

Association of Serum Lactic Dehydrogenase Level with Severity of Preeclampsia

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ABSTRACT

Background & objective: : The present study was undertaken to measure the levels of lactic dehydrogenase (LDH) in normal pregnancy, mild preeclampsia and severe preeclampsia and compare them among the three groups of women.

Methods: This cross-sectional analytical study was carried out in the Department of Obstetrics & Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, between January 2014 to December 2014. A total of 120 pregnant women admitted in the above-mentioned hospital were included in the study. Pregnant women with blood pressure $\geq 140/90$ mmHg and proteinuria ≥ 0.3 gm/24 hours were included in the study as case, while pregnant women with normal blood pressure without proteinuria were included as control. Of them 40 women were mildly preeclamptic, 40 severely preeclamptic and 40 were normal pregnant women. While preeclampsia was exposure variable, the outcome variable was LDH level. Lactic Dehydrogenase (LDH) level was measured in all the study subjects. Pregnant women with diabetes, chronic renal disease, hepatic disease, systemic infection and systemic lupus erythematosus, cardiovascular disease, essential hypertension, thyroid disorder and hemorrhagic disorders were excluded.

Result: The case and control groups were almost similar with respect to age with mean age of the cases and controls being 26.1 and 27.2 years respectively ($p = 0.272$). However, preeclamptic patients were comparatively heavy than the normal pregnant women (31.4 ± 7.5 vs. 26.3 ± 3.1 kg/m²) ($p = 0.001$). The preeclamptic women exhibited significantly raised serum LDH level than their normal counterparts did (561.4 ± 301.2 vs. 270.2 ± 89.3 U/L, $p = 0.001$). More than half (52.5%) of the severe preeclamptic women had LDH ≥ 600 U/L as opposed to only 17.5% of the mild preeclamptic patients with risk of having raised LDH in severe preeclamptic patients being > 5 -fold (95% CI of OR = 1.8 – 14.5) higher than that in the mild preeclamptic patients ($p = 0.001$). The LDH level was also found to increase with increasing severity of preeclampsia ($p < 0.001$). Both systolic and diastolic blood pressures of mild and severe preeclamptic patients had significantly linear correlations with serum LDH levels. Proteinuria in preeclamptic patients were also significantly correlated with LDH level ($r = 0.636$, $p = 0.001$). Categorically both systolic and diastolic blood pressures in severe form of preeclampsia were associated with higher level of LDH (> 800 U/L) ($p = 0.003$ and $p = 0.012$ respectively).

Conclusion: The study concluded that LDH level increases in preeclampsia patients and rise of serum LDH is associated with severity of preeclampsia.

Key words: Serum lactic dehydrogenase (LDH) level, severity, preeclampsia etc.

INTRODUCTION:

Pre-eclampsia (PE) is one of the most common hypertensive disorder occurring during pregnancy. Preeclampsia is a multi-system disorder that complicates 3–8% of pregnancies in Western countries and constitutes a major source of morbidity and mortality worldwide.^{1,2} If preeclampsia

is not diagnosed or treated early it may turn into eclampsia & increases the risk of abruptio-placenta, acute renal failure (ARF) disseminated intravascular coagulation (DIC), HELLP (H: haemolysis, EL: Elevated liver enzyme and LP: Low Platelet count) syndrome, cerebral haemorrhage, intrauterine growth retardation (IUGR), preterm delivery, low

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birth weight and fetomaternal death.^{3,4} The incidence of preeclampsia in developing countries ranges from 1.8-16.7%⁵ with 16% incidence in Bangladesh being reported by Sultana et al.⁶

PE is still regarded as “a disease of theories” and its etiopathology has remained poorly understood.⁷ But current concepts include abnormal placentation, endothelial dysfunction, inflammatory activation, oxidative stress and predisposing maternal factors. The most accepted theory about etiology of PE is endothelial dysfunction. Investigations show that, poor placental perfusion due to abnormal trophoblast implantation gives rise to production of blood borne agents that causes generalized endothelial cell damage which gives rise to symptoms of hypertension, proteinuria and sudden oedema, characteristic of PE.⁸ Although the identified risk factors for preeclampsia are different, some risk factors are commonly documented like nulliparity, family history, preeclampsia in previous pregnancy, multiple gestation, and pregestational diabetes mellitus, chronic hypertension, chronic renal disease and some autoimmune diseases.⁹

