

ANALYSIS OF SERUM URIC ACID LEVELS IN EARLY SECOND TRIMESTER AS AN EARLY PREDICTOR FOR PREECLAMPSIA

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ABSTRACT

BACKGROUND

Hypertensive disorders complicate 5-10% of all pregnancies. Screening for these factors in the second trimester of pregnancy will help in early detection of hypertensive disorders of pregnancy, thus enabling.

1. Early identification of patients at risk of developing preeclampsia and eclampsia.
2. Prophylactic medication to prevent hypertension or to reduce its severity.
3. Proper antenatal care.

The aim of the study is to study the accuracy of serum uric acid levels in early second trimester (14-20 weeks) as early predictor of preeclampsia.

MATERIALS AND METHODS

100 pregnant normotensive women between 14-20 weeks gestation with singleton pregnancy irrespective of parity were selected randomly and serum levels of uric acid was estimated. Regular follow up of the cases was done till delivery. Number of cases developing preeclampsia was noted. Results were analysed statistically.

RESULTS

Out of the 100 patients enrolled in the study, 11 developed preeclampsia while rest 89 remained normotensive. Mean value of uric acid in preeclampsia cases was 6.28 ± 0.86 mg/dL while that in normotensive cases was 3.42 ± 0.94 mg/dL. This result was statistically significant.

CONCLUSION

Serum uric acid level at 14-20 weeks of gestation was significantly raised in the cases who developed preeclampsia as compared to those who remained normotensive. Hence, serum uric acid estimation at 14-20 weeks of gestation could be used as an effective parameter for predicting preeclampsia.

KEYWORDS

Preeclampsia, Uric Acid, Hypertension, Haemorrhage.

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BACKGROUND

Hypertensive disorders complicate 5-10% of all pregnancies. The deadly triad of hypertensive disorders, haemorrhage and infection contribute greatly to the maternal morbidity and mortality.¹ The World Health Organization (WHO) systematically reviews maternal mortality worldwide, 16% of maternal deaths were reported to be due to hypertensive disorders. This proportion is greater than three other leading causes that include haemorrhage-13%, abortion-8% and sepsis-2%.

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The hypertensive disorders of pregnancy cover a spectrum of conditions, of which preeclampsia poses the greatest potential risk and remains one of the most common causes of maternal death.² Preeclampsia is a multisystem disorder of pregnancy. The cardinal clinical features of the condition are hypertension and proteinuria occurring after 20 weeks gestation in women who were not previously known to be hypertensive.³

Hypertension during pregnancy is defined as a systolic blood pressure of 140 mmHg or more or diastolic blood pressure of 90 mmHg or more on two occasions at least 6 hours apart, but within 7 days.⁴

Proteinuria is defined as 24-hour urinary protein excretion ≥ 300 mg or persistent 30 mg/dL (1+dipstick) protein in random urine sample or urine protein-creatinine ratio ≥ 0.3 .⁵

Measurement during early pregnancy or across pregnancy of various biological, biochemical and biophysical markers implicated in preeclampsia syndrome. Pathophysiology has been proposed to predict its



development later in pregnancy. Most of these have resulted in testing strategies with poor sensitivity and with poor positive predictive value for preeclampsia.⁶ Currently, no screening tests are predictably reliable, valid and economical.⁷

Uric Acid During Pregnancy

Uric acid is a product of purine degradation catalysed by the enzyme xanthine dehydrogenase/xanthine oxidase (XDH/XO).⁸ Its concentrations are influenced by diet (i.e., high protein and fructose), alcohol consumption, increased cell turnover, enzymatic defects in purine metabolism or altered kidney function.⁹ In pregnancy, uric acid concentrations initially fall 25-35% due to the effects of oestrogen, expanded blood volume and increased glomerular filtration rate.¹⁰ However, concentrations slowly rise to those observed in nonpregnant women by term gestation (4-6 mg/dL).¹¹

One of the earliest laboratory manifestations of preeclampsia is hyperuricaemia.¹¹ It likely results from reduced uric acid clearance from diminished glomerular filtration, increased tubular reabsorption and decreased secretion.⁷ It is used by some to define preeclampsia, but Crossen and coworkers¹² reported that its sensitivity ranged from 0 to 55% and specificity was 77 to 95%.

Hyperuricaemia is a common finding in preeclampsia. The elevation of uric acid in preeclamptic women often precedes hypertension and proteinuria.¹³ There are several potential origins for uric acid in preeclampsia, abnormal renal function, increased tissue breakdown, acidosis and increased activity of the enzyme xanthine oxidase/dehydrogenase.¹⁴

The increase in uric acid level appears to coincide with the increase in the blood pressure and precede the development of proteinuria. Uric acid levels have been used for early diagnosis of preeclampsia. A disproportionate fall in uric acid clearance is a key feature of preeclampsia. The serum level of uric acid rises as preeclampsia progresses; a level >5.5 mg/dL is a strong indicator of the disease and a level >7.8 mg/dL is associated with significant maternal morbidity.¹⁵

The degree of uric acid elevation correlates with the severity of proteinuria and renal pathological changes and with foetal demise.

RESULTS

Variables	Mean±S.D.		Total	T value	P value
	Normotensive	Preeclampsia			
Age in Years	25.07±2.91	24.82±3.68	25.04±2.98	0.2609	0.7947
BMI (kg/m ²)	22.52±2.33	21.49±1.50	22.41±2.27	1.2884	0.2006

Table 1. Characteristics of Patients

Mean age among preeclampsia group is 24.82 years and mean BMI in this group is 21.49 kg/m². Normotensive group has mean age of 25.07 years and BMI of 22.52 kg/m². Comparison of the age and BMI for both preeclampsia and normotensive groups are almost alike.

