



CORRELATION OF SERUM URIC ACID LEVELS WITH MATERNAL AND PERINATAL OUTCOMES IN ANTENATAL FEMALES WITH PREGNANCY INDUCED HYPERTENSION

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Hypertensive disorders are the most common medical complications of pregnancy rampant globally. Of the Hypertensive disorders of pregnancy, preeclampsia complicates 2-8% of all pregnancies. Kidneys are the most commonly affected organ and hyperuricaemia is the earliest indication of a change in renal function and predates the onset of heavy proteinuria and severe hypertension. **Material And Methods:** 150 cases with pregnancy induced hypertension admitted in department of Obstetrics and Gynaecology, SRMSIMS, Bareilly from November 2018-May 2020 were studied for correlation of rising levels of serum uric acid with maternal and fetal outcomes and the severity of disease progression was observed. **Results:** Majority of the antenatal women among the study population were unbooked primigravidas with mean age 24.9 ± 4.5 years and 10.7% women had family history of hypertension. Maternal outcomes in respect to abnormal fundoscopy, abnormal liver and renal function tests were more deranged when serum uric acid concentration was above 5.5 mg/dL and this was statistically significant. Similarly, there was a statistically significant difference when fetal parameters were studied in terms of APGAR at <7 mins, NICU admission, intrauterine fetal demise, prematurity and low birth weight with significant p value of 0.0053, 0.0152, 0.0024, 0.0415 and 0.0105 respectively at serum uric acid concentrations of <3.5, 3.5-5.5 and >5.5 mg/dL. **Conclusion:** Serum uric acid levels in patients with preeclampsia are associated with severity of the disease. Higher serum uric acid levels in pregnancy induced hypertension indicates heightened risk of progression to adverse maternal and perinatal outcomes.

KEYWORDS

Preeclampsia, Uric acid concentration, Maternal and Fetal outcomes.

INTRODUCTION

Hypertensive disorders are the most common medical complications of pregnancy rampant globally and despite various advancement in health-care, still remain the leading cause of maternal and perinatal morbidity and mortality worldwide.¹ It is estimated that over 63,000 women and 500,000 babies worldwide die annually from preeclampsia.²

Of the Hypertensive disorders of pregnancy, preeclampsia complicates 2-8% of all pregnancies.³ It is a multisystem disorder leading to widespread endothelial dysfunction affecting almost all the vessels, particularly those of uterus, kidney, liver, placental bed and brain. Kidneys are the most commonly affected organ and 'glomerular endotheliosis' is the characteristic lesion seen in patients of preeclampsia.⁴

Because of the serious consequences of this syndrome, it becomes a challenge to screen antenatal patients for risk of developing pregnancy induced hypertension and predict the disease progression. Till date, several biomarkers like antiangiogenic factors such as soluble fms-like tyrosine kinase-1 and soluble endoglin, pro-angiogenic factors such as vascular endothelial growth factor and placenta growth factor have been identified make an early diagnosis. However, the choice of a biomarker should not only be related to its biological characteristics and its participation in the pathogenesis of the disease, but also to the feasibility of being used as a screening tool. A marker that requires complex technology and does not show a positive cost-benefit would be inapplicable especially in low income countries.

Uric acid is the final metabolite in the process of purine metabolism during the breakdown of DNA, RNA and ATP, produced by enzyme Xanthine Oxidase/Xanthine dehydrogenase and excreted mainly in urine. It is mainly metabolized by kidneys, accounting upto 70% of daily excretion. It is freely filtered by glomeruli, with reabsorption and secretion in proximal convoluted tubule of the kidney.

Due to physiological changes in pregnancy, glomerular filtration rate and renal plasma flow increase by 50% after conception. Serum uric acid concentration initially falls upto 16 weeks gestation by 25-30%, due to increase in renal clearance, secondary to increased glomerular filtration rate and reduced proximal tubular reabsorption, then stabilizes, between 17 to 28 weeks of pregnancy. In third trimester, Serum Uric acid level increases due to increase in fetal production,

decreased binding to albumin and a decline in uric acid clearance.⁵ The normal serum uric acid in the third trimester is 4-6 mg/dl (237.9 – 356.9 $\mu\text{mol/l}$).⁶

Serum uric acid levels are raised in women with hypertensive pregnancies due to fetal production, impaired clearance from kidneys, increased tissue breakdown, acidosis, increased oxidative stress and increased activity of xanthine oxidase enzyme causing more conversion of xanthine to uric acid.⁷ Also, due to the interaction of uric acid with proinflammatory cytokines, increased levels of uric acid in the plasma of patients with preeclampsia may indicate a direct contribution to the pathophysiology of this syndrome by its ability to promote inflammation.⁸

Hyperuricaemia is the earliest indication of a change in renal function and predates the onset of heavy proteinuria and severe hypertension.⁹ The purpose of this study is to compare the rising levels of serum uric acid levels with maternal and fetal outcomes in antenatal women with pregnancy induced hypertension and to predict the severity of disease progression. This is an effort to screen the various high risk pregnancies for hypertensive disorders and thereby reduce the morbidity and mortality related to it.