Lactate dehydrogenase (LDH) is an intracellular enzyme (remains in many body tissues, especially heart, liver, kidney, skeletal muscle, brain, blood cells, and lungs) which converts lactic acid to pyruvic acid and its elevated level indicates cellular death and leakage of enzyme from the cell.¹⁰ Increased levels of LDH were found in association with preeclampsia in a limited number of studies.¹¹⁻¹³ The normal value of LGH ranges from 78 – 433 U/l in first trimester, 80-447 U/l in second trimester and 82-524 U/l in third trimester of pregnancy.¹⁴ The enzyme is most often measured to evaluate the presence of tissue damage. Acute clinical symptoms that endanger fetal life in preeclampsia correlate with distinct activity of AST and LDH.¹⁵ Serum LDH levels can therefore, be used to assess the extent of cellular death in women with preeclampsia. LDH is a useful biochemical marker that reflects the severity of the occurrence of preeclampsia,¹⁰ which in turn, may help deciding further management strategies to improve maternal and fetal outcome.¹⁶

Jaiswar and colleagues¹⁶ studied the association of severity of preeclampsia with serum LDH levels and

found that the enzyme was significantly elevated in women with severe disease. Higher LDH levels had significant correlation with high blood pressure as well as poor maternal and perinatal outcome. The authors concluded that high serum LDH levels correlate well with the severity of the disease and poor outcomes in patients of preeclampsia. But no study has yet been done in the context of our population. Faced with this context, the present study intended to find the association between severity of preeclampsia and serum LDH levels carries utmost significance, for the findings derived from the study would better help in managing the patients of preeclampsia.

METHODS:

This cross-sectional analytical study was conducted in the outpatient and inpatient Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka over a period 1 year from January to December 2014. Pregnant women with preeclampsia (case) and normotensive healthy pregnant women (control) were enrolled in this study. Pregnant women with blood pressure $\geq 140/90$ mmHg and proteinuria ≥ 0.3 gm/24 hours were included in the study as case, while pregnant women with normal blood pressure without proteinuria were included as control. The cases were again subdivided into mild preeclampsia (pregnant women with blood pressure $\geq 140/90$ mmHg to $< 160/110$ mmHg and proteinuria ≥ 0.3 gm/24 hours on 2 occasions at least 6 hours apart on bed rest) and severe preeclampsia (systolic blood pressure of ≥ 160 mmHg or diastolic blood pressure of ≥ 110 mmHg on 2 occasions at least 6 hours apart on bed rest). However, patients with diabetes, chronic renal disease, hepatic disease, systemic infection, cardiovascular disease, essential hypertension, systemic lupus erythematosus, hemorrhagic disorders & thyroid disorder were excluded from the study. A total of 120 pregnant women-80 cases and 40 controls were consecutively included in the study.

Having institutional approval (from the Institutional Review Board of BSMMU, Dhaka) obtained and consent from the patients, data were collected by history taking, clinical examination and laboratory

investigations of the subjects using a semi-structured questionnaire containing the key variables of interest. While preeclampsia was exposure variable, the outcome variable was LDH level. A blood sample of 10 ml was collected from the antecubital vein (in an arm without intravenous infusion ongoing) each patient into a heparinized syringe for evaluation of LDH & haematological investigations. The collected blood was centrifuged for 10 minutes at 3000 rpm and was sent for test instantly. The blood pressure was measured on the right arm, with the patient lying on her side at 45° to the horizontal. In the outpatient setting, sitting posture was preferred to measure blood pressure. 24-hrs urine protein was measured by quantitative method. LDH concentration was measured by spectrophotometric kinetic method using Flex reagent cartridge on the dimension clinical chemistry system.

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences), version 16.0. Descriptive statistics, such as frequency and corresponding percentage, was used to analyze qualitative data and mean \pm SD (standard deviation) for quantitative data. Data presented on continuous scale were compared between groups using Unpaired t-Test and that on categorical scale were compared between groups using Chi-square (χ^2) Test. Pearson's correlation test was used to test the relationship between two continuous variables of interest. The level of significance was set at 5% and p-value $<$ 0.05 was considered as statistically significant.

