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# Correlation between various biochemical biomarkers and blood pressure in pregnant women

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## ABSTRACT

**Aims:** To find out the correlation of C-reactive protein, serum uric acid and serum LDH with hypertensive antenatal patients.

**Methods:** The present study was conducted among preeclamptic and eclamptic antenatal patients. Serum was used for estimation of serum levels of CRP, LDH and Uric acid. The data obtained was compiled and analyzed statistically and was expressed in terms of mean±SD and percentage. Student t-test, Chi-square test, Pearson's Correlation Coefficient were used and p value less than 0.05 was considered significant.

**Results:** A positive correlation was found between serum CRP level and systolic blood pressure (r = +0.525, P=0.001) & serum CRP level diastolic systolic blood pressure (r= + 0.493, P=0.001). There was a positive correlation between serum uric acid with systolic (r= +0.454, P <0.001) and diastolic blood pressure (r = +0.471, p < 0.001). There was positive correlation between Serum LDH with systolic (r =+0.385, p value of r <0.001) and diastolic BP (r = +0.420, p value of r < 0.001).

**Conclusion:** Hyperuricemia, increased serum CRP and LDH level can be used as biomarkers for identifying women at risk of preeclampsia and its complications along with adverse effects. We conclude that CRP, serum LDH and Serum Uric acid are reliable and inexpensive markers to predict severity of hypertensive disorders of pregnancy.

**Keywords:** antenatal care, hypertension, pre-eclampsia

## INTRODUCTION

In pregnancy, many changes occur in metabolic, biochemical, physiological, haematological and immunological processes. These changes are reversible within a few days to a few months post delivery.[1] Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection. Despite decades of intensive research, the exact cause that how pregnancy incites or aggravates hypertension remains still unsolved. Indeed hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics.[2] When blood pressure is 140/90 mm of Hg or greater for the first time after

20 weeks of gestation with no proteinuria, it is called as gestational hypertension.[3]

Amongst many of the markers, CRP is found to be the good predictor of the probability of severity of future maternal and perinatal events. The CRP is one of the acute phase proteins measured in plasma. C-reactive protein (CRP) is a sensitive marker of systemic inflammation and is primarily synthesized in hepatocytes in response to infection and tissue injury,[4] which is stimulated by the release of proinflammatory cytokines.

Lactate Dehydrogenase (LDH) is an intracellular cytoplasmic enzyme. LDH enzymes are ubiquitous to all the major organ systems e.g. heart, kidney, muscle, leukocytes and erythrocytes. Cellular enzymes in the extracellular space, although of no further metabolic function in this space, are still of benefit because they serve as indicators suggestive of disturbance of cellular integrity induced by pathological conditions and is used to detect cell damage or cell death. Serum LDH is abnormal in most of disorders, therefore the total serum LDH is highly sensitive but nonspecific test. In order to optimize the diagnostic value, LDH isoenzymes can be measured. This can be further used as help in making decision, regarding the management strategies to improve the maternal and fetal outcome.[5-8]

Serum uric acid levels reflect the circulating xanthine oxidase activity and oxidative stress production. There are studies which demonstrate that the development of preeclampsia is associated with hyperuricemia.[9,10] But yet, the role of uric acid in preeclampsia is less clear. Some studies reported an independent association between uric acid and preeclampsia, but others found prognostic and also diagnostic significance.[11,12] Thus, the study was conducted to find out the correlation of C-reactive protein, serum uric acid and serum LDH with hypertensive antenatal patients.

## METHODS

The present study was a prospective, observational and clinically randomized study conducted in the Department of Obstetrics and Gynaecology in collaboration with Department of Biochemistry and Department of Microbiology, Govt. Medical College, Rajindra hospital, Patiala, Punjab during the period 2018-2019 after getting ethical clearance from the institutional ethical committee. 200 pregnant women were included in study after fulfilling inclusion criteria.

Inclusion criteria consisted of gestational age > 20 weeks, primi/multigravida, antenatal patients of age 18 - 40 years and all antenatal patients' normotensive as well as hypertensive, which do not fall under exclusion criteria. Exclusion criteria comprised of patients with known renal disease, diabetes, hepatic dysfunction, alcoholism, dyslipidaemia, RH negative blood group, cardiac and infectious diseases; pre-existing hypertension before pregnancy or on any type of anti- hypertensive treatment; multiple pregnancy; PROM (Premature rupture of membranes) and any symptomatic infectious disease. After fulfilling inclusion and exclusion criteria and taking informed consent, all the subjects were divided into 2 groups, study group included of preeclamptic & eclamptic antenatal patients (n=150) and control group included of normotensive antenatal women (n=50).

