

**STUDY OF SERUM URIC ACID LEVELS IN
PREGNANCY INDUCED HYPERTENSION****DR. LAXMI NARAYANA S^{*1}, DR. M. D. SULEMAN² AND DR. B. VODELU³**¹*MD. Asst. Professor, Department of Biochemistry, Gandhi Medical College, Secunderabad, Telangana, India.*²*MD. Professor & Head, Department of Biochemistry, Gandhi Medical College, Secunderabad, India.*³*MD. Associate Professor, Department of Biochemistry, Gandhi Medical College, Secunderabad, India.***ABSTRACT**

The aim of the present study is to understand and investigate the association/relationship of selected physical and biochemical parameters among pregnant women with hypertension and without hypertension. The 54 cases were selected from the antenatal outpatient, Gandhi Hospital, Secunderabad, Telangana state with age group between 18-24 years, primigravide with known last menstrual period and gestational age between 20-30 weeks. Among 54 women, 36 were pregnancy induced hypertensive, considered as experimental group and remaining 18 were normotensive taken as control group. The experimental group was further categorized into three groups based on the degree of hypertension. Serum Uric Acid levels had significantly increased only in the group-3 of experimental group, but not in the group- 1 & 2. This observation clearly suggests that as the diastolic blood pressure increases, serum Uric Acid levels also increase, thereby resulting in an increased risk of adverse pregnancy outcomes. Based on the present study results, it can be suggested that serum Uric Acid levels can act as a good marker for early detection of pregnancy induced hypertension.

KEY WORDS: Pregnancy Induced Hypertension, serum Uric Acid.**DR. LAXMI NARAYANA S**MD., Asst. Professor, Department of Biochemistry,
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INTRODUCTION

Pre-eclampsia / Eclampsia is a form of hypertensive disorder during pregnancy. It is one of the most potential complications contributing to preterm labour / delivery, perinatal mortality, maternal mortality and morbidity¹, intra-uterine growth retardation (IUGR)^{2,3}, low birth weight infants and many such related problems^{3,4}. Several studies involving estimations of serum Uric Acid, Albumin and Creatinine levels as biochemical markers for the prediction of the subsequent development of Pre-eclampsia, were reported to be performed late in the second and third trimesters of pregnancy when the disease process usually manifests^{5,6}. Among these, Pre-eclampsia / Eclampsia remain one of the largest single causes of maternal and fetal mortality and morbidity, whereas uncomplicated Gestational Hypertension carries a far better prognosis. Over the years, a lot of interest has been directed at studies on the role of serum Uric Acid (SUA), Urea (SU) and Creatinine (SCr) in the pathogenesis of Pregnancy Induced Hypertension (PIH), such as Pre-eclampsia / Eclampsia and Gestational Hypertension. The association between raised serum Uric Acid (UA) levels and Pregnancy Induced Hypertension (Pre-eclampsia / Eclampsia) was first reported almost a century ago⁷. Raised serum Uric Acid (UA) is one of the characteristic findings in Pre-eclampsia. Several studies have reported a positive correlation between elevated maternal serum UA and adverse maternal and fetal outcomes^{8,9,10}. The results of some studies in normotensive pregnant women suggest that serum Uric Acid levels begin to rise before the appearance of hypertension⁵. A number of studies^{11,12,13,14} have evaluated several tests and parameters, including serum UA during the first and second trimester of pregnancy, as potential predictor of Pre-eclampsia, but with mixed results. The serum UA levels were found to be significantly elevated in the pre-eclampsic pregnancies (with reference to the normotensive) in a number of studies^{15,16}. Another study described that there were insignificant changes in the SUA and SCr in both the cited groups¹⁷. It is important therefore, to undertake a detailed study on the aspects of

serum Uric Acid levels and identify women who are at high risk of developing PIH during early pregnancy. This would not only help to facilitate in reducing the risk of Pre-eclampsia / Eclampsia but also help in determining those patients who were more likely to be benefited from interventional measures. Therefore, the present study was aimed to understand and investigate the association / relationship of selected physical and biochemical parameters among pregnant women with hypertension (PIH subjects / Experimental group) and without hypertension (Normotensive / Control group). To achieve this aim, biochemical parameter like serum Uric Acid levels, and physical parameters like age and body weight of the subjects, gestational age and systolic and diastolic blood pressures were estimated both in normotensive pregnant women and pregnancy induced hypertension (PIH) women and further evaluate whether these estimated levels serve as potential predictors of PIH (Pre-eclampsia / Eclampsia). This report is a continuing one to our earlier studies¹⁸.