RESULTS:

There was no significant difference between case and control groups with respect to age with mean age of the cases and controls being 26.1 and 27.2 years respectively (p=0.272). However, preeclamptic patients were significantly heavier than the normal pregnant women (31.4 \pm 7.5 vs. 26.3 \pm 3.1 kg/m²) (p=0.001) (Table I). The mean LDH level of preeclamptic women was staggeringly high compared to that in normal pregnant women (561.4 \pm 301.2 vs. 270.2 \pm 89.3 U/L, p=0.001) (Table II). Over half (52.5%) of the severe preeclamptic patients exhibited

LDH \geq 600 U/L as compared to only 17.5% of the mild preeclamptic patients. The risk of having elevated LDH in severe preeclamptic patients is $>$ 5-fold (95% CI of OR=1.8–14.5) higher than that in mild preeclamptic patients (p=0.001). The mean LDH in severe preeclamptic patients was also significantly higher (698.4 \pm 348.3 U/L) than that in mild preeclamptic patients (424.5 \pm 154.9 U/L) (Table III).

Table I: Distribution of the patients according to age and BMI

Demographic variables	Preeclampsia (n = 80)	Normal pregnancy (n = 40)	t-value	p-value
Age (years)	26.1 \pm 4.6	27.2 \pm 5.3	1.10	0.272
BMI (kg/m ²)	31.4 \pm 7.5	26.3 \pm 3.1	4.07	0.001

Data were analyzed using **Unpaired t-Test** and were presented as **mean \pm SD**.

Table II: Distribution of the patients according to LDH

Outcome variable	Preeclampsia (n = 80)	Normal pregnancy (n = 40)	t-value	p-value
LDH (U/L)	561.4 \pm 301.2	270.2 \pm 89.3	5.96	0.001

Data were analyzed using **Unpaired t-Test** and were presented as **mean \pm SD**.

Table III: Distribution of the study patients according to LDH level with preeclampsia

LDH (U/L)	Severe preeclampsia (n = 40)	Mild preeclampsia (n = 40)	OR (95%CI of OR)	p-value
\geq 600	21(52.5)	7(17.5)	5.2(1.8-14.5)	0.001
$<$ 600	19(47.5)	33(82.5)		

Data were analyzed using **Chi-square (χ^2) Test**; Figures in the parentheses denote corresponding %.

Correlation between blood pressures and LDH level:

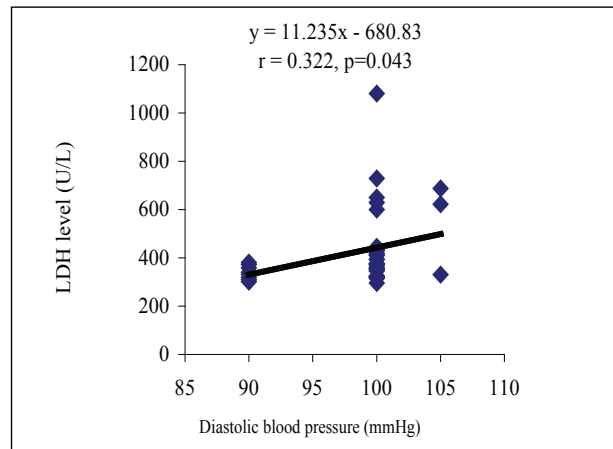
As systolic blood pressures of mild and severe preeclamptic patients were correlated with their serum LDH using Pearson's correlation test, significantly linear correlations were found between the variables of interest (r=0.360, p=0.022 and r=0.447, p=0.004 respectively) (Fig. 1-A & 1-B). Likewise, when diastolic blood pressure (DBP) of mild and severe preeclamptic patients were correlated with LDH level they were found to bear significantly linear correlations with LDH levels (r=0.322, p=0.043 and r=0.412, p=0.008 respectively) (Fig. 2-A & 2-B).

