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# Role of Maternal Serum Lactate Dehydrogenase as a Biochemical Marker in Pre-Eclampsia

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***Abstract:***
***Background:*** *Pre-eclampsia is a syndrome affecting all organs and has both maternal and foetal complications. Maternal multi organ vascular endothelial damage in pre-eclampsia leads to excessive leakage of lactate dehydrogenase into the maternal serum.*
***Objective:*** *(1) Role of serum lactate dehydrogenase as a biochemical marker in pre-eclampsia so as to decrease maternal morbidity and mortality. (2) Correlation of the levels of serum lactate dehydrogenase with Severity And Complications Of Pre-Eclampsia.*
***Methodology:*** *This observational study was conducted at Lalla Ded Hospital Srinagar over a period of 18 months in which 100 patients were included in study group and 100 patients were included in control group. All patients were subjected to detailed and comprehensive history, physical examination, routine investigations and estimation of serum lactate dehydrogenase levels.*
***Statistical Analysis****: Data was described as mean±standard deviation and percentages. The parametric data was analysed by student's t-test whereas Mann-Whitney 'U' test and Chi square tests were applied for non-parametric data. All p-values of less than 0.05 were considered significant. Softwares used were Statistical Package for Social Sciences (SPSS), Minitab and Microsoft Excel.*
***Results:*** *Among study group 60% were in age group(25-29 years),28% in age group (20-24years), 12% in age group (30-34years) and mean gestational age was 32.5± 2.0 weeks with max (36 weeks) and min (28 weeks). BMI in study group was (27.8± 1.6 kg/m2). Kidney function test in study group :S.urea-28.6±7.6mg/dl(14,61) S.cretinine-0.8±0.5mg/dl(0.3,5).Mean±SD 24 hours urinary proteins in the study group was 0.99±1.76 g/day while as in the control group it was 0.16±0.10 g/day. In study group, 28 patients had raised serum lactate dehydrogenase levels, 65 patients had normal serum lactate dehydrogenase levels and 7 patients had low serum lactate dehydrogenase levels and in the control group, only 2 patients had raised serum lactate dehydrogenase levels, 84 patients had normal serum LDH levels and 14 patients had low serum LDH levels. Mean Serum lactate dehydrogenase level in mild pre-eclampsia was 347.6IU/L and in severe pre-eclampsia 564.7IU/L and that associated with warning symptoms 766.1IU/L.*
***Keywords:*** *Pre-eclampsia, Serum lactate dehydrogenase, Hypertension*
***Abbreviation:*** *LDH- lactate dehydrogenase, BP- blood pressure, HELLP- haemolysis, elevated liver enzymes, low platelet count, BMI- body mass index, NADH-nicotineamide adenine dinucleotide reduced form, $NAD^+$ nicotineamide adenine dinucleotide oxidised form.*

## I. Introduction

Pre-eclampsia is a pregnancy specific syndrome characterized by new onset hypertension and proteinuria occurring usually after 20 weeks of gestation [1]. It is defined as the blood pressure of ≥ 140/90mmHg in a women without a previous history of arterial hypertension along with presence of proteinuria ≥ 300mg in 24 hours urine collection or ≥1+ by qualitative urine examination after 20 weeks of pregnancy [2]. Pre-eclampsia is classified into mild and severe.

Pre-eclampsia is a syndrome, which affects virtually all maternal organ systems[3]. The dreadful complications associated with pre-eclampsia include eclampia ,HELLP (haemolysis ,elevated liver enzymes and low platelets count)syndrome, pulmonary oedema, acute renal failure, abruptio placentae and intracranial bleeding[4].Risk factors associated with pre-eclampsia include nulliparity, previous history of pre-eclampsia, chronic renal disease, chronic hypertension, antiphospholipid antibody syndrome, diabetes mellitus, twin gestation, hydatidiform mole ,age more than 40 years, high body mass index and African-American race[5]. As

