Original Research Article

Correlation of serum lactate dehydrogenase and uric acid levels with severity parameters of preeclampsia

Mamatha Kunder[1], Deena C Mendez[1,*], Shashidhar K N[1], Munikrishna M[2]

[1]Dept. of Biochemistry, Sri Devraj Urs Medical College, Karnataka, India
[2]Dept. of Obstetrics and Gynaecology, Sri Devaraj Urs Medical College, Karnataka, India

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ABSTRACT

Introduction: Preeclampsia (PE) is a pregnancy specific disease with multisystem complications. In PE endothelial cell injury leads to alteration of various biochemical parameters. Levels of serum lactate dehydrogenase (LDH) & uric acid are known to be elevated in PE. This study was conducted to correlate these two parameters with severity parameters of PE such as blood pressure & proteinuria and to associate these parameters with severity of PE.
Aim: To compare serum LDH and uric acid levels between healthy pregnant and preeclamptic women, and to correlate their levels with severity parameters such as BP & proteinuria.
Materials and Methods: This is a case-control study conducted between normotensive pregnant (n=50) and preeclamptic women (27 mild PE & 23 severe PE). Serum uric acid was estimated by Uricase method and LDH by enzymatic method. ANOVA and Pearson's correlation tests were used to analyse the data. The results are expressed as Mean + SD and P value <0.001 was considered statistically highly significant.
Results: Serum uric acid (mild 7.53 + 1.35; severe 8.16 + 1.57) and LDH (mild 405.56 + 42.69; severe 735.22 + 108.36) levels were significantly elevated in PE group compared to controls (uric acid 4.53 + 1.30; LDH 227.68 + 58.85). The correlation analysis of LDH with systolic blood pressure (SBP) & proteinuria in severe PE group indicated a positive association. However, when uric acid was correlated, SBP associated negatively and proteinuria correlated positively.
Conclusion: LDH can be used as a biochemical marker for severity of PE as its levels correlated with other severity parameters of PE unlike that of serum uric acid.

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1. Introduction

Preeclampsia (PE) complicates 6-8% of all pregnancies and leads to both maternal and fetal complications.[1] It is a multisystem disorder and it is diagnosed on the basis of persistent hypertension and proteinuria with or without edema.

Preeclampsia is a disorder whose pathogenesis is still not clearly understood. One of the theories suggested for the cause of PE is that, endothelial dysfunction is brought about by certain factors released from ischemic placenta leading to poor uterine and placental perfusion.[2] High glucose consumption and lactate production is normally present in human placenta and glycolysis is a major

energy pathway.[3,4] Hypoxia increases metabolic pathways so, it further enhances glycolysis and increases activity of LDH which converts pyruvate to lactate.[3,5] LDH is an intracellular cytoplasmic enzyme which is highly sensitive, is of diagnostic significance in several disorders and serves as an indicator of disturbance of cellular integrity in pathological conditions. Studies have associated elevated levels of LDH in PE with complications such as abruption placenta, renal failure and Haemolysis Elevated Liver Enzymes Low Platelet count (HELLP) syndrome.[6]

The state of hypoxia in PE causes increased oxidative stress with reduced antioxidant capacity. The increased purine catabolism due to placental hypoxia result s in increased production of uric acid. This is one of the reasons for increased uric acid levels besides trophoblast breakdown and cytokine release.[7] Besides the increased production, the

* Corresponding author.
E-mail address: deenaharper@gmail.com (D. C. Mendez).

levels of uric acid are increased in PE due to decreased excretion.[8]

Though studies have been carried out to measure serum levels of LDH & uric acid so as to consider them as biochemical markers for PE, studies on the correlation of these two parameters with severity markers of PE such as blood pressure & proteinuria are minimal. This study was an attempt in this direction so as to associate these parameters with severity of PE.

2. Aims and Objectives

The aim of the present study was to compare serum LDH and uric acid levels in healthy pregnant women and women with PE, and to correlate their levels with severity parameters such as BP & proteinuria.

3. Materials and Methods

This is a case- control study carried out for a period of six months from March 2017 to September 2017 by the Department of Biochemistry, Sri Devaraj Urs Medical College (SDUMC). The subjects included in this study were pregnant women attending or admitted in the Department of Obstetrics and Gynaecology, RL Jalappa Hospital and Research Centre, the teaching hospital of SDUMC, a constituent college of Sri Devaraj Urs Academy of Higher Education and Research, Kolar, Karnataka, India. Informed written consent was obtained from all enrolled subjects and Institutional Ethical Committee (No. DMC/KLR/IEC/81/2016-17) approval was obtained.

