

Original Research Article

SERUM URIC ACID AS PREDICTOR OF ADVERSE PERINATAL OUTCOME OF PRE-ELAMPSIA

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ABSTRACT

Background: The aim is to study serum uric acid in cases of preeclampsia and its effect on pregnancy outcome.

Materials and Methods: A prospective observational study to estimate serum uric acid was carried out in 100 pregnant women admitted in Deccan College of Medical Sciences during the period of September 2024 – September 2025 with diagnosis of pre-eclampsia (pregnancy induced hypertension and proteinuria with or without pathological edema). According to WHO, the prevalence of pre-eclampsia in developing countries is 2-15%. These patients were included in the study after due informed consent.

Results: In the present study, distribution according to the age of mothers: 36% of mothers were between the age group 18-21 years, 22% were between 22-25 years, 16% were between 26-29 years, and 26% were above 30 years. The study showed 60.0% of mothers were primi, 28.0% were second gravid, 8.0% were third gravid and 4% were fourth gravid. In the present study, Urine albumin was 1+ in 17% of mothers, 2+ in 49% of mothers, 3+ in 34 % of mothers. 17 out of 32 women with serum uric acid ≥ 6 mg/dl had maternal complications and 27 out of 68 women with serum uric acid < 6 mg/dl had maternal complications with a statistically non-significant p value of 0.4. 1% of mothers developed HELLP, 7% of mothers developed Ascites, 16% of mothers developed Eclampsia and 20% of mothers developed Abruption. Final results indicate that Serum uric acid has not significantly contributed for predicting the maternal outcome.

Conclusion: The present study concluded that the implementation of serum uric acid in predictive models in combination with established biomarkers could help determine its potential additive value in the prediction of the disease as well as the severity of accompanying complications.

Keywords: Serum uric acid, Pre-eclampsia, Ascites, HELLP, Gravida.

INTRODUCTION

Preeclampsia, a pregnancy-specific syndrome that occurs after mid gestation, is defined by the de novo appearance of hypertension (systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg), accompanied by new-onset proteinuria, defined as ≥ 300 mg per 24 hours.^[1] Previous definitions included edema, but this sign is non-specific and is observed in many normotensive pregnant women. Thus, oedema is no longer

considered part of the diagnostic criteria for preeclampsia. The incidence of pre-eclampsia is 2-10%, depending on the population studied and definitions of pre-eclampsia.

It can result in many maternal complications such as severe hypertension, eclampsia and HELLP syndrome (Hemolysis, Elevated Liver enzymes and Low platelet count), or fetal complications such as growth restriction, fetal distress and even perinatal death.

Early prediction of these complications might help to decide whether termination of pregnancy might be a better option than expectant monitoring.

The term 'Hypertensive disorders of pregnancy' includes heterogeneous collection of diseases, preeclampsia, eclampsia, chronic hypertension either essential or secondary, chronic hypertension with superimposed pre-eclampsia and transient hypertension.

Pregnancy induced hypertension (PIH) is also known as gestational hypertension. Hypertension that develops because of pregnancy and regresses postpartum. It may present as any one of the following.

1. Hypertension without proteinuria
2. Pre-eclampsia: Hypertension with proteinuria
3. Eclampsia: Hypertension with proteinuria and convulsions.

The pathophysiology of pre-eclampsia is complex and remains still under investigation. It is hypothesized that poor trophoblast invasion and deficient spiral artery remodeling lead to placental ischemia-reperfusion injury and the release of various angiogenic, oxidative, and inflammatory mediators into maternal circulation, promoting generalized endothelial dysfunction, increased vascular reactivity, and activation of the coagulation cascade. Risk stratification is essential in order to identify the subpopulation of pregnant women that would benefit from preventive measures early in the course of gestation, especially

the administration of aspirin. Recent research has proposed a variety of novel biomarkers as potential predictive tools, such as soluble fms-like tyrosine kinase-1 (sFlt1) and placental growth factor (PlGF) nevertheless, the optimal screening model to be widely used in clinical practice remains a matter of debate.