pre-eclampsia is a multisystem disorder with different clinical characteristics ;prevention, diagnosis and therapy of this disease requires a close interdisciplinary cooperation[6].The etiology of pre-eclampsia is unknown but is thought to be related to hypoxia in the placenta[7].The factors currently considered to be important include abnormal placental implantation, maternal immunological tolerance, cardiovascular, genetic, nutritional and environmental factors[8].The general consensus is that pre-eclampsia is an endothelial cell disorder resulting in mild to moderate microangiopathy of target organs such as brain, liver, kidney and placenta[9].Several circulating markers of endothelial cell injury have been shown to be elevated in women who develop pre-eclampsia before they become symptomatic and these include endothelins, cellular fibronectin, plasminogen activator inhibitor-1 and altered prostacyclin/thromboxane profile[10]. There is an increasing evidence that altered endothelial cell function plays an important role in the pathogenesis of pre-eclampsia [11].The multi organ dysfunction in severe pre-eclampsia caused by vascular endothelial damage including maternal liver, kidney, lungs, nervous system, blood and coagulation system leads to excessive leakage of lactate dehydrogenase and its elevated levels in serum.

It would be apparent from above that for reduction of overall maternal and foetal morbidity and mortality , easy and reliable methods to diagnose pre-eclampsia and if possible to grade the severity is essential. Battery of laboratory tests have been used over the years which include urinary proteins, protein/creatinine ratio, serum uric acid, serum creatinine, platelet count, prothrombin time, activated partial thromboplastin time, fibrinogen time, peripheral blood smear, indirect bilirubin level, serum aspartate aminotransferase, alanine aminotransferase and serum lactate dehydrogenase [12,13].

Small quantity of lactate dehydrogenase is always present in plasma. Following tissue damage, the damaged tissue releases lactate dehydrogenase into blood. It is abundant in red blood cells and can function as a marker for haemolysis[14].Acute clinical symptoms that endangers life in pre-eclampsia correlates with the distinct activity of the lactate dehydrogenase[15].Elevated lactate dehydrogenase levels in pre-eclampsia indicates both tissue damage and haemolysis[14,11]. It reflects severity as well as occurrence of complications in pre-eclampsia[16,17].Pre-eclamptic patients with higher levels of lactate dehydrogenase are at high risk of developing subsequent complications with poor maternal and foetal outcome. This shows that lactate dehydrogenase is a useful and reliable biochemical marker in pre-eclampsia. Identification of these high risk patients with elevated lactate dehydrogenase levels, their close monitoring and prompt management may prevent these complications with subsequent decrease in maternal and foetal morbidity and mortality[17].

This study was conducted to evaluate serum lactate dehydrogenase levels in pre-eclamptic patients and normotensive pregnant women so as to know its value as a biochemical marker in pre-eclampsia. Its role in early detection of severity and complications in pre-eclampsia was also studied so as to decrease maternal and foetal morbidity and mortality.

## II. Objectives

- Role of serum lactate dehydrogenase as a biochemical marker in pre-eclampsia so as to decrease maternal morbidity and mortality.
- Correlation of the levels of serum lactate dehydogenase with severity and complications of pre-eclampsia.

This observational study was conducted for a term of 18 months in the Department of Gynaecology and Obstetrics ,Lalla Ded Hospital, Government Medical College, Srinagar. This study was conducted in two groups:

Study Group: It included 100 patients who presented with blood pressure constantly ≥ 140/90mmHg and proteinuria ≥300mg/24hours with no urinary tract infection and no previous history of hypertension.

Control Group: It included 100 normal pregnant women (non-hypertensive, non-diabetic of matching age and gestational age).

Inclusion Criteria: Primigravida, Singleton pregnancy, age range between 20-35 years, third trimester pregnancies, all patients with blood pressure ≥ 140/90mmHg or rise of 30 mmHg systolic and 15 mmHg diastolic pressure on at least two occasion 6 hours apart, ≥300mg proteinuria in 24 hours were included in the study.

Exclusion Criteria: All pregnancies with urinary tract infections, previous history of hypertension, history of chronic renal disease or pathological vaginal discharge, molar pregnancies, chronic hypertension and proteinuria before conception or 20 weeks of gestation were excluded from the study.

After an informed consent, detailed and comprehensive history, physical examination (general and systemic), routine investigations (Haemoglobin, Bleeding time, Clotting time, Blood grouping, Platelet count, Blood sugar, Kidney function test, Liver function test, Urine analysis, Ultrasonography, Electrocardiography) were performed.Then samples were collected for the estimation of serum Lactate dehydrogenase levels.