MATERIALS AND METHODS

The present study was carried out in the Department of Biochemistry, Gandhi Medical College, Secunderabad, A.P. The cases in the present study were selected from the antenatal outpatient, Gandhi Hospital, Secunderabad according to specific criteria like women with age group between 18-24 years, primigravide with known last menstrual period and gestational age between 20-30 weeks. If menstrual history and examination findings were not correlating, ultrasonography was done to find out the exact period of gestation. Those with known hypertension, diabetes mellitus, multiple pregnancy and ultrasound proven congenital malformation in the fetus were excluded. All 54 women included in the present study were subjected to a detailed history taking, systematic examination, obstetric examination and routine antenatal investigations. Among 54 women, 36 were Pregnancy Induced Hypertensive (BP >140/90 mmHg) who were

considered as experimental group and remaining 18 were normotensive (BP <140/90 mmHg) taken as controls. The experimental group was further categorized into three groups, having 12 women in each group, based on the degree of hypertension. The Group-1 was having diastolic blood pressure of 90 to 95 mmHg, the Group-2 with diastolic blood pressure of 96 to 100 mmHg and the Group-3 having diastolic blood pressure more than 100 mmHg.

Collection of samples

Under strict aseptic conditions, 3 ml of venous whole blood sample was collected from each subject in a plain, dry and properly labelled bottle. Precautions were taken to prevent haemolysis. Samples were brought to Clinical Biochemistry Laboratory, Gandhi Hospital and centrifuged after clotting and retraction at room temperature. Clear serum was collected and subsequently analysed for the following parameters: serum Uric Acid. Serum uric acid levels were measured by colorimetric assay.

Statistical Analysis

The data was subjected to descriptive statistical analysis to find out Means and Standard Deviation values and One Way Analysis of Variance (One Way ANOVA) to decipher the intra and inter group variations of the study subjects from both control and experimental groups. In addition, the correlation coefficients were also used for all the groups studied to understand the extent of relationships between the important variables pertaining to physical and biochemical parameters like age, weight, gestational age, systole, diastole and serum Uric Acid. $P < 0.05$ and $P < 0.01$ were considered statistically significant.

RESULTS

The descriptive statistics (Mean and SD) of control group constituting 18 normotensive pregnant women and the total experimental group (n=36) as well as different groups based on the degree of diastolic blood pressure (group-1, 2 and 3) for age, body weight, gestational age, systole, diastole and serum Uric Acid are summarized Table 1.

Table 1
Descriptive statistics of individual clinical data of Control group (n=18) and experimental group (n=36)

Parameter	Control group Mean±Std.	Experimental group Mean ± Std.				P value
		GROUP-I (n=12)	GROUP-II (n=12)	GROUP-III (n=12)	TOTAL (n=36)	
Age	20.7±1.81	22.1±1.78	22.0±2.04	21.9±1.73	22.0±1.80	.976
Weight	46.86±3.3	48.8±1.57	51.4±1.99	52.9±2.29	51.04±2.59	.000
G.Age (Weeks)	26.89±4.13	23.0±1.60	27.3±0.98	31.2±1.03	27.17±3.59	.000
Systole (mmHg)	121.67±7.46	142.0±2.09	142.7±2.15	147.2±2.76	143.9±3.26	.000
Diastole (mmHg)	76.67±5.86	92.3±1.67	96.7±0.98	101.8±1.80	96.9±4.21	.000
SUA (mg/dL)	3.76±0.78	3.48±0.54	4.04±0.39	4.90±0.57	4.14±0.77	.000

G. Age- Gestational age; SUA- serum Uric Acid

Table 2
Correlation coefficients of physical and biochemical parameters
in control group (n=18) and experimental group (n=36)