AIM

To study the correlation of rising levels of serum uric acid levels with maternal and fetal outcomes in antenatal women with pregnancy induced hypertension and to predict the severity of disease progression.

MATERIAL AND METHODS

This was a prospective case study conducted in the department of Obstetrics and Gynaecology, Shri Ram Murti Institute of Medical Sciences, Bareilly on 150 women diagnosed with pregnancy induced hypertension attending the antenatal clinic (out-patient department) and those admitted in the ward and labour room from November 2018-May 2020. Ethical clearance was obtained from Institutional ethical committee.

Inclusion Criteria:

- Singleton pregnancy.
- Gestation age >20 weeks. Gestational age was calculated from the first day of the last menstrual period.
- All patients diagnosed to have systolic blood pressure ≥ 140 mm

Hg and/or diastolic blood pressure ≥ 90 mmHg on at least two occasions 4 hours apart taken using an appropriate sized cuff and Korotkoff phase - V (disappearance of sound as diastolic blood pressure).

Exclusion Criteria

1. History of chronic hypertension and proteinuria before conception or development of hypertension before 20 weeks of gestation.
2. Patients with chronic renal disease.
3. Patients with history of recurrent urinary tract infection.
4. Molar pregnancy.
5. Multiple pregnancies.
6. Patients with associated liver dysfunction.
7. Patients who delivered before completion of collection of 24-hour urine sample.

Serum uric acid levels were drawn intravenously at the hospital after each patient had rested for 30 minutes and the samples were sent to the chemical pathology laboratory. The study population was divided into 3 groups based on the levels of serum uric acid (group 1: <3.5 mg/dL, group 2: 3.5 - 5.5 mg/dL and group 3: >5.5 mg/dL). The results were analysed on software IBM SPSS version 20.0.

OBSERVATIONS

Majority patients in the study population were primigravida belonging to low socio-economic status wherein 56% cases were term pregnancies. 42% of patients were preterm, and only 2% of total cases were post term. 46% women had serum uric acid concentration > 5.5 mg/dL with mean age 23.1 ± 2.5 years and BMI 25.8 ± 2.9 kg/m². Majority cases were unbooked (62.7%) and 10.7% women had family history of hypertension.

Demographic variables	Serum Uric Acid (mg/dL)		
	< 3.5	$3.5 - 5.5$	> 5.5
Age (years)	24.6 ± 4.2	22.9 ± 3.1	23.1 ± 2.5
Body Mass Index (kg/m ²)	21.9 ± 3.7	23.7 ± 1.5	25.8 ± 2.9
Parity	Second gravida (25.6%)	Primi (27.9%)	Primi (29.4%)
Socioeconomic status	Low (10.7%)	Low (18.5%)	Low (21.5%)

48% patients had mild preeclampsia and 52% had severe preeclampsia. Organ affection was seen more in cases of severe preeclampsia as compared to mild preeclampsia. Abnormal funduscopy was seen in 29.45% cases of severe pre-eclampsia whereas only 5.56% of mild preeclampsia had abnormal fundal changes. Similarly, liver function tests and renal function tests were deranged in 92.30% and 97.43% respectively in severe preeclampsia. The p-value were statistically significant in all cases.

Among all the cases with abnormal funduscopy, 55.6% had serum uric acid concentration > 5.5 mg/dL. Similarly, the laboratory parameters for liver function tests and renal function tests was deranged more with higher uric acid concentration i.e. 66.7% and 78.7% women respectively and this was statistically significant with p value of 0.0472. The values for mean serum bilirubin, SGOT, SGPT and serum alkaline phosphatase among cases with serum uric acid concentration > 5.5 mg/dL was 2.49 ± 1.62 mg/dl, 159 ± 87.9 IU/L, 157 ± 65.2 IU/L and 229 ± 68.3 IU/L respectively and this was statistically significant with p value of 0.00218.

Organ Dysfunction	Serum Uric Acid (mg/dL)			p Value
	< 3.5	$3.5 - 5.5$	> 5.5	
Abnormal Funduscopy (n=27)	3 (11.1%)	9 (33.3%)	15 (55.6%)	0.0125
Deranged LFT (n=96)	10 (10.4%)	22 (22.9%)	64 (66.7%)	0.0095
Deranged KFT (n=127)	12 (9.5%)	15 (11.8%)	100 (78.7%)	0.0182
P Value	0.0472			

A statistically significant change in renal function test (p value 0.0152) were observed among patients of preeclampsia. The values for mean serum urea and serum creatinine among cases with serum uric acid concentration > 5.5 mg/dL was 31.49 ± 1.45 mg/dl and 2.12 ± 0.8 IU/L. Among the study population, 95.33% cases pregnancy was terminated while 4.67% were managed conservatively. Only 4 out of 150 cases had antepartum eclamptic fits. No case of postpartum eclampsia was

noted. 48.95% underwent vaginal delivery against 51.04% cases who underwent cesarean section. No statistically significant result was found while comparing the type of labor (p Value = 0.2048).