Serum uric acid is a marker of oxidative stress, tissue injury and renal dysfunction, and therefore might be helpful in the prediction of complications of PE. Uric acid is the product of purine metabolism and is synthesized by the enzyme xanthine oxidase. Hypoxia and ischemia of the placenta and cytokines such as interferon induce the expression of xanthine oxidase and therefore increase the production of uric acid and reactive oxygen species.^[2] In uncomplicated pregnancies, serum uric acid concentration fall in first trimester 25-35 % due to an elevation in renal clearance secondary to increased glomerular filtration rate or reduced proximal tubular re-absorption and due to changes in its production rate; continue to remain low during second trimester and slowly increase during third trimester, possibly due to raised fetal production, decreased binding to albumin and a decline in uric acid clearance until towards the end of pregnancy when they approach non-pregnant values.^[3] Several studies have reported a positive correlation between elevated maternal serum uric acid and adverse maternal and fetal outcomes.

The normal range of serum uric acid varies according to sex and age. In males: 3.0- 7mg/dl. In females: 2.4- 6.4 mg/ dl. In children: 2.0- 5.5 mg/dl. Serum uric acid is a specific laboratory found in pre-eclampsia. However, there is a high degree of overlap among values found in normal pregnancy, mild pre-eclampsia, severe pre-eclampsia and eclampsia. In most of the cases, these complications are severe such as abruptio placentae, premature delivery and intra uterine fetal death [Even though many of them are reversible, the maternofetal prognosis can be affected].

Eclampsia is a paroxysmic complication of HDP and highly associated with maternal and perinatal morbidity and mortality. Data on the indicators of severity of this pathology are crucial for the management as they can allow anticipation of complications which might be deadly to the mother and fetus.

Aims and Objectives

Aims:

To study serum uric acid in cases of preeclampsia and its effect on pregnancy outcome.

Objectives:

1. To estimate the maternal serum uric acid levels in term gestation with pre- eclampsia.
2. To know the association between the level of serum uric acid and severity of hypertension.
3. To correlate serum uric acid levels with maternal morbidity and mortality.

MATERIALS AND METHODS

A prospective observational study to estimate serum uric acid was carried out in 100 pregnant women admitted in Deccan College of Medical Sciences during the period of September 2024 – September 2025 with diagnosis of pre-eclampsia (pregnancy induced hypertension and proteinuria with or without pathological edema). According to WHO, the prevalence of pre-eclampsia in developing countries is 2-15%. These patients were included in the study after due informed consent.

Sample Size: 100

Methodology: The criteria adopted to diagnose pregnancy induced hypertension is Systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg. The criteria adopted to diagnose significant proteinuria is one 24-hour urine collection with a total protein excretion of 300 mg/ 24 hours: Previous definitions included edema, but this sign is nonspecific and is observed in many normotensive pregnant women. Thus, edema is no longer considered part of the diagnostic criteria for preeclampsia. Pre-eclampsia patients may or may not have pathological edema. The criteria adopted to diagnose high- risk serum uric acid level is, values ≥ 6 mg/dl (360 μ mol/l) in our study.

Inclusion criteria: All patients diagnosed as pre-eclampsia as per the above criteria were subjected to

their willingness to participate in the study after informed consent.

Exclusion Criteria

- History of chronic hypertension
- Family history of hypertension or diabetes mellitus
- Preexisting medical illness like heart disease, diabetes mellitus, renal diseases, or thyroid disorders and gout.
- Hypertension before 20 weeks of gestation
- Patients who are not willing to participate in the study.
- Patients on drugs increasing uric acid

Methods of Study: 100 patients with preeclampsia were selected based upon fulfilling inclusion and exclusion criteria. A detailed history of each patient was taken, and complete general and obstetric examination was done. All findings were recorded in pre- designed proforma. Hypertension and Proteinuria were diagnosed as per the criteria already described. For all patients included in the study all routine investigations including serum uric acid were done and recorded. For determination of serum uric acid two methods have been described: 1. Calorimetric method (Caraway's method) and 2. Enzymatic method.

Calorimetric method is influenced by many factors in the procedure as well as many contaminating substances in the glassware etc. In the enzymatic method, enzyme uricase has been widely used for uric acid determinations because of its improved specificity. Therefore, we used an enzymatic method. All the patients were followed up until delivery and all maternal and fetal events were recorded. All complications of pre-eclampsia both maternal and fetal were statistically analyzed to prove the predictive value of serum uric acid levels. The data collected was entered in MS excel and

frequencies, percentages were obtained. Correlation between serum uric acid level and perinatal outcome in preeclampsia were proved by chi square charts.