A total of 100 subjects were included in the study of which 50 were diagnosed with PE (27 with mild PE & 23 with severe PE) and 50 age matched normotensive pregnant women served as controls. Normal pregnancy was diagnosed based upon clinical and ultrasound evaluation. PE was diagnosed by the presence of hypertension ($\geq$140 mmHg systolic BP and $\geq$90 mmHg diastolic BP) on two occasions with 4-6 hours apart, proteinuria ($\geq$ 1+ by urine dipstick method) with or without pathological oedema. PE was considered as severe based on any of the two following criteria : $\geq$ 160 mmHg systolic BP; $\geq$ 110 mmHg diastolic BP; dipstick proteinuria of 3+ or more. All the other cases were considered as mild PE. All the women included were in the age group of 19-36 years and were primigravida with over 20 weeks of gestation.

Pregnant women with pre-existing diabetes, gestational diabetes mellitus, chronic hypertension, gouty arthritis, liver diseases, renal failure, coronary heart disease and multiple pregnancies were excluded from the study.

Blood was collected from antecubital vein in redvacutainers with the total volume of 3ml and the serum was separated and stored at -70^0 C until analysis. Samples were thawed at room temperature, vortexed and centrifuged before analysis. Basic biochemical parameters were

estimated by standard methods. Serum uric acid was estimated by Uricase method[9] and LDH by enzymatic method.[10] All parameters were analysed using Dry Chemistry Vitros 250 analyser (Ortho Clinical Diagnostics).

3.1. Statistical analysis

The data were statistically analysed by SPSS software version 22 (licensed version). The results are expressed as Mean + SD. For statistical differences in means between groups ANOVA (Analysis of variance) with post-hoc test was used. Pearson's correlation coefficient was used to analyse the correlation between continuous variables. p value < 0.05was considered statistically significant and <0.001as highly significant.

4. Results

The baseline physical and biochemical characteristics of the normal, mild and severe preeclamptic subjects are depicted in Table 1.

The gestational age was in the range of 34 to 37 weeks for normal, and 31 to 36 weeks for mild and severe PE subjects. The blood pressure was elevated significantly in mild and severe cases of PE in comparison to normal and was significantly higher in severe PE compared to mild PE. The data on proteinuria is as per the criteria definedfor PE.[11]

Serum uric acid levels showed a significant rise in PE group (Mild 7.53 + 1.35; Severe 8.16 + 1.57) compared to controls (4.53 + 1.30) which was statistically highly significant. In the case of LDH, mild (405.56 + 42.69) and severe (735.22 + 108.36) preeclamptic women presented significantly higher levels when compared to normotensive pregnant women (227.68 + 58.85).

The correlation analysis of uric acid with LDH presented a positive correlation in both mild and severe PE groups. However, the correlation was not statistically significant (Figure 1).

Correlation studies of the severity parameters, SBP & proteinuria with the levels of LDH indicated a weak positive picture while the association with uric acid concentration was weakly negative in mild PE group (Figure 2). On the other hand, the correlation analysis of serum LDH with SBP & proteinuria in severe PE group indicated a positive association. When uric acid was correlated with the severity parameters, SBP associated negatively and proteinuria correlated positively (Figure 3).