Estimation of Serum Lactate Dehydrogenase Levels:

This method is based on the reduction of pyruvate to lactate in the presence of NADH (nicotineamide adenine dinucleotide, reduced form) by the action of lactate dehydrogenase enzyme. Pyruvate that remains unchanged reacts with 2,4-dinitrophenylhyrazone, which was determined calorimetrically in an alkaline medium.

**Principle Of This Method:**

NADH and pyruvate are converted into lactate and NAD+

Pyruvate + NADH + $H^+$ → Lactate +$NAD^+$

The rate of NADH decrease is directly proportional to the lactate dehydrogenase activity. The rate of formed $NAD^+$ is determined by the decrease in the asorbance.

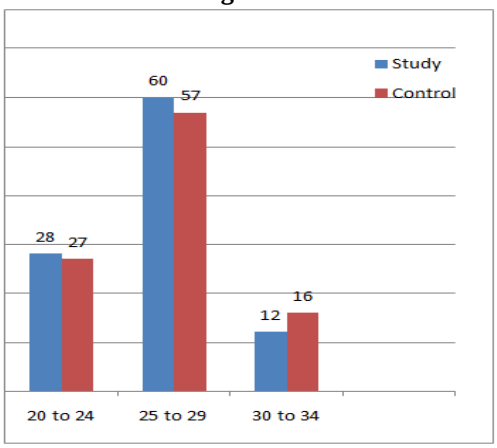
Normal serum lactate dehydrogenase level ranges from 240 to 480 IU/L. Hence, any significant difference in the serum lactate dehydrogenase levels of cases and controls were evaluated.

**Statistical Analysis**

Data was described as mean±standard deviation and percentages. The parametric data was analysed by student's t-test whereas Mann-Whitney 'U' test and Chi square tests were applied for non-parametric data. All p-values of less than 0.05 were considered significant. Softwares used were Statistical Package for Social Sciences (SPSS), Minitab and Microsoft Excel.

## III. Results

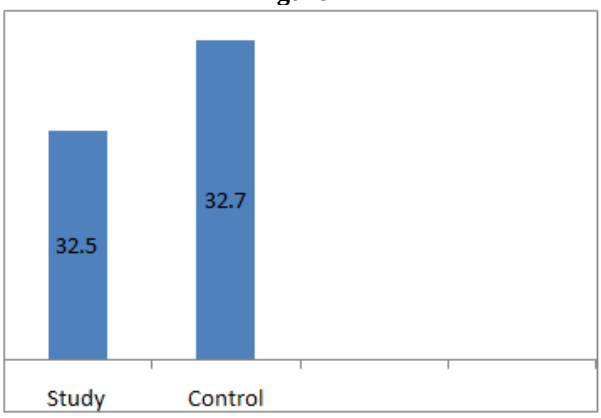
**Figure 1**




**Maternal Age (years) of the studied subjects**

Maximum number of patients , that is 60% in the study group and 57% in the control group were in the age group of 25-29years. Among the study group 28% patients were in the age group of20-24 years and 12% were in the age group of 30-34 years. In the control group, 27%women were in the age group of 20-24 years and 16% women belonged to the age group of 30-34 years. Mean age in the study group was 26.2±2.8 years and in the control group was 26.0±2.9 years. This difference was not statistically significant.

**Figure 2**




**Gestational Age (weeks) of the Studied Subjects**

Mean gestational age in the study group was 32.5±2.0 weeks with a maximum gestational age of 36 weeks and minimum of 28 weeks. In the control group mean gestational age was 32.7±2.0 weeks with a maximum gestational age being 36 weeks and minimum gestational age being 30 weeks. This difference was not statistically significant.

**Table 1**

| **Body mass index (kg/m2) of Studied subjects** | | |
|---|---|---|
| Group | mean±SD | P value |
| Study | 27.8±1.6(24.3,31.3) | 0.000(Sig) |
| Control | 25.5±2.2 (20.8,31.0) | |

The mean body mass index in the study group was 27.8± 1.6kg/m2 and in the control group was 25.5± 2.2kg/m2.So the mean body mass index in the study group was significantly higher than the control group. The results were statistically significant (p value <0.001).