AIMS AND OBJECTIVES

- Study of serum uric acid in early second trimester as early predictor of preeclampsia.
- To find out its sensitivity and specificity of alteration of serum uric acid levels in early second trimester of pregnancy as a parameter for preeclampsia in later part of pregnancy.

MATERIALS AND METHODS

This study was conducted in Department of Obstetrics and Gynaecology in MVJ Medical College and Research Hospital, Hoskote, Bangalore, from October 2014 to August 2016 over a period of 2 years on 100 pregnant normotensive and non-proteinuric women selected randomly between the gestational age of 14-20 weeks attending the ANC clinics, irrespective of parity. Patients were selected as per inclusion and exclusion criteria.

All the women were subjected to detailed history regarding age, parity, past obstetric history, menstrual history, medical history, drug history and family history. Height, weight and blood pressure were measured. Routine antenatal investigation was done.

Uric acid was measured using a colorimetric assay (Pointe Scientific Inc.) kit U7581-120 using uricase. Statistically analysed by Student's 't' test and significance was expressed in term of 'P' value (p <0.001). The cases were followed up in antenatal clinic and were examined 4 weekly till 28 weeks, fortnightly up to 36 weeks and thereafter weekly till delivery.

A p-value of 0.05 or less was considered for statistical significance. SPSS version 16 software was used for all the analysis.

Inclusion Criteria

- Primi/multigravida with singleton pregnancy with gestational age 14-20 weeks.
- All selected patients between age group of 18-35 will be screened for serum uric acid in their early second trimester (14-20 weeks) and will be followed up till delivery.

Exclusion Criteria

- Multiple pregnancy.
- Women with history of medical, metabolic and renal diseases.

Variables	Groups		Total	T value	P value
	Normotensive	Preeclampsia			
SBP on 1 st visit	111.24±9.27	110.00±8.94	111.10±9.20	0.42	0.6754
DBP on 1 st visit	70.45±5.42	68.18±6.03	70.20±5.50	1.2948	0.1984
SBP at delivery	114.94±9.06	152.73±6.47	119.1±14.78	13.3899	<0.0001 HS
DBP at delivery	75.84±5.18	97.27±9.05	78.2±8.81	11.7705	<0.0001

Table 2. Comparison of Mean±SD of Systolic and Diastolic Blood Pressure (mmHg) between Preeclampsia and Normal Group

Comparison of blood pressure at time of booking (14-20 weeks) between preeclampsia and the normotensive group did not vary significantly. Blood pressure for preeclampsia cases at the time of delivery was significantly higher in comparison to the B.P. of the normotensive group. This is true for both diastolic and systolic blood pressure.

Serum Uric Acid (Mean±SD)	Normotensives (N=89)	Preeclampsia (N=11)	Total N=100	P-value
	3.42±0.94	6.28±0.86	3.74±1.12	<0.0001 highly significant

Table 3. Mean Uric Acid Concentration among Normotensives and Preeclampsia Group

Mean SD value for normotensives is 3.42±0.94 and for preeclampsia group is 6.28±0.86, which was highly significant.

DISCUSSION

Uric acid is one of the good predictor of hypertensive disorders in pregnancy and can be of great help in predicting the disease. In preeclampsia, uric acid level increases in pregnancy, so predicting the value can help to correlate with maternal and foetal morbidity and always it has been proved to be a reflection of disease rather than a cause and it has antioxidant properties that protects from oxidative stress, contributes directly to endothelial dysfunction by its proinflammatory effects, as well as to hypertension during preeclampsia.

Uric acid is the end product of purine catabolism catalysed by the enzyme xanthine oxidase/dehydrogenase. The oxidase form of the enzyme producing uric acid and superoxide will be increased proportionally with hypoxia. Thus, increased uric acid production occurs in a setting of hypoxia, local acidosis or increased tissue breakdown or with reduced renal function and can increase oxidative stress- all of which would indicate more severe preeclampsia.¹⁶ Uric acid is also found to be associated with carotid atherosclerosis and its increase is an independent risk factor for cardiovascular diseases, which mediate altered vascular function and inflammation. Its elevation maybe due to imbalance between oxygen free radicals and NO.¹⁷ Because uric acid is also known to have antioxidant activity in the serum, its level may rise as a compensatory mechanism to counteract the increased oxidative stress under the conditions of metabolic syndrome or atherosclerosis.

CONCLUSION

Serum uric acid levels were significantly higher in preeclampsia and could be a useful indicator of the maternal and foetal complication in hypertensive patients. Despite the existence of many different potential markers for preeclampsia, the reliability of these markers in predicting preeclampsia has been inconsistent between different studies. Furthermore, preeclampsia is a

multifaceted disorder, certain say it is not one, but several diseases. Therefore, there is a need for high quality, large scale multicenter trials, which enrol patients with different risks of developing the syndrome and throughout multiethnic background in order to assess the predictive value of different markers and finally propose the best marker combination for a routine use in clinical settings.

This study shows that hyperuricaemia (serum uric acid >5.5 mg/dL) in midtrimester of pregnancy is highly significant in predicting the development of preeclampsia (p=0.010) later. Lancet et al had also concluded that mean serum uric acid values (5.5 mg/dL) were significantly higher in women with preeclampsia compared to controls. High BMI (>23 kg/m²) was found to be highly significant (p=0.2006) predictor of preeclampsia in our study. Raised diastolic pressure (80-90 mmHg) was not statistically significant (p=0.117) predictor of preeclampsia.

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