Maternal Complications	Serum Uric Acid (mg/dL)			p Value
	< 3.5	$3.5 - 5.5$	> 5.5	
Post Partum MgSO ₄ (n=15)	0	1 (6.7%)	14 (93.3%)	0.00695
Post Partum Hemorrhage (n=5)	1 (20.0%)	2 (40.0%)	2 (40.0%)	0.0125
Admission to ICU (n=4)	0	1 (25.0%)	3 (75.0%)	0.00512
Mortality (n=0)	0	0	0	0

No case of post partum MgSO₄ and ICU admission was observed at serum uric acid concentration < 3.5 mg/dL while at levels above 5.5 mg/dL 93.3% cases required postpartum MgSO₄, 40% cases had postpartum haemorrhage and 3 cases were admitted to ICU for management and this difference was statistically significant. No mortality was observed in either group.

Fetal Complications	Serum Uric Acid (mg/dL)			p Value
	< 3.5	$3.5 - 5.5$	> 5.5	
APGAR < 7 at 5 mins (n=59)	6 (10.2%)	16 (27.1%)	37 (62.7%)	0.0053
NICU Admission (n=12)	1 (8.3%)	3 (25.0%)	8 (66.7%)	0.0152
IUFD (n=18)	2 (11.1%)	5 (27.8%)	11 (61.1%)	0.0024
Prematurity (n=46)	5 (10.9%)	7 (15.2%)	34 (73.9%)	0.0415
Low Birth Weight (n=76)	10 (13.1%)	12 (15.8%)	54 (71.1%)	0.0105

16% babies had birth weight < 2 kg, 37% babies has birth weight between 2 - 2.5 kg and 47% had birth weight > 2.5 kg. Among these 87% were live births while 13% were documented to be intrauterine fetal demise.

There was a statistically significant difference when fetal parameters were studied in terms of APGAR at < 7 mins, NICU admission, intrauterine fetal demise, prematurity and low birth weight with significant p value of 0.0053, 0.0152, 0.0024, 0.0415 and 0.0105 respectively at serum uric acid concentrations of < 3.5 , 3.5 - 5.5 and > 5.5 mg/dL.

DISCUSSION

In our study, we found that with increase in serum uric acid concentration the frequency of organ involvement increases. Similarly, adverse fetal outcomes were observed at uric acid concentration > 5.5 mg/dL.

Yuquan et al. (2023), in a retrospective cohort study of 249 singleton pregnant women observed that increased serum uric acid level was associated with 2.3-fold increased odds of progression to preeclampsia and 1.5-fold increased odds of developing clinically significant adverse maternal or infant conditions (aOR 1.49 (1.03–2.17)).¹⁰

In another study by Corominas et al. (2022), it was reported that uric acid level at cut-off point ≥ 1.5 had a very low positive predictive value, but a high negative predictive value of 99.5% for preeclampsia and thus concluded that Uric acid level less than 1.5 may be a helpful parameter with a strong exclusion value and high sensitivity for those women who are not expected to develop preeclampsia.¹¹ Ugwuany et al. (2021), reported that females with elevated serum uric acid levels (> 6 mg/dL) were found to be 4 times more likely to have severe preeclampsia (P = 0.022, OR = 4.00, 95% CI = 1.225–13.056), 66 times more likely to have APGAR score < 7 in the first minute (P < 0.001, OR = 66.00, 95% CI = 6.991–623.128), and 3 times more likely to have lower birth weight (P = 0.038, OR = 3.400, 95% CI = 1.073–10.775) than those with normal serum uric acid levels.¹²

Singh A et al (2014), in their study on 126 cases of hypertensive disorders of pregnancy a study, found Fifty seven women with serum uric acid level < 5.5 mg% (Group A) and 43 with serum uric acid level ≥ 5.5 mg% (Group B). In those developing hyperuricemia 54.81% had mild hypertension, 40.91% had severe hypertension. Adverse perinatal outcome with serum uric acid level ≥ 5.5 mg/dl had stillbirth in 7%, had low birth weight in 27.9%, 11.6% were admitted in special care baby unit and 18.6% had APGAR < 7 at five minute, concluded that Perinatal morbidity and mortality was increased in women with raised uric acid level.¹³

On the other hand, Nischintha et al. (2014) concluded direct correlation between serum uric acid and spot urine protein-creatinine ratio, but observed no statistically significant difference between proteinuria and hyperuricemia with respect to the various fetal and maternal outcome parameters.¹⁴

CONCLUSION

There is significant association between serum uric acid levels in preeclampsia with perinatal outcomes. Since the level of serum uric acid has been seen to have considerable clinical implications in the course of pregnancy and on maternal and perinatal outcomes, the early detection of even minor degree of raised serum uric acid level is important to improve both maternal and fetal morbidity and mortality. Serum uric acid levels in patients with preeclampsia are associated with severity of the disease. Higher serum uric acid levels in pregnancy induced hypertension indicates heightened risk of progression to adverse maternal and perinatal outcomes. However, our being a very small study, large randomized control trials are needed before establishing its efficacy as predictor of adverse maternal and fetal outcomes.

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