**Table 2**

| **Haematological parameters of the Studied Subjects** | | | |
|---|---|---|---|
| | Group | mean±SD | P value |
| Haemoglobin (gm%) | Study | 9.9±1.1(7.1,11.9) | 0.000 (sig) |
| | Control | 9.3±1.2(7.2,12.5) | |
| Platelets (lac/mm3) | Study | 1.4±0.4(0.68,2.4) | 0.018 (sig) |
| | Control | 1.6±0.5 (0.7,3.5) | |

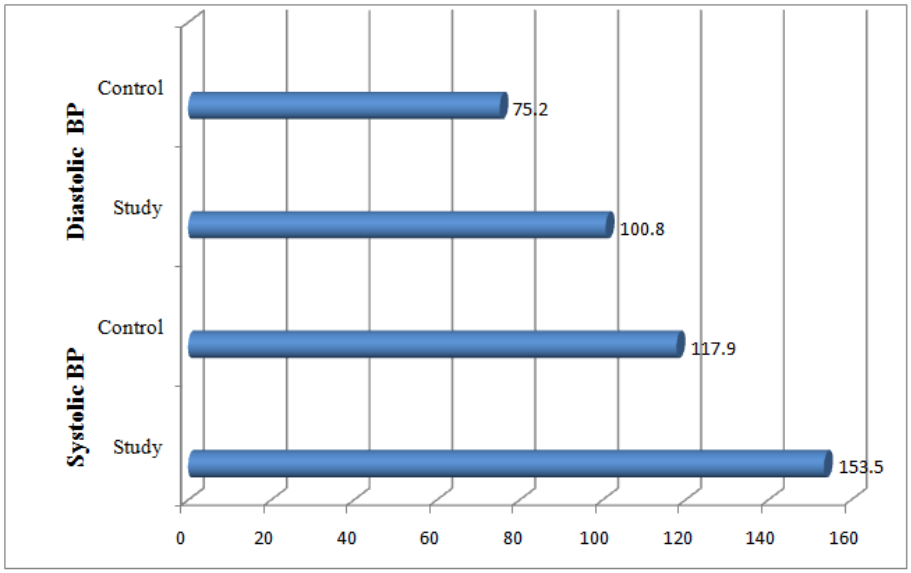
Mean haemoglobin level in the study group was significantly higher than the control group. The mean platelet count in the study group was lower than the control group and this difference was statistically significant.

**Table 3**

| **Kidney function tests in the studied subjects** | | | |
|---|---|---|---|
| | STUDY | CONTROL | P value |
| S.Urea (mg/dl) | 28.6±7.6(14.61) | 15.6±3.2(10,20) | 0.000 |
| S.Creatinine (mg/dl) | 0.8±0.5(0.3,5) | 0.6±0.2(0.3,0.9) | 0.012 |

Mean serum urea concentration in the study group was significantly higher than the control group with a p value of <0.001. The same pattern was seen in serum creatinine concentration which was higher in the study group than that in the control group. These results were statistically significant.

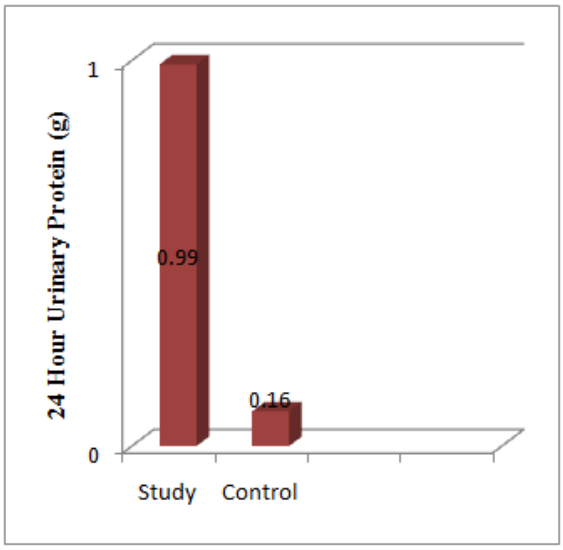
**Figure 3**




**Blood Pressure of Studied Subjects**

Mean blood pressure (systolic and diastolic pressure) in study group was significantly higher than the control group with a p value of <0.001.