5. Discussion

In this study, it was found that serum levels of LDH & uric acid were higher in preeclamptic group when compared to normotensive group. This was in accordance with the other studies conducted.[12,13] The preeclamptic group was subdivided further into mild and severe groups. When the serum LDH & uric acid levels were compared between these
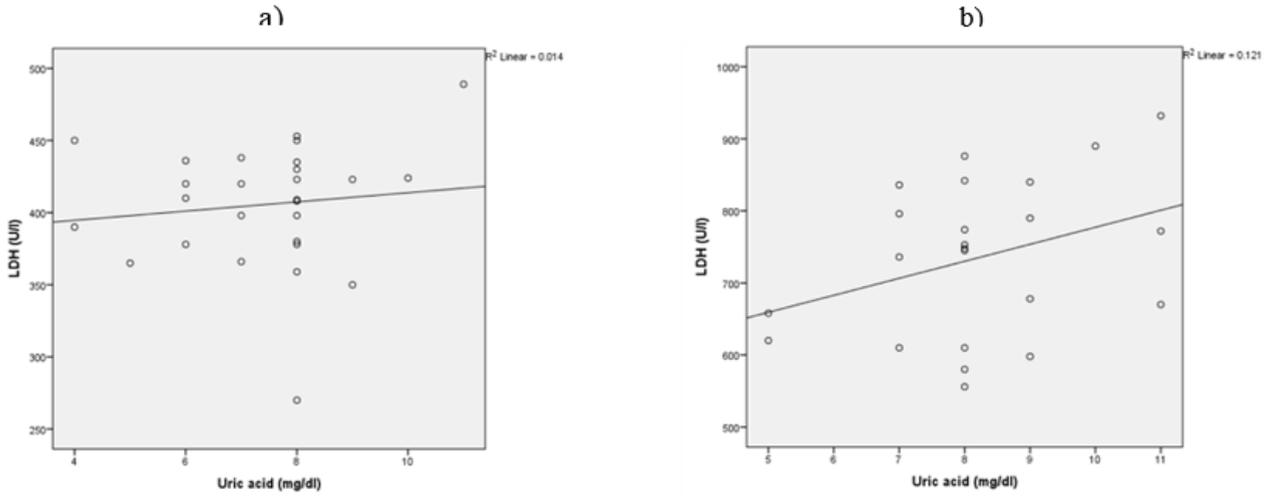
Fig. 1: Correlation of Serum uric acid with LDH concentration in a) mild (r=0.119; p=0.553)&b) severe PE groups (r=0.347; p=0.104)