Parameters	Age	Weight	G Age	Systole	Diastole	SUA
Age	1.000	NS	.508*	.638**	.551*	NS
Weight		1.000	NS	NS	NS	NS
G Age			1.000	.551**	.849**	.514*
Systole				1.000	.942**	NS
Diastole					1.000	NS
SUA						1.000
Experimental group (n=36)						
Age	1.000	NS	NS	NS	NS	NS
Weight		1.000	.714**	.388*	.683**	.593**
G Age			1.000	.738**	.961**	.789**
Systole				1.000	.770**	.632**
Diastole					1.000	.736**
SUA(mg/dL)						1.000

*G Age- Gestational age; *.Correlation is significant at (P < 0.05), **.Correlation is significant at (P < 0.01), NS = Not significant.*

The data of mean age (years), body weight (Kg) and gestational age (weeks) of the control group was found to be 20.7 ± 1.81 , 46.86 ± 3.3 and 26.89 ± 4.13 respectively and that of total PIH group 22.0 ± 1.80 , 51.04 ± 2.59 and 27.17 ± 3.59 respectively. Considering the blood pressure of control group, the mean systole and diastole was observed to be 121.67 ± 7.46 and 76.67 ± 5.86 respectively. Whereas, mean values of experimental PIH group were observed to be relatively higher (143.9 ± 3.26 and 96.9 ± 4.21 respectively) compared to control group. Hence, the control group can be considered as normotensive. The mean values of the biochemical parameter serum Uric Acid was observed to be relatively higher (4.14 ± 0.77) in the experimental PIH group as compared to the mean value (3.76 ± 0.78) in control group. The correlation coefficients pertaining to physical and biochemical parameters of the control and PIH (Experimental) groups are presented in Table 2. It was observed that the age was not significantly correlated with body weight and biochemical parameter serum Uric Acid in control group. However, no significant correlation was observed with any of the parameters studied in the experimental PIH group. Considering the body weight in control group was not significantly correlated with any of the parameters. Whereas, significantly correlated with all the physical as well as biochemical

parameters in the experimental PIH group at 1% level of significance. Considering the systole it was observed to be significantly correlated with age, gestational age and diastole ($P < 0.01$) and not significantly correlated with SUA in the control group whereas, significantly correlated with body weight and all the biochemical parameters like gestational age, diastole, and SUA ($P < 0.01$) in the PIH group. On the other hand diastole was observed to be significantly correlated with age ($P < 0.05$), gestational age and systole ($P < 0.01$) while not significantly correlated with SUA in the control group. Whereas, significantly correlated with all the physical (except age) and biochemical parameters ($P < 0.01$) in the experimental PIH group. Serum Uric Acid was not significantly correlated with any of the parameters (except gestational age) in the control group. However, significantly correlated with all the physical (except age) and biochemical parameter studied ($P < 0.01$) in the experimental PIH group. It was observed that the age was significantly correlated with gestational age, systole ($P < 0.01$) and diastole ($P < 0.05$) and not significantly correlated with the body weight and serum Uric Acid in control group. On the other hand, no significant correlation was observed between age and with any of the parameters studied in the experimental group.

Table 3
Multiple comparisons of different parameters studied in experimental group

Dependent variable	Groups	Mean difference	Std. Error	Sig.
Age (years)	1 & 2	NS	.758	NS
	1 & 3	NS		NS
	2 & 3	NS		NS
Weight (Kg)	1 & 2	-2.667*	.807	.002
	1 & 3	-4.167*		.000
	2 & 3	NS		.072
Gest. Age (Weeks)	1 & 2	-4.33*	.504	.000
	1 & 3	-8.17*		.000
	2 & 3	-3.83*		.000
Diastole (mmHg)	1 & 2	-4.33*	.624	.000
	1 & 3	-9.50*		.000
	2 & 3	-5.17*		.000
Systole (mmHg)	1 & 2	NS	.960	NS
	1 & 3	-5.17*		.000
	2 & 3	-4.50*		.000
SUA (mg/dL)	1 & 2	-.558*	.207	.011
	1 & 3	-1.417*		.000
	2 & 3	-.858*		.000