**Figure 4**




**24 Hours Urinary Protein (gms) in the Studied Subjects**

Mean±SD 24 hours urinary proteins in the study group was 0.99±1.76g/day while as in the control group was 0.16±0.10 g/day. These results were found to be statistically significant with a p value of <0.001

**Table 4**

| **Liver function tests of studied subjects** | | | |
|---|---|---|---|
| | **Study** | **Control** | **P Value** |
| Sr. Bilirubin | 0.8±0.3(0.2,1.4) | 0.6±0.2(0.2,0.9) | 0.000(Sig) |
| AST (U/L) | 30±13.3(10,62) | 23.1±6.2(11,33) | 0.000(Sig) |
| ALT (U/L) | 27.1±8.1(10,39) | 21.3±5.8(10,30) | 0.000(Sig) |

Mean serum bilirubin concentration in the study group was significantly higher than the control group with a p value of >0.001.Mean ±SD AST and ALT level in the study group was higher than that in the control group and the difference was statistically significant with a p value of < 0.001.

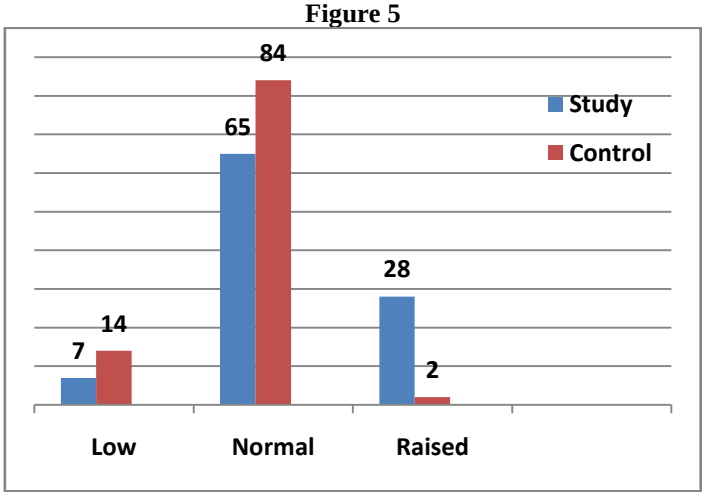
**Table 5**

| Serum Lactate Dehydrogenase Levels (IU/L)in Pre-eclampsia | | | | | | |
|---|---|---|---|---|---|---|
| | | Min | Max | Mean | SD | P value |
| Pre-eclampsia | Mild | 230.9 | 584.6 | 347.6 | 99.1 | 0.000 |
| | severe | 285.1 | 906.6 | 564.7 | 162.5 | (Sig) |
| Warning Symptoms and Signs | Present | 482.6 | 906.6 | 766.1 | 175.5 | 0.000 |
| | Absent | 230.9 | 689.4 | 375.9 | 116.4 | (Sig) |

**Table 5** The mean serum lactate dehydrogenase level in mild pre-eclampsia was higher than severe pre-eclampsia with a p value of <0.001. Serum lactate dehydrogenase level in those patients of severe pre-eclampsia having associated warning symptoms and signs was significantly higher than those patients of severe pre-eclampsia without warning symptoms and signs with a p value of < 0.001.

The mean serum lactate dehydrogenase level in mild pre-eclampsia was higher than severe pre-eclampsia with a p value of <0.001. Serum lactate dehydrogenase level in those patients of severe pre-eclampsia having associated warning symptoms and signs was significantly higher than those patients of severe pre-eclampsia without warning symptoms and signs with a p value of <0.001.

**Figure 5**




**Serum Lactate Dehydrogenase Levels of the Studied Subjects**

In the study group of 100 patients, 28 patients had raised serum lactate dehydrogenase levels, 65 patients had normal serum lactate dehydrogenase levels and 7 patients had low serum lactate dehydrogenase levels. In the control group, out of 100 patients , only 2 patients had raised serum lactate dehydrogenase levels, 84 patients had normal serum LDH levels and 14 patients had low serum LDH levels. The mean serum LDH levels was significantly higher in the study group than the control group with a p value of < 0.001.

