A LONGITUDINAL STUDY OF SERUM URIC ACID LEVEL IN NORMAL PREGNANCY AND PREGNANCY INDUCED HYPERTENSION AMONG PATIENTS ATTENDING ANTENATAL OUTPATIENT DEPARTMENT OF GAUHATI MEDICAL COLLEGE, GUWAHATI

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ABSTRACT: AIMS AND OBJECTIVES: To estimate serum uric acid level in normal pregnancy and pregnancy induced hypertension at different duration as pregnancy advances and to evaluate its place in determining severity of pregnancy induced hypertension. MATERIALS AND METHODS: A longitudinal study was carried out among forty cases of normal pregnancy and forty cases of pregnancy induced hypertension attending antenatal outpatient department of Gauhati Medical College and Hospital. Serum uric acid level was estimated colorimetrically by using Uricase method in the Department of Physiology, Gauhati Medical College. Statistical analysis was carried out applying ANOVA test using IBM SPSS 16. RESULTS: Serum Uric Acid level was found to be significantly higher in study group as compared to control group. The mean values of serum uric acid level in study group were 4.07 mg/dl, 4.44 mg/dl and 5.27mg/dl as compared to 3.14mg/dl, 3.11mg/dl and 3.71mg/dl in control group at 20-24 weeks, 24-28 weeks and 32-40 weeks of gestation respectively. Also, the level of serum uric acid was found to be increased with increasing severity of pregnancy induced hypertension. CONCLUSION: A definite rise in serum uric level was found in cases of pregnancy induced hypertension and its level increases with increasing severity of the disease. KEYWORDS: Uric acid, Antenatal, Gestation, Pregnancy induced hypertension.

INTRODUCTION: Pregnancy is a physiological process which can become pathological or high risk when it is associated with various medical or surgical complications. Hypertension is one of the common complications met with in pregnancy and contributes significantly to the cause of maternal and perinatal morbidity and mortality. Hypertension is a sign of underlying pathology, which may be preexisting or appears for the first time during pregnancy. Identification of this clinical entity and its effective management play a significant role in the outcome of pregnancy, both for the mother and the baby. Cunningham et. al.[1] describe hypertension in pregnancy as a major cause of maternal and perinatal morbidity and mortality. Hypertension is a sign of underlying pathology, which may be preexisting or appears for the first time during pregnancy. Identification of this clinical entity and its effective management play a significant role in the outcome of pregnancy, both for the mother and the baby. Cunningham et. al.[1] describe hypertension in pregnancy as a major cause of maternal and perinatal morbidity, complicating 5-10% of all pregnancies worldwide whereas pregnancy induced hypertension has been identified in 3.9% of all pregnancies. Pregnancy induced hypertension being the type of hypertensive disorder that develops as a direct result of gravid state. It is characterized by hypertension, edema or proteinuria or both induced by pregnancy after 20th weeks of gestation.[2]

It is synonymous with preeclampsia and eclampsia. Hypertension during pregnancy can be classified into: 1) Preeclampsia-eclampsia, 2) Chronic hypertension, 3) Chronic hypertension with superimposed preeclampsia and 4) Gestational hypertension.[3]

Early feature of Pregnancy induced hypertension is reduced renal clearance of uric acid causing its rise in plasma. Over years, a lot of interest has been directed at studies on the role of serum uric acid in the pathogenesis of PIH, such as preeclampsia.[4] Estimation of serum uric acid is a simple procedure
and it is a diagnostic test.[5] Farah Saleh in his study serum uric acid as predictor model for pre-eclampsia found that the study was in accordance with international literature confirms the clinical utility of serum uric acid as a marker with high predictive value to detect cases of gestational hypertension progressing to pre-eclampsia.[6]

In our study, left radial arterial blood samples were collected from forty normal pregnant women and forty pregnant women with pregnancy induced hypertension at 20-24 weeks, 24-28 weeks and 32-40 weeks of gestation. Serum uric acid level was estimated calorimetrically by using Uricase method. Serum uric acid level was found to be elevated with advancing gestation in study group.[7] Also, there was a positive correlation between elevated serum uric acid level and pregnancy induced hypertension.[8,9]

MATERIALS AND METHODS: Type of study – Longitudinal study.

Study Procedure: 2ml of radial arterial blood was collected from normal pregnant women (control group) and pregnant women with pregnancy induced hypertension (study group) at 20-24 weeks, 24-28 weeks and 32-40 weeks of gestation and anticoagulated with EDTA.

Serum uric acid level of each was estimated calorimetrically by using Uricase method.
Blood pressure was measured in supine position by using Sphygmomanometer. Phase 1 and IV sound were taken as Systolic and Diastolic blood pressure respectively.

Proteinuria was measured by dipstick (+++ or more was considered as significant proteinuria).

Sample Size: Forty pregnant women with pregnancy induced hypertension constitute the ‘study group’ and forty cases of normal pregnancy constitute the ‘control group’.

Inclusion Criteria: Pregnant women suffering from pregnancy induced hypertension (Blood pressure≥140/90mm Hg and/or proteinuria) during 20-28 weeks of gestation or later on during follow up till term were selected in the ‘study group’ against subjects without those complications constituting the ‘control group’.

Exclusion Criteria: Cases with heart disease, diabetes mellitus, severe anemia, hydatidiform mole, Rh–ve women, multiple pregnancy, hemoglobinopathy, sexually transmitted disease were excluded from the study.

