



## SIGNIFICANCE OF VARIOUS BIOCHEMICAL MARKERS TO ASSESS SEVERITY OF HYPERTENSIVE DISORDERS OF PREGNANCY

### Biochemistry

**Dr. Manpreet Kaur Dhillon** Senior Resident, Department of Biochemistry, Government Medical College, Patiala  
- Corresponding Author

**Dr. Gurdeep Kaur Bedi** Professor, Department of Biochemistry, Government Medical College, Patiala

### ABSTRACT

Hypertensive disorders of pregnancy or Pregnancy induced hypertension (PIH) is a common gestational disorder which is associated with maternal and fetal morbidity and mortality. Yet the etiology of this disorder is little understood. Alterations in levels of liver function and renal function markers have been suggested to be linked to severity of PIH. Present study aimed to evaluate levels of various biochemical markers and their importance in assessing severity of PIH.

**Material and methods:** 50 patients with PIH which constituted study group and 50 normotensive pregnant women constituted control group. Collected samples were analysed for uric acid, urea and creatinine levels which predict renal functions and liver transaminases (SGOT and SGPT) which predict liver functions.

**Result:** Serum Uric acid levels significantly increased ( $p < 0.001$ ), levels being  $4.27 \pm 0.83 \text{ mg/dl}$  in normal pregnant women and  $5.56 \pm 0.78 \text{ mg/dl}$  in PIH patients. There was no difference in levels of urea and creatinine among two groups. The increase in SGOT and SGPT levels in study group as compared to control group shows statistically significant association ( $p \text{ value} = 0.008$ ).

**Conclusion:** Serum uric acid and liver transaminases are strongly associated with pre eclampsia, suggestive of their predictive role in assessing hepatorenal damage in patients presenting with pregnancy induced hypertension.

### KEYWORDS:

Pregnancy induced hypertension, Uric acid, SGOT, SGPT

### INTRODUCTION

Pregnancy induced hypertension is one of the most common disorders seen in human pregnancies<sup>[1]</sup>. It can be classified as Gestational hypertension, Pre-eclampsia (PE) and eclampsia syndrome<sup>[2]</sup>. Though relatively benign on its own, in roughly half of the cases of gestational hypertension the disorder progresses into preeclampsia, a dangerous condition that can prove fatal to expectant mothers<sup>[3]</sup>. The underlying cause of gestational hypertension in humans is commonly believed to be an improperly implanted placenta<sup>[1]</sup>. A lot of studies have been conducted to find any relation of uric acid, urea and creatinine with PIH.

Normally in pregnancy the clearance of urate is high whereas in preeclampsia the renal tubular function is affected earlier than the glomerular function and decreased clearance of uric acid precedes changes in glomerular filtration rate leading to hyperuricemia. Where majority authors concluded that hyperuricemia is associated with severity of pre eclampsia, there are still others who preclude from this opinion<sup>[4,5,6]</sup>. Similarly, conflicting results have been deduced in context to urea and creatinine. Various studies found that there is no significant difference in the mean value of creatinine and urea in preeclamptic and normotensive pregnant women<sup>[4]</sup>. This is in contrast to certain studies which showed increased urea and creatinine levels in study group<sup>[7]</sup>.

In PIH, placental dysfunction initiate the systemic vasospasm, ischaemia and thrombosis that eventually damage the maternal organs. Thrombus formation or haemorrhage causes liver injury, hepato cellular necrosis and causes elevation of liver enzymes.<sup>[8]</sup>

The present study aimed at evaluating the levels of above mentioned hepatorenal biochemical markers and assess the severity of PIH.

### MATERIAL AND METHODS

This is a prospective study which study was conducted in Department of Biochemistry, Rajindra Hospital, Patiala on 50 patients with pregnancy induced hypertension which constituted study group, out of which, 15 (30%) were mild pre eclamptic, 25 (50%) were severe pre eclamptic and 10 (20%) were eclamptic. 50 normotensive pregnant women constituted control group.