## IV. Discussion

Pre-eclampsia is a specific disease of pregnancy with multisystem complications[17]. Altered endothelial cell function plays an important role in pathogenesis of pre-eclampsia. Lactate dehydrogenase is one of the important markers of tissue damage. In the present study role of LDH as a biochemical marker in pre-eclampsia has been studied.

The results showed that there was no statistical difference in age and gestational age in our study and this was similar to observations made by other studies [11].

Mean body mass index (BMI) among the pre-eclamptic patients was 27.8±1.6 kg/m2 and among normotensive pregnant women was 25.5±2.2 kg/m2 in our study which was statistically significant. The mean BMI of pre-eclamptic patients was significantly higher than normotensive pregnant women and this observation was comparable to study done by Rubina Aziz et al 2008 [11]. In our study, among the cases mean systolic and mean diastolic BP was 153.5±11.3 mmHg and 100.8±10.2mmHg respectively. In controls mean systolic BP and mean diastolic BP was 117.9±10.1 mmHg and 75.2±6.4mmHg respectively. So the mean BP of pre-eclamptic patients was significantly higher than the normotensive pregnant women. 24 hour urinary proteins in pre-eclamptic patients (0.99± 1.7g/day) was also significantly higher than the normotensive women (0.16±0.10g/day). Mean Haemoglobin level in study group was 9.9±1.1 g% while in control group it was 9.3±1.2 g%. Results were statistically significantly high in study group and was comparable with other studies [18,19,20].Platelet count was lower among study group (1.4±0.4 lacs/mm3) than controls (1.6±0.5lacs/ mm3) and was comparable to studies by Verhaeghe et al [21] and Bayhan et al [22].

Mean serum urea and creatinine levels was also high in study group than control group and correlated with other studies [18,19]. Mean serum Aspartate transaminase, Alanine transaminase and serum bilirubin of the study group and control group was compared and found to be higher in pre-eclamptic patients which was comparable to other studies [11,18,21]. In our study serum lactate dehydrogenase levels in the study group and control group was compared and was 395.4±146.3 IU/L and 307.2±68.2 IU/L respectively. This was statistically significant. It was observed that serum LDH was raised in 28% of pre-eclamptic patients while as only 2% normotensive patients had raised levels. The mean serum LDH level in patients with mild pre-eclampsia was 347.6±99.1IU/L while as in severe pre-eclampsia it was 564.7±162.5 IU/L which was significant. This observation was comparable to studies done by Qublan Hussain et al in 2005 [17], Keren K Malik et al[23] and Nurhan Celik et al in 2008 [18] and Ozgur Dermirtas et al in 2005 [24].

Serum lactate dehydrogenase levels in pre-eclamptic patients with warning symptoms and signs ( headache,blurring of vision, nausea, vomiting, epigastric pain, oliguria, thrombocytopenia, elevated liver enzymes) was studied and found to be raised (766±175.5 IU/L) while as in pre-eclamptic patients without these symptoms and signs it was found to 375.9±116.4 IU/L only and was comparable to other studies [11].

Our study showed that serum LDH levels were higher in patients of pre-eclampsia as compared to normotensive patients and levels also increased with the severity of pre-eclampsia and in those patients who had associated warning symptoms and complications.

## V. Conclusion

Pre-eclampsia is a syndrome complex commonly encountered by obstetrician. It has complications for both mother and foetus. Though it is not preventable but the severity and complications can be contained to some extent if high risk patients are identified. Serum Lactate dehydrogenase levels indicates celluar damage in pre-eclampsia and its estimation is easy and non- invasive. It predicts the severity as well as complications in pre-eclampsia. It can be used as a reliable biochemical marker to identify high risk patients for close monitoring , prompt and correct management and hence help in preventing complications. Thus, it can be used as a potential added diagnostic test for early detection of the severity and occurrence of various maternal and foetal complications. Thereby it can help in decreasing maternal, foetal and neonatal morbidity and mortality in pre-eclampsia.

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