Under all aseptic conditions, 5ml blood sample was taken by venepuncture in a plain vacutainer. Sample was allowed to clot for sometime and then centrifuged. Serum was

separated out and stored in aliquot. Serum was used for estimation of serum levels of CRP, LDH and Uric acid.

The semiquantitative CRP test was based on the principle of latex agglutination. Polysterine latex particles are coated with purified CRP antibodies. The presence or absence of visible agglutination immediately after removing the slide from the rotator was examined macroscopically. The presence of agglutination indicates a CRP concentration equal or greater than 6 mg/L.

Estimation of serum LDH was done by Kit method via semi- auto analyser. LDH catalyzes the oxidation of lactate to pyruvate accompanied by the simultaneous reduction of NAD to NADH. LDH activity in serum is proportional to the increase in absorbance due to the reduction of NAD.

Estimation of Uric acid was done by Kit method via fully automated Bio chemistry analyser (EM-360).

The data obtained was compiled and analysed statistically using IBM SPSS version 22 software. Data was expressed in terms of mean±SD and percentage. Student t-test, Chi-square test, Pearson's Correlation Coefficient were used whenever found suitable and necessary. The statistical test is considered significant when calculated p value is less than 0.05 and considered highly significant when p value less than 0.001.

## RESULTS

Table 1 and figure 1-3 shows positive correlation between CRP & SBP ($p<0.001$), positive correlation between S. uric acid & SBP ($p<0.001$) as well as positive correlation between S. LDH & SBP ($p<0.001$).

Table-1: Correlation of CRP, serum Uric Acid, Serum LDH with Systolic blood pressure

| Correlation between | Pearson's correlation coefficient (r) | p-value | Remarks |
|---|---|---|---|
| CRP & SBP | +0.525 | 0.001 | Highly significant Positive correlation |
| S. uric acid & SBP | +0.454 | 0.001 | Highly significant Positive correlation |
| S. LDH & SBP | +0.385 | 0.001 | Highly significant Positive correlation |