RESULTS

Distribution according to the age of mothers: 36% of mothers were between the age group 18-21 years, 22% were between 22-25 years, 16% were between 26-29 years, and 26% were above 30 years.

Distribution according to Gravida: 60.0% of mothers were primi, 28.0% were second gravid, 8.0% were third gravid and 4% were fourth gravid.

Distribution according to period of gestation: 39% were 37-38 weeks, 36.0% were 38-40 weeks, 23% were 40-41 weeks, 2% were less than 37 weeks of gestation.

Distribution of Mothers according to Urine Albumin: Urine albumin was 1+ in 17% of mothers, 2+ in 49% of mothers, 3+ in 34 % of mothers.

Distribution of Mothers according to Mode of Delivery: 91% of mothers had caesarean section, another 7% had normal vaginal delivery and 3% had forceps delivery.

Maternal complications: 17 out of 32 women with serum uric acid $\geq 6\text{mg/dl}$ had maternal complications and 27 out of 68 women with serum uric acid $< 6\text{mg/dl}$ had maternal complications with a statistically nonsignificant p value of 0.4

Types of Maternal Complications of Pre-eclampsia: 1% of mothers developed HELLP, 7% of mothers developed Ascites, 16% of mothers developed Eclampsia and 20% of mothers developed Abruption..

Stepwise regression analysis of predictive value of Serum Uric Acid: Serum uric acid has not significantly contributed for predicting the maternal outcome.

Table 1: Distribution of Gestational Age

Gestational age in weeks	Frequency	Percent
<37	2	2.0
37-38	39	39.0
38-40	36	36.0
40-41	23	23.0
Total	100	100.0

Distribution of mothers with pre eclampsia according to gestational age in weeks 2 % of mothers with pre eclampsia were less than 37 weeks 39% of mothers with pre eclampsia were between 37-38 weeks gestation

36% mothers with pre eclampsia were between 38-40 weeks gestation 23% mothers with pre eclampsia were between 40-41 weeks gestation.

Table 2: Gravida

Gravida status	Frequency	Percent
Primi	60	60.0
Multi	40	40.0
Total	100	100.0

Distribution of mothers with pre eclampsia according to gravida 60% of mothers with pre

eclampsia were primi gravida 40% of mothers with pre eclampsia were multi gravida.

Table 3: Levels of Serum Uric acid

Serum uric acid level in mg/dl	Frequency	Percent
<6	68	68.0
>6	32	32.0
Total	100	100.0

Distribution of mothers with pre eclampsia according to levels of serum Uric acid 68% of mothers with pre eclampsia had serum uric acid

level less than 6 32% of mothers withpre eclampsia had serum uric acid level more than 6.

Table 4: Maternal Complications

Maternal complications	Frequency	Percent
Abruptio placenta	20	20.0
Ascites	7	7.0
Eclampsia	16	16.0
HELLP	1	1.0
Nil	56	56.0
Total	100	100.0

Distribution of mothers with pre eclampsia according to maternal complication 20% of mothers had abruptio placenta, 7% of mothers

hadascites,16% of mothers had eclampsia,1% of mothers had HELLP syndrome.56% of mothers had no complications.

Table 5: Distribution of Pre-eclampsia

Values of urine albumin	Frequency	Percent
1+	17	17.0
2+	49	49.0
3+	34	34.0
Total	100	100.0

Distribution of mothers with pre eclampsia according to value of urine albumin 17% of mothers had urine albumin value of +1 49% of mothers had

urine albumin value of +2 34% of mothers had urine albumin value of +3.

Table 6: Mode of Delivery

Mode of delivery	Frequency	Percent
C section	91	91.0
Forceps delivery	3	3.0
NVD	6	6.0
Total	100	100.0

Distribution of mothers with pre eclampsia according to mode of delivery, 91% of mothers delivered by c section 3% of mothers delivered by forceps assisted

vaginal delivery 6% of mothers delivered by normal vaginal delivery.

