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## STUDY OF SERUM LACTATE DEHYDROGENASE AND URIC ACID IN PREECLAMPSIA

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**Abstract:** BACKGROUND: Preeclampsia is an unpredictable multiorgan disorder unique to human pregnancy. It is associated with significant maternal and foetal morbidity and mortality worldwide. There is no single test that fulfills all the criteria for a good predictor of preeclampsia. LDH is a useful biochemical marker that reflects the severity of the occurrence of preeclampsia. **OBJECTIVES:** This study was done to compare serum levels of lactate dehydrogenase (LDH), and uric acid (UA) among women with preeclampsia, normal pregnancy and non-pregnant healthy controls and to evaluate role of their estimation in preeclampsia. **METHODS:** this is the case-control hospital based study carried in the department of biochemistry kurnool Medical College. Normal pregnant women (n=50), women with preeclampsia (n=50) were included in the study. Both the groups were in their third trimester and of same age and same gestational age. Preeclamptic group was further divided into two subgroups **group I** preeclampsia (n=25) and, 25 **group II** (n=25) preeclampsia. Serum levels of LDH and UA were measured using commercially available kits. Statistical analysis was done using SPSS 17.0. **RESULTS:** Serum levels of LDH, and UA were significantly increased in women with preeclampsia compared with controls. **CONCLUSION:** Elevated levels of serum LDH indicates the tissue damage related to endothelial vascular damage and are the main cause of the occurrence of preeclampsia. Serum LDH, and UA levels gradually increase as the disease severity increases

**Keywords:** Preeclampsia, LDH, Uric acid, Endothelial dysfunction



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## INTRODUCTION

Preeclampsia is a clinical manifestation characterized by hypertension, proteinuria and edema that occurs after 20th week of pregnancy. It is a multisystem disorder of pregnancy with potentially severe consequences for both mother and child.<sup>1</sup> The etiology of preeclampsia is unknown but thought to be related to hypoxia in the placenta and endothelial dysfunction.<sup>2</sup> It affects about 5-8% of all pregnancies and is a major cause of maternal, fetal and neonatal mortality and morbidity.<sup>3</sup>

## PATHOPHYSIOLOGY

Although the exact cause of preeclampsia remains unclear, many theories center on problems of placental implantation and the level of trophoblastic invasion.<sup>4,5</sup> It is important to remember that although hypertension and proteinuria are the diagnostic criteria for preeclampsia, they are only symptoms of the pathophysiologic changes that occur in the disorder. One of the most striking physiologic changes is intense systemic vasospasm, which is responsible for decreased perfusion of virtually all organ systems. Perfusion also is diminished because of vascular hemo concentration and third spacing of intravascular fluids. In addition, preeclampsia is accompanied by an exaggerated inflammatory response and inappropriate endothelial activation.<sup>5</sup> Activation of the coagulation cascade and resultant microthrombi formation further compromise blood flow to organs.<sup>6</sup>

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. Preeclampsia is a multisystem disorder and leads to a lot of cellular death. So, serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease.<sup>7</sup> Hence Serum LDH Levels can be further used as help in making decision, regarding the management strategies to improve the maternal and fetal outcome. Uric Acid is the major end products of Purine metabolism. The cause of hyperuricemia in pre eclampsia has been attributed to either a decreased excretion or to an increased production of uric acid. Decreased uric acid clearance, reflected by altered tubular function. Increased breakdown of purines in placenta as explanation of over production of uric acid.<sup>8</sup> Soluble uric acid impairs nitric oxide generation in endothelial cells inducing endothelial dysfunction. Hyperuricemia is one of the most consistent and earliest detectable changes in Pre eclampsia and has cited a better predictor of fetal risk. Hence we are conducting this study to know the effects of LDH and uric acid levels in PIH patients and their outcome.

**2. MATERIALS AND METHODS:** A study of serum lactate dehydrogenase and uric acid in preeclampsia from Government General Hospital, affiliated to Kurnool Medical College,

Kurnool. The study was approved by Ethical and Research Committee of Government General Hospital to use human subjects in the research study. The study was conducted from April 2014 to February 2015.

**SUBJECTS:** A total number of 50 subjects were selected for the present study based on the inclusion and exclusion criteria.

**CASES:** Out of 100 subjects, 25 **group I** preeclampsia, 25 **group II** preeclampsia were considered as cases. **Case group I-** It included 25 diagnosed cases of preeclampsia in age group of 20-45 years.

Pregnant female of  $\geq 20$  weeks of gestation with blood pressure  $\geq 140/90$  mm of Hg noted first time during pregnancy on  $\geq 2$  occasions at least 6 hours apart with proteinuria of  $\geq 1+$  ( $\geq 30$ mg/dl) by dipstick method in a random urine sample was considered as having preeclampsia. **Case group II-** It included 25 diagnosed cases of gestational hypertension in age group of 20-45 years. Pregnant female of  $\geq 20$  weeks of gestation with blood pressure  $\geq 140/90$  mm of Hg noted first time during pregnancy on  $\geq 2$  occasions at least 6 hours apart without proteinuria was considered as having gestational hypertension

**CONTROLS:** Out of 100 subjects, 50 healthy pregnant women were considered as Controls.

**INCLUSION CRITERIA:** STUDY GROUP- the study group includes 50 preeclampsia women. Preeclampsia defined as blood pressure constantly greater than 140/90 mmHg with proteinuria with no UTI and no previous history of hypertension. CONTROL GROUP- includes 50 normal pregnant women with age and gestational age matched with the study group. All women would be followed from the time of admission and early postpartum period and babies till 7<sup>th</sup> day of delivery.