Data Collection Procedure: Relevant information of the pregnant women was obtained by examining them in the antenatal outpatient department and results obtained from estimation of serum uric acid were recorded.

Instruments: For estimation of serum uric acid, Photo colorimeter, Centrifuge machine, pipettes, test tubes, Uric acid kit (Coral) were used. For recording Blood Pressure, Sphygmomanometer was used. Proteinuria was measured by dipstick.

Quality Control: The instruments to be used for study were checked for quality control before doing the study.

Plan of Analysis: The statistical analysis was carried out by applying ANOVA test using IBM SPSS 16.
Ethical Considerations: Permission to carry out the study was obtained from the Head of the departments of Physiology and Obstetrics and Gynecology, Gauhati Medical College and Hospital. Consents were taken from the participants by signing in the previously prepared Informed Consent Form.

OBSERVATIONS AND RESULTS: Our study comprised of 80 pregnant women between age group of 18 - 35 years attending antenatal outpatient department during 20-28 weeks of gestation. Out of the 80 cases selected for study, 40 cases of pregnancy induced hypertension constitute the ‘study group’ while 40 cases of normotensive pregnancy constitute the ‘control group’. The cases were followed from 20 weeks of gestation at monthly interval up to term for estimation of serum uric acid level. Blood pressure level of ≥ 140-90 mm of Hg was considered as hypertensive. Proteinuria of +++ or more was considered significant.

Serum uric acid level was found to be significantly higher in study group as compared to control group (P<0.000). This is shown in Table 1.

| Weeks of Gestation | Control Group | Study Group | P value |
|--------------------|---------------|-------------|---------|
|                    | Mean | SD | Mean | SD |                     |
| 20-24 weeks        | 3.14* | 0.06 | 4.07 | 0.52 | <0.000              |
| 24-28 weeks        | 3.11** | 0.48 | 4.44 | 0.53 | <0.000              |
| 32-40 weeks        | 3.71*** | 0.17 | 5.27 | 0.59 | <0.000              |
| P value            | Between * & ** >0.05 | Between ** & *** <0.000 | < 0.000 between all groups |

Table 1: Showing the Mean Serum Uric Acid level in both study and control groups at different weeks of gestation.

Similar study was conducted by Dr. Habibunnisha B. Sirajwala found mean serum uric acid levels in pre-eclampsia was 7.52± 0.77 mg/dl as compared to 3.70±0.94 mg/dl in controls.[10]
Among the study group, 18 cases were found to belong to severe and 22 cases were of mild variety of pregnancy induced hypertension. Mean serum uric acid levels in mild variety of PIH were 3.74±0.41, 4.12±0.46 and 4.87±0.44 as compared to 4.47±0.34, 4.81±0.32 and 5.75±0.34 in severe PIH at 20 - 24 weeks, 24 - 28 weeks and 32 - 40 weeks of gestation respectively. This is shown in Table 2.

| Weeks of gestation | Control | Mild PIH | Severe PIH | Total cases |
|--------------------|---------|----------|------------|-------------|
| 20-24 Weeks        | 3.14    | 3.74     | 4.47       | 4.07        |
| 24-28 Weeks        | 3.11    | 4.12     | 4.81       | 4.44        |
| 32-40 Weeks        | 3.71    | 4.87     | 5.75       | 5.27        |

Table 2: Serum Uric Acid level in both mild and severe PIH at different weeks of gestation

Serum uric acid level in control group was found to remain below 4mg/dl during middle and late pregnancy, whereas the level rose from 4.04mg/dl to 5.27mg/dl in study group. Ravi I. Thadhani et al. in their study found that serum uric acid usually falls to levels well below 4mg/dl during early to middle pregnancy, but in patients with pre-eclampsia, levels often rise to more than 4.5mg/dl.[11]
**DISCUSSION:** In this study, serum uric acid level in the study group was found to be significantly higher than in the control group and is comparable to that of the studies which showed serum uric acid level to be higher in pregnancy induced hypertension.[12]

Mean serum uric acid level in severe Pregnancy induced hypertension was found to be 5.75 mg/dl and that in control group was 3.71 mg/dl (during 32-40 weeks of gestation), showing a definite rise (2.04 mg/dl) in severe PIH.[13] Mean serum uric acid level in mild Pregnancy induced hypertension was found to be 4.87 mg/dl and that in control group was found to be 3.71 mg/dl (during 32-40 weeks of gestation) showing slight increase (1.16 mg/dl) in mild PIH.

Mean serum uric acid level in mild PIH was found to be 4.87 mg/dl as compared to 5.75 mg/dl in severe PIH. This shows that when severity of Pregnancy induced hypertension increases, serum uric acid level also increases. This is supported by Sanjay Gupta and Girija Wagh showing uric acid as a marker of severity of disease at both renal and placental levels.[14]

**CONCLUSION:** Our study shows a definite rise of serum uric level in pregnancy induced hypertension as compared to normal pregnancy. There was a significant rise of serum uric acid level in mild and severe pregnancy induced hypertension. Since serum uric acid level increases with increasing severity, it can be used for diagnosing severity of pregnancy induced hypertension.[15] However, single random estimation of serum uric acid cannot be relied upon for diagnosis of pregnancy induced hypertension and its severity. Only serial estimation of serum uric acid at frequent intervals with rising titer can be useful. As there is early and definite rise of serum uric acid level in preeclampsia,[16,17] it can be used as an early diagnostic tool and there is obvious scope for further study on this observation.

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