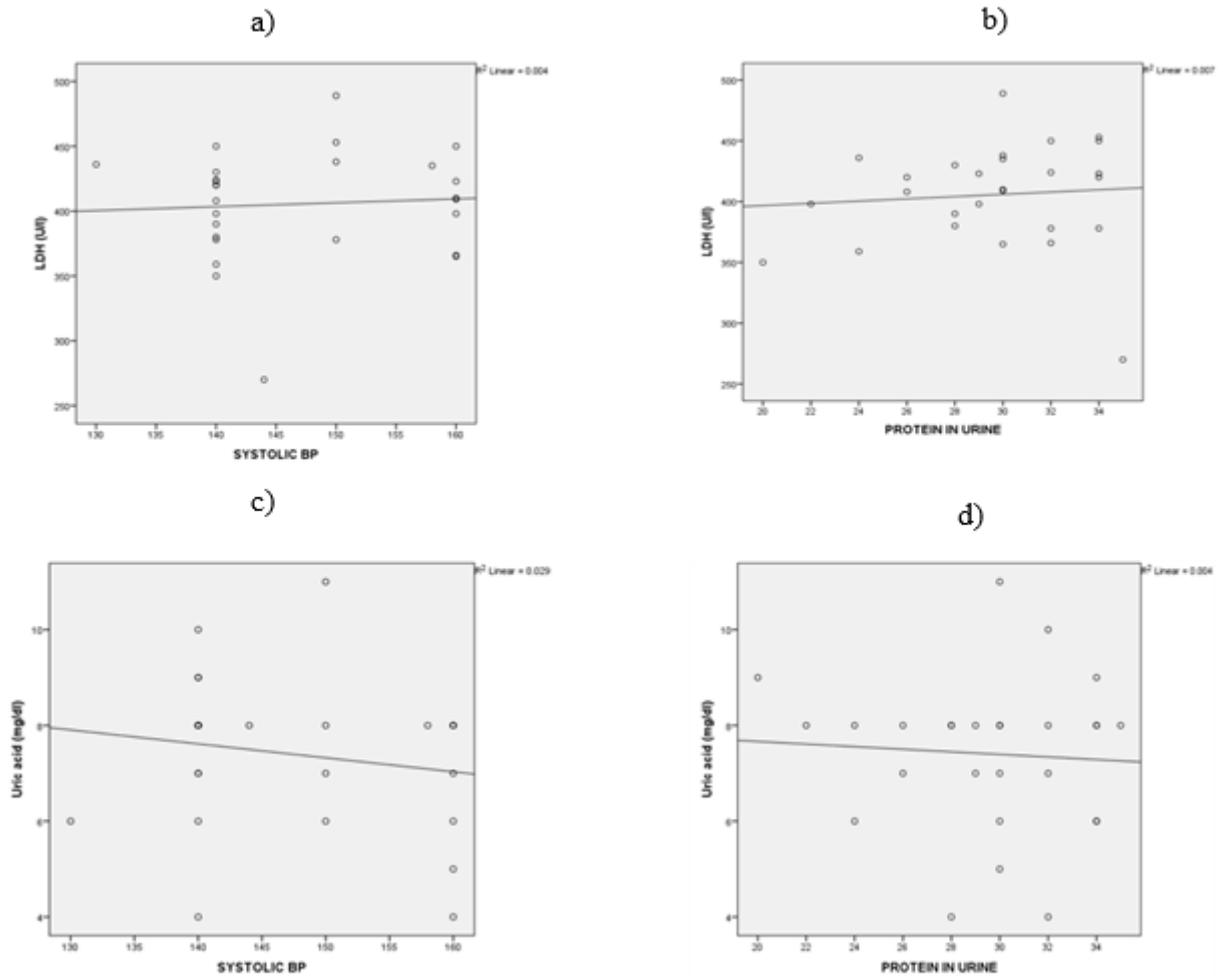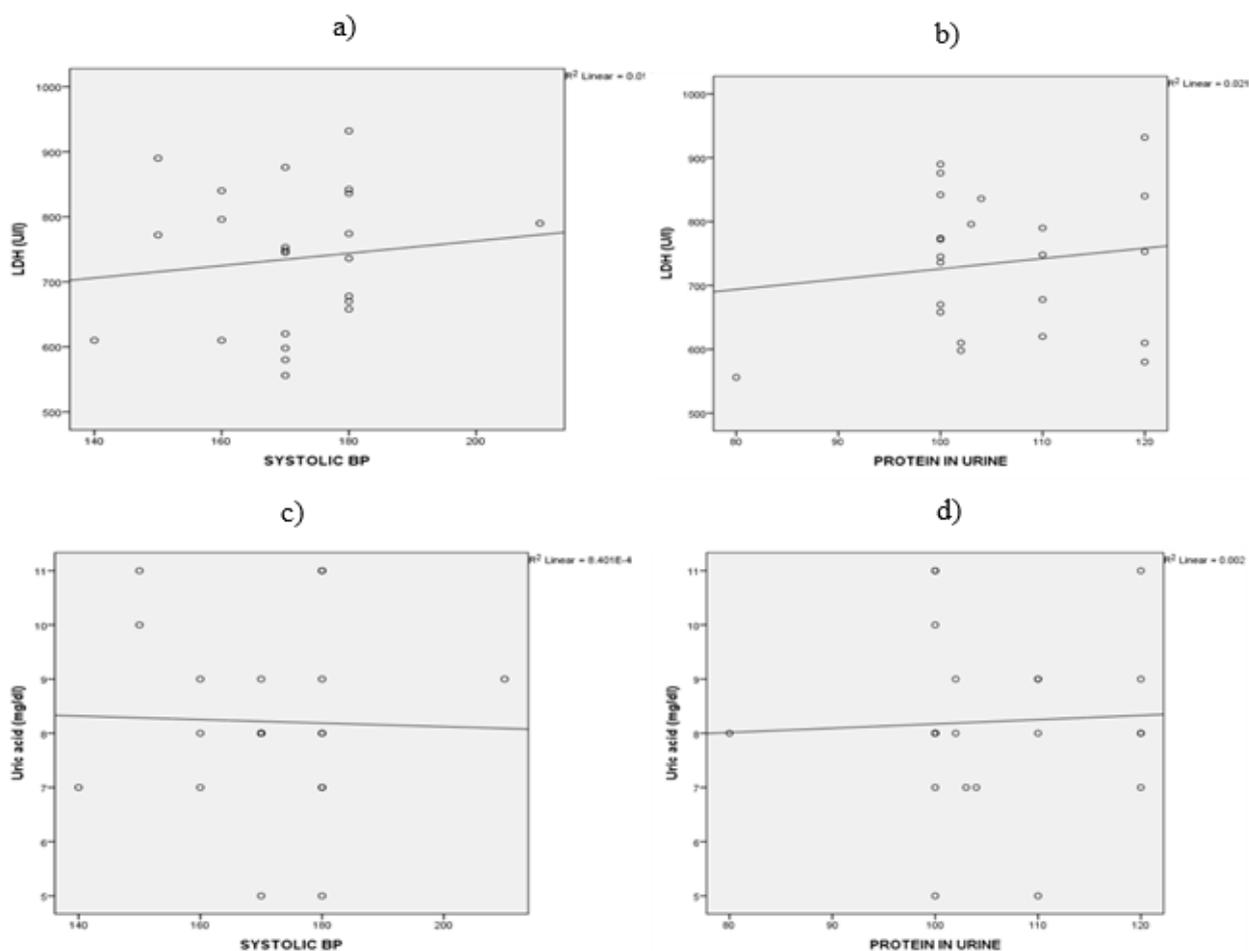**Fig. 2:** Correlation of Serum LDH with severity parameters (SBP & Proteinuria) a) r=0.066, p=0.744; b) r=0.085, p=0.674 and uric acid with severity parameters c) r=-0.170, p=0.396; d) r= -0.066, p=0.744 in mild PE group