Correlation between urine protein and LDH level

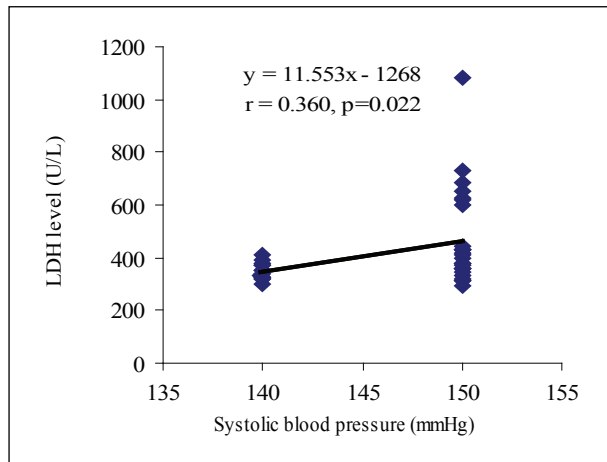
Pearson’s correlation statistics showed that urine protein in preeclamptic patients bears significantly liner correlation with LDH level ($r=0.636$, $p=0.001$) (Figure 3).

Association between blood pressure and LDH levels:

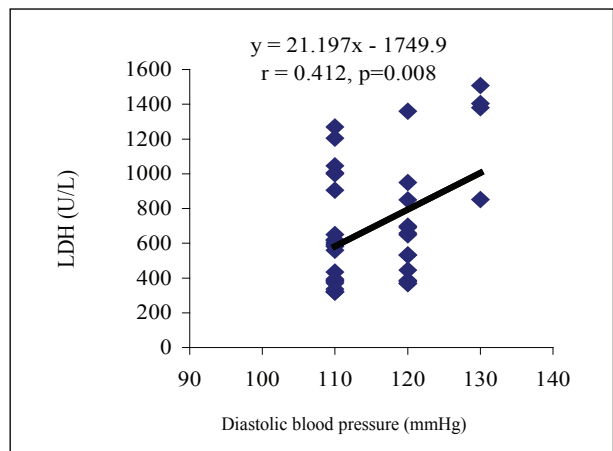
As blood pressure data were categorized according to severity and LDH data were stratified into three categories (from as low as < 600 U/L to as high as >800 U/L) and crosstab analysis was done between the two variables, a significant association was observed between blood pressure and LDH level with higher the systolic and diastolic blood pressures, higher the LDH level ($p=0.003$ and $p=0.012$ respectively) (Table V).



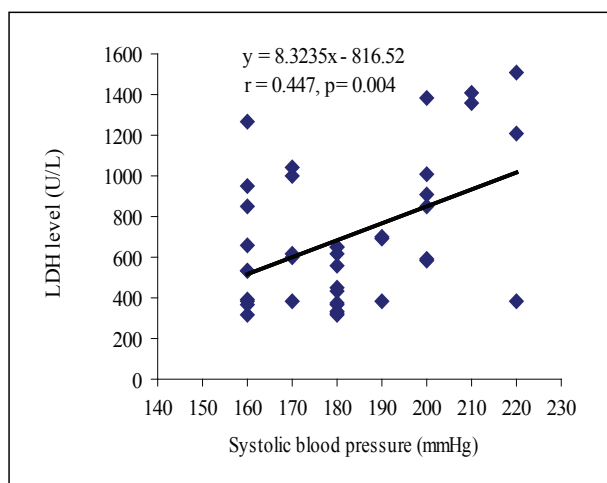
Significant positive correlation ($r = 0.322$; $p = 0.043$) in mild preeclampsia (Fig. 2-A)



Significant positive correlation ($r = 0.360$; $p = 0.022$) in mild preeclampsia (Fig.1-A)



Significant positive correlation ($r = 0.412$; $p = 0.008$) in severe preeclampsia (Fig. 2-B)



Significant positive correlation ($r = 0.447$; $p = 0.004$) in severe preeclampsia (Fig. 1-B)