Table 4
Comparison between controls Vs PIH subjects

	F	Sig.	T	Df	Sig (2-tailed)
Diastole	4.195	.046	14.599	52	.000
Systole	19.749	.000	15.329	52	.000
SUA	.278	.601	1.708	52	.094

*- The mean difference is significant at the 0.05 level

The data subjected to One Way Analysis of Variance of physical and biochemical parameters in the experimental group showed that all the parameters (systole, diastole) were found to be significantly different between the three groups of PIH ($P < 0.001$). Multiple comparisons of different parameters studied in the PIH group are presented in Table 3. It was observed that the mean difference among the three groups of PIH, age did not show any significant difference. On the other hand, highly significant differences were observed in the mean difference of the parameters like weight, gestational age, diastole, serum Uric Acid levels ($P < 0.05$) in all the three groups. Considering the mean difference among the three groups of PIH with regard to systole, highly significant difference was observed between the groups 1 & 3 and 2 & 3 respectively. However, there was no significant difference observed between group 1 & 2 ($P < 0.05$). The data of

comparisons between control and total experimental group of PIH women (Table 4) showed a significant increase in mean systole ($P < 0.01$) and diastole ($P < 0.05$), in experimental group when compared with the control group. Statistical analysis on comparison between controls and individual group of PIH women (groups 1 to 3 of experimental subjects) showed a significant increase in mean values of systole and diastole ($P < 0.01$) in all the three groups of PIH when compared to control group. In the present study, the normotensive pregnant women when compared to total PIH group it was observed that the parameters like systolic and diastolic blood pressures were significantly increased in the PIH group similar to the earlier reports^{19,20}. However, when considering the different groups of PIH, it can be observed that there was a significant increase in systole and diastole as compared to control group. While serum Uric Acid levels had significantly increased only in

the group-3 of the PIH, but not in the group-1 and 2 of PIH. This may be due to the fact that the group-3 of PIH women had the diastolic blood pressure more than 100 mmHg contributing to an increased level of serum Uric Acid production. This observation clearly suggests that as the diastolic blood pressure increases, serum Uric Acid levels also increases, thereby resulting in an increased risk of adverse pregnancy outcomes. This is in accordance with the studies^{21,22}. Hyperuricemia is one of the acknowledged characteristic features of PIH. On the basis of histology findings at renal biopsy PIH was categorized into 3 types of increasing severity²³. Serum Uric Acid levels were found to be increased significantly in PIH and hyperuricemia is associated with the severity of PIH and foetal outcome²⁴. Tubular dysfunction is associated with Hyperuricemia²⁵ due to increased reabsorption of Uric Acid, which is coupled with tubular sodium reabsorption. It has been proposed that the Hyperuricemia is of benefit as it acts as an antioxidant²⁶. Elevated serum Uric Acid levels in maternal blood may be due to altered renal handling of urate in PIH women which depends on the severity of Hypertension. Serum Uric Acid levels determined at 24 weeks gestation, might predict the subsequent development of PIH. Hyperuricemia is a valuable marker to differentiate PIH from all other causes of

hypertension during pregnancy where decrease in uric acid clearance does not occur. Therefore, an increased level of Uric Acid reflects the disease severity in PIH and fetal outcome. Uric Acid is an antioxidant and its increased levels is of benefit and potentially important. Therefore, high serum Uric Acid levels act as both marker of PIH and also act as a protective agent against free radicles. Finally, based on the results of the present study and the observations made by several other researchers as described above, it is suggested that the serum Uric Acid levels can act as good marker for early detection of PIH, thereby helps to initiate early treatment so as to minimize and/or avoid the adverse effects of PIH.

CONCLUSION

Finally, it can be concluded that the serum Uric Acid levels can act as "Potential Markers" for early detection of PIH, thereby helping in initiating early treatment to minimize / avoid the complications of PIH. In this direction, it is also opined that, further studies on larger population are needed to understand in detail the mechanisms / interactions between these biochemical molecules in the development of Pregnancy Induced Hypertension.

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