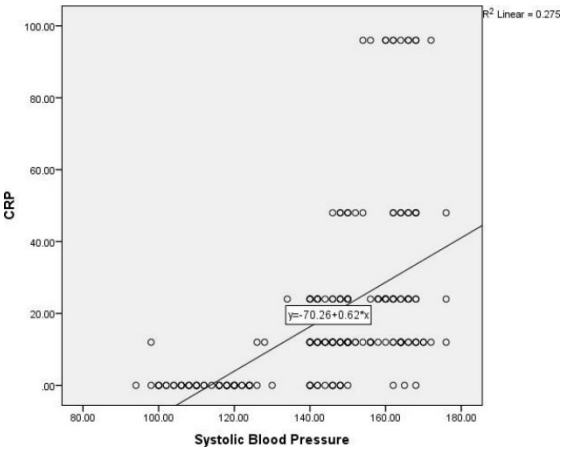


Figure-1: Correlation of CRP with Systolic Blood Pressure

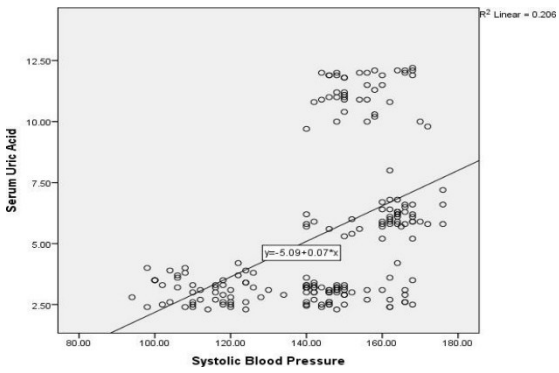


Figure 2: Correlation of S. Uric Acid with Systolic Blood Pressure

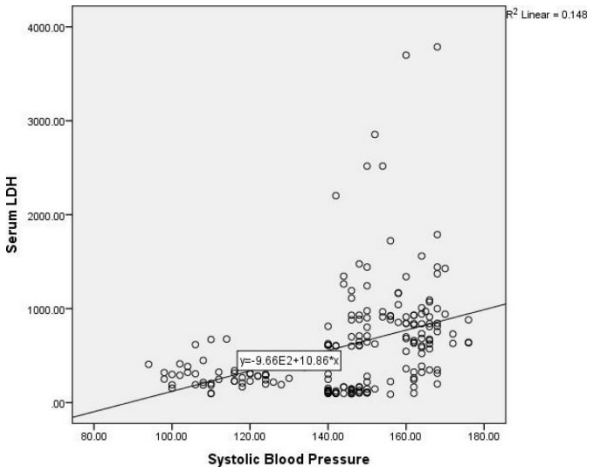


Figure-3: Correlation of LDH with Systolic Blood Pressure

Table 2 and figure 4-6 shows positive correlation between CRP & DBP (p<0.001), positive correlation between S. uric acid & DBP (p<0.001) and positive correlation between S. LDH & DBP (p<0.001).

Table-2: Correlation of CRP, serum Uric Acid, Serum LDH with Diastolic blood pressure

| Correlation between | Pearson's correlation coefficient (r) | p-value | Remarks |
|---|---|---|---|
| CRP & DBP | + 0.493 | 0.001 | Highly significant Positive correlation |
| S. uric acid & DBP | +0.471 | 0.001 | Highly significant Positive correlation |
| S. LDH & DBP | +0.420 | 0.001 | Highly significant Positive correlation |

A positive correlation is found between serum CRP level and systolic blood pressure (r = +0.525, P=0.001) & serum CRP level diastolic systolic blood pressure (r= + 0.493, P=0.001). There was a positive correlation between serum uric acid with systolic (r = +0.454, P <0.001) and diastolic blood pressure (r = +0.471, p < 0.001). There was positive correlation between Serum LDH with systolic (r =+0.385, p value of r <0.001) and diastolic BP (r = +0.420, p value of r < 0.001).

Figure-4: Correlation of CRP with Diastolic Blood Pressure

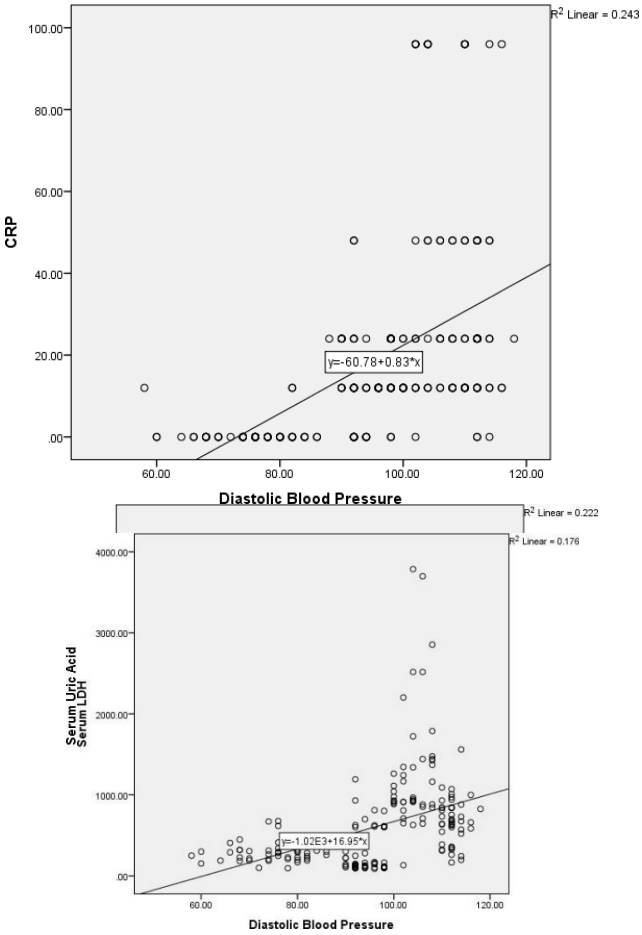


Figure-5: Correlation of S. Uric Acid with Diastolic Blood Pressure

Figure-6: Correlation of LDH with Diastolic Blood Pressure

## DISCUSSION

Oxidative stress and inflammation are important contributors. [13] Various traditional and newer biomarkers were suggested for diagnosis and prognosis of preeclampsia. In view of this, the present study was done to assess clinical utility of some of the promising biochemical markers like serum uric acid, CRP and serum LDH which are inexpensive and can be of some diagnostic and prognostic significance.