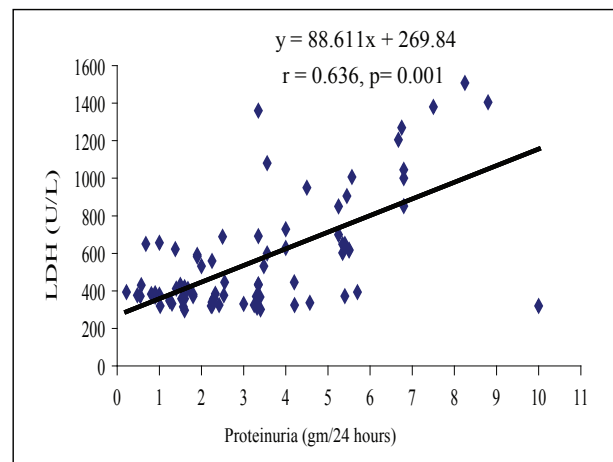


Figure 3: The scatter diagram shows significant positive correlation ($r = 0.636$, $p = 0.001$) between proteinuria and LDH level.

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Table V: Association between blood pressure with LDH levels in various groups

Blood pressure	LDH level			p-value
	< 600 U/L (n=52)	600-800 U/L (n=14)	> 800 U/L (n=14)	
Systolic blood pressure				
< 140 mmHg	0(0.0)	0(0.0)	0(0.0)	0.003s
140-160 mmHg	39(75.0)	7(50.0)	4(28.6)	
> 160 mmHg	13(25.0)	7(50.0)	10(71.4)	
Diastolic blood pressure				
< 90 mmHg	0(0.0)	0(0.0)	0(0.0)	0.012s
90-110 mmHg	45(86.5)	10(71.4)	7(50.0)	
> 110 mmHg	7(13.5)	4(28.6)	7(50.0)	

Data were analyzed using **Chi-square (χ^2) Test** and were presented as **n(%)**.

DISCUSSION:

This cross-sectional analytical study was carried out to measure LDH level in normal pregnant women and in pregnant women with preeclampsia and also to compare LDH level between normal pregnant women and women with mild and severe preeclampsia. The result of the study demonstrated that there was no significant difference between case and control groups in terms of age ($p = 0.272$). Begum and colleagues¹⁷ showed that approximately 63% of the cases (preeclampsia) and 75% controls were in the age range 20-30 years with mean ages of former and latter cohorts being 23.7 and 24.2 years respectively ($p > 0.05$). Similarly, several studies¹⁸⁻²¹ observed similar age range in mild preeclampsia, severe preeclampsia and in normal pregnant women. In the present study preeclamptic patients were much heavier than the normal pregnant women ($p = 0.001$). The BMI > 30 kg/m² could be one of the factors that may predispose pregnant women to the increasing risk of preeclampsia.²¹⁻²³ So, it should be considered as a modifiable risk factor and preventing programs should target heavier women to reduce their weight to normal range.

The preeclamptic women demonstrated significantly higher serum LDH level compared to their normal counterparts. Over half (52.5%) of the severe preeclamptic women exhibited LDH ≥ 600 U/L as

compared to only 17.5% of the mild preeclamptic patients with risk of having raised LDH in severe preeclamptic patients being > 5 -fold (95% CI of OR = 1.8-14.5) higher than that in the mild preeclamptic patients ($p = 0.001$), bearing consistency with other studies.^{10,16,18,23} Our study also demonstrated that the level of LDH increases with increasing severity of the disease indicating that LDH level goes up as the preeclampsia turns severe which is also consistent with the findings of several other studies.^{10,16,23}

Both systolic and diastolic blood pressures of mild and severe preeclamptic patients were found to bear significantly linear correlations with serum LDH levels. Proteinuria in preeclamptic patients also showed a significantly linear correlation with LDH level ($r = 0.636$, $p = 0.001$). Categorically both systolic and diastolic blood pressures in severe preeclampsia were associated with higher level of LDH (> 800 U/L) ($p = 0.003$ and $p = 0.012$ respectively). Other studies reported highly significant positive correlation of systolic & diastolic blood pressures with serum LDH.^{16,24}

CONCLUSION:

The study concluded that LDH level increases in pregnant women with preeclampsia and rise of serum LDH is associated with severity of preeclampsia. Serum LDH level linearly increases corresponding to the increase in blood pressure and proteinuria in preeclamptic patients.

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