The diagnosis of preeclampsia was confirmed using the "Report of the American College of Obstetricians and Gynecologists' Task Force on

Hypertension in Pregnancy" criteria. Based on these criteria, patients with systolic blood pressure  $\geq 140 \text{ mmHg}$  and/or diastolic blood pressure  $\geq 90 \text{ mmHg}$  (measured after a period of rest of four hours, twice daily) and proteinuria ( $\geq 300 \text{ mg protein/24 h}$ ) were diagnosed as preeclampsia. The diagnosis of eclampsia was based on the presence of tonic-clonic seizures in patients that were followed up with the diagnosis of preeclampsia with no systemic disease that may cause seizures<sup>[1]</sup>.

**Inclusion Criteria included** Pregnant females with upto 35 years of age and with gestation 20 weeks or more.

**Exclusion criteria included** all cases of previous history of essential hypertension or chronic hypertension due to any other cause, any associated renal, hepatic, cardiac or neurological disorders not due to pregnancy induced hypertension, known cases of diabetes mellitus type 1 and 2, PCOS, associated molar pregnancy and multiple pregnancy.

Venous Samples obtained from both groups were collected in plain vacutainers. Levels of SGOT and SGPT were evaluated using IFCC kinetic method on autoanalyzers<sup>[9]</sup>. Urea and creatinine levels were evaluated with colorimetric urease method and colorimetric Brod and Sirota respectively<sup>[10,11]</sup>. Colorimetric method of Caraway was done to determine uric acid levels<sup>[12]</sup>. The data obtained was statistically analysed. Results obtained were statistically

analyzed using student t-test. A p-value less than 0.05 was considered significant.

### RESULT

No statistically significant differences were found in age, gravidity, parity, weight and height among the demographic data between the groups.

Systolic and diastolic blood pressures were significantly higher in the eclamptic and preeclamptic patient groups compared to the healthy pregnant women ( $P < 0.001$  and  $P < 0.001$ , respectively).

Serum Uric acid levels significantly increased ( $p < 0.001$ ) with the severity of PIH, levels being  $4.27 \pm 0.83 \text{ mg/dl}$  in normal pregnant women and  $5.56 \pm 0.78 \text{ mg/dl}$  in PIH patients. The mean blood urea level in the study group was  $31.46 \pm 6.48 \text{ mg\%}$  against  $30.14 \pm 6.12 \text{ mg\%}$  in the control group, mean serum creatinine level was  $0.990 \pm$

0.27 mg% in the study group against 0.998±0.255 mg% in the control group. The p value of blood urea and serum creatinine was 0.880 and 0.298 respectively and hence non significant. (Table no. 1)

Mean value of SGOT in study group and control group were 33.36 ± 11.05 IU/L and 28.44 ± 6.34 IU/L (normal range is 6 to 40 IU/L). The mean value of SGPT in study and control group were 29.90 ± 10.45 IU/L and 25.26 ± 5.85 IU/L (normal range is 6- 40 IU/L). The increase in SGOT levels in study group as compared to control group shows statistically significant association (p value= 0.008) . Similarly increase in SGPT levels among study group in comparison to control group shows statistically significant association (p=0.008).(Table No. 2)

TABLE NO. 1

PARAMETER	STUDY GROUP	CONTROL GROUP	P VALUE	SIGNIFICANT
Uric acid (mg/dl) Normal range = 2-6mg%	5.56±0.78	4.27±0.83	0.000	S**
Urea (mg/dl) Normal range = 20-40mg%	31.46±6.48	30.14±6.12	0.880	NS*
Creatinine (mg/dl) Normal range= 0.7-1.4 mg%	0.99±0.27	0.998±0.255	0.298	NS

\*NS Non significant \*\* S Significant

FIGURE1

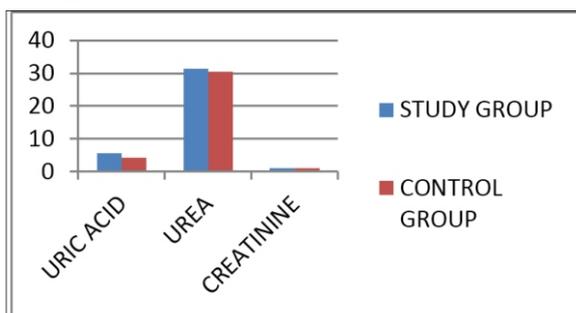
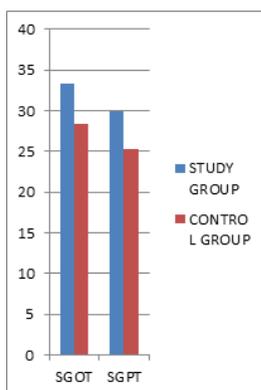


