclampsia & eclampsia group. Their levels significantly positively correlated with systolic and diastolic BP.

Conclusion: Serum LDH and UA levels gradually increase as the disease severity increases. Regular monitoring of their serum levels in women with HDP may give a clue of disease severity and associated organ damage.

Keywords: Lactic acid dehydrogenase, uric acid, prognostic markers, hypertensive disorders

Introduction

Hypertensive disorders of pregnancy are one of the most complication in pregnancy and together they form one member of the deadly triad, along with haemorrhage and infection, that contribute greatly to maternal morbidity and mortality rates. These conditions, however, are largely preventable and once detected, they are treatable. Preeclampsia is a multisystem disorder that

complicates 5-15% of pregnancies in India.[1]Pre-eclampsia, is a pregnancy induced disorder characterized by hypertension and proteinuria [2,3]. Hypertension during pregnancy is diagnosed when the systolic pressure is 140 mmHg or more, and /or diastolic pressure of 90 mmHg or more, measured on two occasions at least 6 hours apart within 7 days.Preeclampsia is a multisystem disorders and lead to a lot of cellular death. LDH is an intracellular enzyme and its level is increased in these women due to cellular death.

Lactate Dehydrogenase (LDH) is mainly an intracellular enzyme. It is responsible for interconversion of pyruvate and lactate in the cells. Its levels are several times greater inside the cells than in the plasma. So its levels are increased in the scenario of increased cell leakiness, hemolysis and cell death .[4]Uric acid (UA) is an end product of purine metabolism. It is filtrated through glomeruli and almost completely reabsorbed in proximal convoluted tubules (PCT) by both active and passive carrier mediated process. It is also actively secreted into the tubules. 85% of total excreted UA is derived by tubular secretion.[5]Hyperuricemia is found to be one of the earliest laboratory manifestations of preeclampsia. It is likely to be resulted from reduced UA clearance from reduced glomerular filtration rate (GFR) and reduced tubular secretion. Its increased levels suggest serious impending damage to kidney functions[6].

So, serum LDH levels and Uric acid can be used to assess the extent of cellular death and thereby the severity of disease. Nevertheless, the accurate identification of women at risk, early diagnosis, and prompt and appropriate management may help to improve maternal outcome, and possibly perinatal outcome, as well. Currently, there are no clinically available tests that perform well in distinguishing women who will develop preeclampsia from those who will not.[7]

Aims and objectives

- The aim of the present study was to compare serum LDH levels and Uric acid levels in normal pregnant women and in women with preeclampsia and eclampsia.
- The objective of the study was to compare serum LDH and Uric acid levels in the normal pregnant women and in women with preeclampsia and eclampsia in ante-partum period and to correlate their levels with the severity of the disease.

Materials and methods

A cross sectional study was conducted taking women with hypertensive pregnancy & healthy pregnant women as cases and healthy nonpregnant women as controls. This was a prospective comparative study conducted in the department of Obstetrics and Gynaecology in SMS medical college for 1 year. 140 Pregnant women were enrolled in this study are divided into following groups:

Group 1: Healthy normal pregnant women (controls, n=80).

Group 2: Patients of preeclampsia and eclampsia(subjects). This was further subdivided into following subgroups

- Mild preeclampsia (n=32)
- Severe preeclampsia (n=32)
- Eclampsia(n=16)

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

- <600 IU/l
- 600-800IU/l
- >800 IU/l

Subjects were also divided according to the serum uric acid levels into following groups:

- <6 mg/dl
- >6 mg/dl

Inclusion criteria: Singleton pregnancy, age 18 - 30 years, pre-eclamptic women whose blood pressure was normal during first 20 weeks of gestation, no previous history of

hypertension, all the cases were in the third trimester of pregnancy. Exclusion Criteria: The women with h/o chronic hypertension, diabetes mellitus, drugs intake, smoking, alcoholism, liver, cardiac or renal diseases or any other major illness were excluded from the study.

A proforma was used to record relevant information and patient's data. Blood samples were collected. Serum was separated by centrifugation and used for estimation of serum levels of LDH and Uric Acid. Concentration of serum LDH and UA were analyzed by using analytical kits.

Results

We included 140 patients in our study, of which 40 were normal pregnant women; 40 were mild preeclampsia, 40 were severe preeclampsia and 20 cases were of eclampsia. The majority of patients in control group as well as study group belonged to the age group of 21-25 years.When compared statistically, the age wise distribution in the subjects was almost similar to the control group. No significant difference was found in POG.In the present study, the LDH levels were significantly raised with the severity of the disease (P <0.001). Serum LDH showed (882.6±182.62) significantly higher levels in eclamptic women in comparison to mild preeclampsia (420.7±72.4), severe Pre-eclampsia (574.2±88.2) and normotensive group (191.5000±23.53) (P <0.001).Table-1 shows that the mean level of systolic BP and diastolic BP, serum Uric acid, serum LDH was significantly higher in pre-eclampsia and eclampsia group compared with controls.