**EXCLUSION CRITERIA:** Pregnant women with essential hypertension or hypertension  $< 38$ wks of gestation; Preexisting diabetes mellitus, renal disease, liver disorder, thyroid disorder, epilepsy & with urinary tract infection, cardiovascular disease, smokers, alcoholics, Rh negative pregnancy, multiple gestation and hepatitis.

**COLLECTION OF SAMPLES:** About 5 ml of venous blood from all subjects was collected an aseptically from ante cubital vein. Serum was separated immediately by centrifugation and kept at 4 degrees C until analysis was carried out. **Parameters Measured.** LDH was estimated using commercial kit from AGAPEE diagnostics by kinetic method. The estimations were carried out on semi auto analyzer.

**STATISTICAL ANALYSIS:** The statistical analysis would be done by Chi-square test (for proportional data) analysis of variance and sample "t" test (for parametric data).

**RESULTS:** Table-1 shows that the mean level of systolic BP was significantly higher in Group I, II when compared with controls. The mean levels of diastolic BP and serum LDH were significantly higher in Group I and II when compared with healthy non-pregnant controls. One way ANOVA test showed significant difference in levels of all the parameters among study groups except POG and age of mother which was non-significant. Table-2 shows that the mean level serum LDH, UA was significantly higher in Group I, II when compared with controls Table-3 shows that there is highly significant positive correlation of systolic & diastolic blood pressure with serum LDH and UA concentrations.

**Table 1: comparison of POG ,age and BP among study groups.**

|  | POG<br>(weeks) | AGE<br>(years) | SYSTOLIC BP<br>(mm of Hg) |          | DIASTOLIC BP<br>(mm of Hg) |           |            |
|--|----------------|----------------|---------------------------|----------|----------------------------|-----------|------------|
|  | Mean±SD        | Mean±SD        | T test<br>(p)             | Mean±SD  | T test (p)                 | Mean±SD   | T test (p) |
| <b>Preeclampsia (Group I)</b>              | 34.05±3.26     | 22.4 ±2.35     | 0.521                     | 160±9.46 | < 0.001**                  | 94.78±8.0 | <0.001**   |
| <b>Gestational Hypertension (Group II)</b> | 34.66 ±3.3     | 22.65±2.68     | 0.450                     | 152±4.02 | < 0.001**                  | 93.0±4.19 | < 0.001**  |
| <b>Normal Pregnancy CONTROLS</b>           | 34.24±1.23     | 22.03±2.28     | 0.730                     | 112±4.56 | < 0.05*                    | 72.56±3.5 | 0.123      |

**Table 2: comparison of serum LDH, UA among study groups.**

|  | Serum LDH (IU/L) |               | Serum Uric acid (mg/dl) |               |
|--|------------------|---------------|-------------------------|---------------|
|  | Mean±SD          | T test<br>(p) | Mean±SD                 | T test<br>(p) |
| <b>Preeclampsia (Group I)</b>              | 386.32<br>170.09 | <0.001**      | 5.65 0.56               | <0.001**      |
| <b>Gestational Hypertension (Group II)</b> | 264.1 115.86     | < 0.001**     | 5.43 0.36               | < 0.001**     |
| <b>Normal Pregnancy CONTROLS</b>           | 143.40 45.38     | 0.081         | 5.01 0.51               | < 0.05        |

P-value of unpaired student's t-test between respective case groups and controls.

POG – period of gestation; BP- Blood Pressure.

\* Significant \*\* Highly Significant

**Table 3: Pearson's correlation between Systolic & Diastolic BP and parameters**

|                                 | Serum LDH (IU/L) | Serum Uric Acid (mg/dl) |
|---------------------------------|------------------|-------------------------|
| <b>r-value for Systolic BP</b>  | <b>0.602</b>     | <b>0.612</b>            |
| <b>r-value for Diastolic BP</b> | <b>0.516</b>     | <b>0.319</b>            |

**DISCUSSION:** Globally 8.4 million pregnant women suffer from hypertensive disorders.<sup>9-11</sup> Preeclampsia is considered an idiopathic multisystem disorder that is specific to human pregnancy.<sup>12</sup> The multi organ dysfunction in preeclampsia caused by vascular endothelial damage, including maternal liver, kidney, lungs, nervous system, coagulation system will leads to excessive LDH leakage and elevated levels in serum due to cellular dysfunction, which may cause the occurrence of preeclampsia. These results are also supported by HS Qublan.<sup>13</sup> Hyperuricemia is associated with higher maternal complication rates and fetal growth retardation.<sup>14</sup> Hak et al.<sup>15</sup> suggested that the uric acid levels are reliable predictors of perinatal outcome in preeclamptic women. The present study too showed significantly high levels of serum uric acid in mild PIH, severe PIH and eclamptic women in comparison to normotensive cases.

In majority of preeclamptic women mild to moderately diminish glomerular filtration appears due to reduced plasma volume. Uric acid is considered as biochemical marker of preeclampsia was raised beyond the normal levels in preeclampsia suggested that elevated uric acid levels may be due to either decreased renal urate excretion or increased oxidative stress. The time at which serum uric acid concentration begins to rise is an approximate indicator of the time of onset of the preeclampsia.<sup>16</sup> The value of measuring serum uric acid in hypertensive pregnancy is greatest between 24 to 32 weeks of gestation. Low values indicate a good prognosis for the fetus

**CONCLUSION:** Standard antenatal follow up should be carried out for the early detection and prevention of PIH. Tests like serum LDH, uric acid could help to predict and to deal with the adverse complications of PIH. Elevated levels of lactic dehydrogenase, indicative the cellular damage and dysfunction can be used as a biochemical marker because it reflects the severity of the disease the study concluded that Serum LDH and uric acid gradually increase as the disease severity increases. Regular monitoring of its serum level in women with preeclampsia may give a clue of disease severity.

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