Table 1: Basic & biochemical characteristics of study groups

Maternal age (years)	23.62+2.98	25.11+4.20	25.70+4.35	-
Gestational age (weeks)	37.18+3.05	34.70+3.37	34.96+3.11	* <0.001
Blood Pressure (mmHg)				* <0.001
Systolic (SBP)	120.28+8.70	147.11+9.35	170.87+14.11	
Diastolic (DBP)	80.20+5.88	100.22+8.84	106.52+11.12	
Cases with proteinuria (n (%)				
Traces		4 (14.8)	1(4.3)	
1+		16 (59.3)	3(13.0)	
2+		7 (25.9)	5(21.7)	
3+			14(60.9)	
Serum uric acid (mg/dL)	4.53+1.30	7.53+1.35	8.16+1.57	* <0.001
Serum LDH (U/L)	227.68+58.85	405.56+42.69	735.22+108.36	* <0.001

Fig. 3: Correlation of Serum LDH with severity parameters (SBP & Proteinuria) a) r=0.124, p=0.575; b) r=0.145, p=0.508 & uric acid with severity parameters c) r= -0.029, p=0.896; d) r=0.048, p=0.827 in severe PE group.

groups, it was found that their concentrations were almost doubled in the severe PE women as compared to normal and it was also higher in comparison to mild PE group. This suggests that these parameters are associated with the severity of the disease.

Uric acid is a product of purine degradation catalysed by the enzyme Xanthine Oxidase (XO). Poor uterine and placental perfusion in preeclampsia yields a state of hypoxia. This promotes increased XO activity resulting in increased production of uric acid through heightened maternal, fetal or placental tissue breakdown. This coupled with the production of ROS is implicated as a contributor to oxidative stress in PE.[13] Alternatively, hypovolemia which is an early change in PE, brings about increased uric acid reabsorption which in turn causes increased serum uric acid concentrations.[14]

In the pathophysiology of PE, hypoxic condition in the placenta leads to oxidative stress which in turn increases anaerobic glycolysis leading to increased LDH levels.[3] Studies have shown that LDH activity & gene expression are higher in placentas of preeclamptic women as compared to normal pregnant women.[5] It is also known that vascular endothelial dysfunction is the central pathogenic cause for PE. This dysfunction causes increased sensitivity of the vasculature to vasoactive substances which in turn leads to reduction of perfusion and loss of fluid from the intravascular compartment leading to multiorgan failure. Multiorgan dysfunction leads to excessive LDH leakage and brings about an increase in LDH activity in serum.[15–17]

Correlation studies were carried out between serum LDH & uric acid concentrations and severity markers of PE i.e. SBP and proteinuria in order to confirm the findings. A positive association of serum LDH levels with SBP & proteinuria was observed in both mild and severe PE groups. On the other hand, correlation analysis of severity parameters with serum uric acid levels presented a negative association the exception being with proteinuria in severe cases of PE. This correlation study indicates that serum LDH levels are a better marker for severity of PE as compared to serum uric acid. The findings of this study are similar to that of other studies.[18–20]

6. Conclusion

This study showed that elevated LDH can be used as a biochemical marker for severity of PE as it is correlated with the other severity parameters of PE. Though high serum uric acid levels were observed in PE group, the correlation of uric acid with severity parameters of PE were not as significant. Thus, monitoring plasma LDH levels can serve as a useful tool in the detection of patients with a high risk of developing preeclampsia.

7. Source of funding

8. Conflict of interest

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Author biography

Mamatha Kunder Assistant Professor

Deena C Mendez Assistant Professor

 Shashidhar K N Professor

Munikrishna M Professor