Table 1: Comparison of parameters among study groups.

	CONTROL (Normal pregnant women, n=80)	Mild preeclampsia (n=32)	Severe preeclampsia (n=32)	Eclampsia (n=16)
Age in years	22.83±2.22	22.6±2.22	22.42±2.22	22.03±2.38
POG(weeks)	34.36±1.69	34.03±3.46	34.01±3.23	34.77±3.4
Systolic BP	113.0±5.34	151.3±5.71	161±8.77	164±8.62
Diastolic BP	75.87±5.94	95.0±5.09	110.6±7.0	110.87±5.94
Sr. LDH(IU/l)	191.5±23.5	420.7±72.4	574.2±88.2	882.6±182.62
Sr. Uric acid (mg/dl)	5.02±0.72	5.83±0.71	6.01±0.84	6.42±0.71

Table 2: Showing association between LDH and URIC ACID

	% Patients with LDH <600IU/ml	% Patients with LDH <600IU/ml	% Patients with LDH <600IU/ml	P-value
Uric acid <6mg%	96.2	2.6	1.2	<0.001
Uric acid >6mg%	26.1	33.2	40.7	

Table 3 showing the correlation coefficient of LDH and Uric acid with SBP and DBP.

	r - value for Systolic BP	r- value for Diastolic BP
Sr. LDH	0.508	0.536
Sr. URIC ACID	0.402	0.418

As both LDH and uric acid had similar associations with the parameters assessed, a comparison was done between LDH and uric acid. As in the table 2, majority of patients (40.7%) who had LDH >800 IU/L also had high uric acid levels >6 mg% which was statistically significant. Table-3 shows that there is highly significant positive correlation of systolic & diastolic blood pressure with serum LDH and Uric acid concentrations. Hence, higher levels of LDH and Uric acid is associated with higher Systolic and Diastolic BP.Proteinuria by itself is a marker of severity of the disease and was associated with high LDH and uric acid ($p<0.001$).

Discussion

Pre-eclampsia and LDH

In the study, LDH and Uric acid has been evaluated as a biochemical marker for prognosis according to severity of preeclampsia and eclampsia. In the present study the LDH levels were significantly raised with the severity of the disease (P <=0.001).These finding was in accordance with study done by Qublan H et al[8] and Kozic J et al[9]. They concluded that serum LDH could be a useful marker for prediction of adverse outcome of pregnancy in severe preeclampsia. Serum LDH has also found to be useful predictor for birth of small for gestational age infants in preeclamptic pregnancy [10]. A group of researchers has noted significant usefulness of LDH levels in amniotic fluid at mid-trimester for prediction of fetal growth restriction[11] .In another study by Jaiswar SP et al.[12] the control arm had mean LDH levels of 278.3±119.2 IU/l (normotensives). In mild preeclampsia group, it was 400.45+145.21 IU/l, in severe preeclampsia group it was 646.95±401.64 IU/l and eclampsia group was 1648.10± 1992.29 IU/l. Jaiswer SP, et al.[12] also demonstrated a significant rise in the LDH levels with increasing severity of the disease (P <0.001). In the present study, significantly higher serum LDH level was observed in preeclamptic women than normotensive pregnant women. Literature review suggested that in the progressive endothelial dysfunction in maternal vascular system induced by toxins released from hypoxic placenta cause profound vasoconstriction affecting all organ system including liver. This hypoperfusion induced ischaemic injury to hepatic cells and other organs cause increased release of intracellular LDH to circulation.[13-20] In the present study, increased serum LDH level in preeclamptic women than control women are attributed to these facts. Moreover, the progressively increased LDH level in severe preeclampsia indicates progression of cellular injury with severity of this disorder.

Pre-eclampsia and uric acid

In our study, we found that the mean serum Uric Acid levels were significantly higher in cases when compared with controls. This finding is in accordance with the study done by Punthumapol C et al.[21]Serum uric acid levels consistently increased with increasing systolic & diastolic blood pressure.It is found that estimation of serum UA is as important as proteinuria in identifying the risk of renal involvement and fetal compromise .[22]Maternal hyperuricemia is found to be a strong predictor of maternal disease progression and fetal outcome. Thus, it can be used as useful and inexpensive marker for predicting disease severity, renal function status and fetal growth retardation in women presenting with HDP. [23]

Conclusion

Serum LDH and uric acid values were significantly high in pre-eclamptic patients depending on the severity of the disease indicating the increased cellular turnover in them. Higher LDH and uric acid levels were associated with diagnostic components of preeclampsia. Hence diagnostic and management strategies may be considered

based on S.LDH and uric acid levels and further studies on a larger sample can be done to substantiate our observations on the utility of this parameter as a diagnostic and prognostic component of Preeclampsia. Development of new management strategies based on S. LDH and uric acid levels may help in appropriate decision making thereby avoiding unwanted maternal &fetal deaths.