In our study the mean ± SD of systolic blood

pressure level in subjects of study group (154.27 ± 10.23 mmHg) was much higher than that of normal pregnant women (133.88 ± 9.50 mmHg). The mean ± SD of diastolic blood pressure level in subjects of study group (102.60 ± 7.99 mmHg) was much higher than that of normal pregnant women (75.44 ± 7.14 mmHg). This difference was found to be highly significant (p = 0.001). A study conducted by Gandhi M et al,[14] mean SBP was 157.41 ± 8.36 mm Hg vs 114.52 ±6.32 mm Hg and mean DBP was 96.24 ± 6.65 mm Hg vs 70.13 ± 5.21 mm Hg in study and control group respectively, which were higher in study group. A study conducted by Sharmin S et al,[15] mean SBP was 122.15±6.44 mm Hg vs 148.40±12.35 mm Hg and mean DBP was 74.05±5.97 mm Hg vs 100.00 ±9.74 mm Hg in control and study group respectively, which were higher in study group (p<0.000). In a study conducted by Mandal KK et al,[16] in study group, the mean ± SD of SBP (163.04 ± 24.26 mm Hg) & DBP (104.19 ± 15.32 mm Hg) were much higher than that of normal pregnant women.

The mean weight of women in the study group was 56.97±6.27 kg and in control group 56.86±5.61 kg which was statistically non-significant. In a study conducted by Mandal KK et al,[16] mean weight of women in the study group (57.23 ± 2.15 Kg) is more compared with that of control group (55.87 ± 1.23 Kg), and this difference is statistically significant (p= 0.001).

In the present study 58% patients belonged to rural areas while 42% patients belonged to the urban areas. This does not in any way indicate prevalence of problem in rural women. On the other hand, it is due to the fact that a higher percentage of population in India is still living in rural areas.

A positive correlation is found between serum CRP level and systolic blood pressure (r = +0.525, P=0.001) & serum CRP level diastolic systolic blood pressure (r= +0.493, P=0.001) and this is significant. Mirzaie F et al,[17] determined serum CRP level in PE, and its correlation with the disease severity. A positive correlation is found between serum CRP level and systolic blood pressure (r = +0.6, P=0.001) & serum CRP level diastolic systolic blood pressure (r= + 0.5, P=0.001) and this is significant. Anil B et al,[18] recorded a statistically positive significant correlation between CRP levels and (SBP,DBP) which shows that the elevation of CRP level is proportional to severity of preeclampsia and supported his results by the concept that systemic inflammation is a hallmark in the preeclampsia pathogenesis and serum CRP level may be the marker to predict severity of disease.

There was a positive correlation between serum uric acid with systolic (r = +0.454, P <0.001) and diastolic blood pressure (r = +0.471, p < 0.001). Similar findings were seen in studies done by Sonagra et al,[19] P Josephine et al[20] and Saxena et al.[21] Mustaphi et al[22] observed that when the levels of diastolic BP is increased, the levels of serum uric acid was also increased, concluding a positive correlation between diastolic BP and serum uric acid. Correlation Coefficient r value with systolic BP in similar studies by Sonagra et al,[19] P Josephine et al[20] and Saxena et al[21] were 0.408, 0.287 and 0.214 respectively whereas r value with diastolic BP in same studies were 0.420, 0.235 and 0.367 respectively.

In our study, there was positive correlation between Serum LDH with systolic (r = +0.385, p value of r <0.001) and diastolic BP (r = +0.420, p value of r

< 0.001) and was significant. Sonagra et al[19] found r value of LDH with Systolic & Diastolic blood pressure as 0.504 and 0.546 respectively.

## CONCLUSION

Hyperuricemia, increased serum CRP and LDH level can be used as biomarkers for identifying women at risk of preeclampsia and its complications along with adverse effects. However, further studies are required to determine whether genetic, nutritional defects or diseases related to uric acid or CRP metabolism account for hyperuricemia or increased serum CRP level observed in pregnant women with preeclampsia. We conclude that CRP, serum LDH and Serum Uric acid are reliable and inexpensive markers to predict severity of hypertensive disorders of pregnancy.

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