TABLE NO. 2

PARAMETER	STUDY GROUP	CONTROL GROUP	P VALUE	SIGNIFICANT
SGOT (IU/L) Normal range= 6-40IU/L	33.36±11.05	28.44 ±6.34	0.008	S
SGPT(IU/L) Normal range= 6-40IU/L	29.90 ±10.45	25.26 ±5.85	0.008	S



**DISCUSSION:**

In the present study, mean serum uric acid levels are 5.56mg% in study group and 4.27 mg% in control group(p<0.001) (Figure 1). The findings were comparable to studies done by Tsukimori et al[5] (2008)

who found 6.6±1.5 mg% serum uric acid in the study group. Similar results are depicted by Magna Manjareeka et al<sup>[4]</sup> (2013) and Jeyabalan et al<sup>[13]</sup>(2007). There is highly significant rise in the mean value of serum uric acid concentration in the preeclamptic women as compared with the normotensive pregnant women because in women with preeclampsia, renal plasma flow and glomerular filtration rate are decreased as a consequence of increased afferent arteriolar resistance and/or reduced ultrafiltration coefficient. Shannon A et al (2007) in his study observed that the elevation of uric acid in preeclamptic women often precedes hypertension and proteinuria. Increased uric acid production from maternal, fetal or placental tissues through heightened tissues breakdown could also explain the increased concentration<sup>[15]</sup>.

Elevated uric acid decreases endothelial cell proliferation, migration, placental development, inhibits placental amino acid uptake, trophoblast invasion and the incorporation of trophoblast into endothelial monolayers<sup>[16]</sup>.

Therefore, it can be emphasized that serum uric acid levels are predictive of the hypertensive disorders of pregnancy. We can also speculate that uric acid may play direct roles in the pathological processes of preeclampsia at both the level of the placenta and maternal vasculature.

In the present study, urea and creatinine levels showed no significant results. These results are comparable to Magna Manjareeka et al[4] (2013). But certain studies like Israa A MJ et al[7] (2012) showed increase in blood urea and creatinine levels in pre eclamptic women as compared to normotensive women. These parameters are of little value in the prediction of preeclampsia.

SGOT and SGPT had mean value as 33.36 IU/L and 29.90 IU/L respectively with p value =0.008 which indicated significant association with pre eclampsia(Figure 2).

In a clinical trial conducted by Seymour including 85 patients with PIH, AST, ALT were elevated in 54% of patients with pre-eclampsia, whereas in cases of gestational hypertension they were raised only in 14% of cases. He pointed out that patients with abnormal liver function tests had bad maternal and fetal outcomes<sup>[17]</sup>.

Peralta et al[18] found no difference in levels of AST and ALT between women with preeclampsia and normal control subjects. The elevated liver enzymes are thought to be secondary to obstruction of hepatic blood flow by fibrin deposits in the sinusoid. This obstruction leads to periportal necrosis. In addition to hemolysis and thrombocytopenia, it also became appreciated that elevated serum transaminase levels were commonly found with severe preeclampsia and were indicative of hepatocellular necrosis.<sup>[8]</sup>

**LIMITATIONS:**

Samples are taken after 20 weeks of gestation. Therefore, proper follow of the trends of these biomarkers from beginning is not obtained. However, the present study does add to the existing data.

**CONCLUSION:**

From the present study, it can be concluded that uric acid and liver transaminases are cheaper and easily available markers which are predictive of hepatorenal involvement in patients of hypertensive disorders of pregnancy. Proper screening of patients with symptoms of PIH or with prior history of such condition should be done at the earliest which may be helpful in alleviating maternal and fetal mortality and morbidity.

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