References

1. Mackey AP, Berg CJ, Atrash HK. Pregnancy related mortality from preeclampsia and eclampsia. Am J Obstet Gynecol. 2001;97(4):533-8.
2. Steegers EA, Von Dadelszen P, Duvekot JJ, Pijnenborg R. Preeclampsia. Lancet 2010;376:631–44.
3. Villar K, Say L, Gu¨ lmezoglu AM, Merialdi M, Lindheimer MD, Betran AP, et al. Eclampsia and pre-eclampsia: a health problem for 2000 years. In: Critchley H, MacLean AB, Poston L, Walker JJ, editors. Pre-eclampsia. London: RCOG Press; 2003. pp. 189–207.
4. Clinical enzymology and biomarkers. In: Vasudevan D, Sreekumari S, Vaidyanathan K (eds). Textbook of biochemistry, 6th edn. Jaypee Brothers, New Delhi 2011, pp146-159.
5. Kidney function tests. In: Vasudevan D, Sreekumari S, Vaidyanathan K (eds).Textbook of biochemistry, 6th edn. Jaypee Brothers, New Delhi 2011, pp314-328.
6. Pregnancy hypertension. In : Cunningham F, Lenevo K, Bloom S, Hauth J, Gilstrap L, Wenstrom K, edts. Williams Obstetrics, 23rd edn. McGraw Hill, New York 2011, pp706-728.
7. Pennington KA, Schlitt JM, Jackson DL, Schulz LC, Schust DJ. Preeclampsia: multiple approaches for a multifactorial disease. Dis Model Mech. 2012;5(1):9-18. stet Gynecol. 2001;97(4):533-8.
8. Qublan H, Ammarin V, Bataineh O, Al-Shraideh Z,Tahat Y, Awamleh I et al. Lactic dehydrogenase as a biochemical marker of adverse pregnancy outcome insevere pre-eclampsia. Med SciMonit 11(8): CR393-397, (2005).
9. Kozic J, Benton S, Hutcheson J, Payne B, Magee L, Dadelszen P. Abnormal Liver Function Tests as Predictors of Adverse Maternal Outcomes in Women With Preeclampsia. J ObstetGynaecol Can 33(10): 995–1004, (2011).
10. He S, Bremme K, Kallner A, Blombäck M. Increase concentrations of lactate dehydrogenase in pregnancy with preeclampsia: a predictor for the birth of small-for-gestational-age infants. GynecolObstet Invest 39(4):234-238, (1995).
11. Borna S, Abdollahi A, Mirzaei F. Predictive value of mid-trimester amniotic fluid high-sensitive C-reactive protein, ferritin, and lactate dehydrogenase for fetal growth restriction. Indian J PatholMicrobiol 52: 498- 500, (2009).
12. Jaiswar SP, Gupta A, Rekha S, Natu SN, Shaili Mohan. Lactic Dehydrogenase: A biochemical marker for preeclampsia-eclampsia. JOGI, 2011; 61(6):645-8.
13. Munde SM, Hazari NR, Thorat AP, Gaikwad SB, Hatolkar VS. Gamma glutamyl transferase and Lactate dehydrogenase as biochemical markers of severity of preeclampsia. Int J Med Health Pharm Biomed Eng. 2014;8(1):50-3.
14. Wagner LK. Diagnosis and management of preeclampsia. AmFam Physician. 2004;70(12): 2317-24.
15. Bera S, Gupta S, Roy SS, Kunti S, Biswas S, Ghosh D. Study of liver enzymes especially lactateinduced hypertension. Sch J App Med Sci. 2014;2(5A):1569-72.
16. Staff AC, Benton SJ, Dadelszen PV, Roberts JM, Taylor RN, Powers RWD. et

al. Redefinining preeclampsia using placenta-derived biomarkers. Hypertens. 2013;61:932-42.
17. Var A, Yildirim Y, Onur E, Kuscu NK, Uyanik BS, Goktalay K, et al. Endothelial dysfunction in preeclampsia. GynecolObstet Invest. 2003;56:221-4.
18. Petla LT, Chikkala R, Ratnakar KS, Kodati V, Sritharan V. Biomarkers for the management of pre-eclampsia in pregnant women. Indian J Med Res. 2013;138:60-7.
19. Dutta DC. Text Book of Obstetrics. 6th ed. Calcutta: New Central Book Agency (P) Ltd; 2008:666.
20. Sonagra AD, Dattatreya K, Murthy JDS. Serum LDH, ALP and Uric Acid in hypertensive disorders of pregnancy. IJPBS. 2012;2(3):201-9.
21. Punthumapol C, Kittichotpanich B. Serum calcium, magnesium and uric acid in preeclampsia and normal pregnancy. J Med Assoc Thai 91(7): 968-973, (2008).
22. Roberts J, Bodnar L, Lain K, Hubel K, Markovic N, Ness R et al. Uric acid is as important as proteinuria in identifying fetal risk in women with gestational hypertension. Hypertension 46:1263-1269, (2005).
23. Saleh F, Shukar-ud-Din S, Soomro N. Serum uric acid as predictor model for preeclampsia. Pak J Surg 26(3): 246-251, (2010).