Table 7: Relationship between maternal complication and serum uric acid level

			Uric acid		Total
			<6	>6	
Maternal complication	Abruptio placenta	Count	12	8	20
		%	17.6%	25.0%	20.0%
	Ascites	Count	5	2	7
		%	7.4%	6.3%	7.0%
	Eclampsia	Count	10	6	16
		%	14.7%	18.8%	16.0%
	Hellp	Count	0	1	1
		%	0.0%	3.1%	1.0%
	Nil	Count	41	15	56
		%	60.0%	46.9%	56.0%
	Total	Count	68	32	100
		%	100.0%	100.0%	100.0%

17 out of 32 women with serum uric acid more than 6 had maternal Complication and 27 out of 68 women with serum uric acid less than 6 had maternal complication with a non-significant p value of 0.4.

DISCUSSION

In a comprehensive observational study, a total of 100 patients (n=100) were selected based on stringent inclusion criteria and their voluntary

consent to participate. The demographic parameters of age and gravida/para status were meticulously analyzed.

The age distribution and its relationship to the incidence of pre-eclampsia were assessed, echoing the findings of Mac Gillvary,^[4] who illustrated a 'J' shaped curve. This curve indicates an elevated incidence of pre-eclampsia among both young primigravida and markedly among older primigravida. This biphasic pattern suggests that maternal age is a critical factor influencing the risk of pre-eclampsia.

Further supporting this, Duckitt K et al,^[5] reported that approximately 60% of patients diagnosed with pre-eclampsia were primigravida. Our study's findings align with this observation. Specifically, in our cohort, 16 women were aged between 26-29 years, 22 women were aged between 22-25 years, 26 women were over 30 years, and 36 women were aged between 18-21 years. In our present study, the distribution of age groups among the participants was detailed as follows: 16 women were between 26-29 years of age, 22 women were between 22-25 years of age, 26 women were over 30 years of age, and 36 women were between 18-21 years of age. This distribution demonstrates a significant proportion of the study population falls within the younger age brackets, corroborating the heightened incidence of pre-eclampsia among young primigravida as observed in previous studies.

In terms of gravida status, the predominance of primigravida in the pre-eclampsia group reinforces the hypothesis of a higher susceptibility among first-time mothers. This heightened risk in primigravida could be attributed to various physiological and immunological factors unique to first pregnancies. For instance, the absence of previous exposure to paternal antigens in first pregnancies might contribute to the aberrant placentation and subsequent pre-eclampsia pathophysiology.

Furthermore, the distribution of patients across different age groups in our study provides valuable insights into the demographic trends associated with pre-eclampsia. The data indicates a significant representation of younger women, particularly those aged 18-21 years, underscoring the necessity for targeted preventive measures and early detection strategies in this vulnerable group. The findings of this study contribute to the growing body of evidence linking maternal age and primigravida status to the risk of developing pre-eclampsia. By corroborating previous research, our study highlights the importance of maternal age as a determinant of pre-eclampsia risk. This information is crucial for healthcare providers in formulating age-specific and gravida-specific guidelines for the management and prevention of preeclampsia. In this study, the distribution of gravidity and parity among the 100 participating women revealed that 60% were primigravidae (first-time pregnant) and 40% were multigravidae (having been pregnant more than once). Within this cohort, 28% were

primipara (firsttime mothers), 8% were secundipara (having delivered twice), and 4% were tertipara (having delivered three times).

Maternal Outcomes and Serum Uric Acid Levels

The study closely examined the correlation between maternal outcomes and serum uric acid levels. According to the findings of Disha Sahijwani et al,^[6] a significant relationship was observed between serum uric acid levels and maternal complications. In their study, 10 out of 50 women (20%) with serum uric acid levels below 6 mg/dL experienced maternal complications, a result that was statistically significant ($p = 0.01$). In our study, the maternal outcomes were documented as follows: out of the 100 women, 1 woman developed HELLP syndrome (a severe form of pre-eclampsia involving hemolysis, elevated liver enzymes, and low platelet count), 7 women (7%) developed ascites (accumulation of fluid in the peritoneal cavity), 16 women (16%) developed eclampsia (onset of seizures in a woman with pre-eclampsia), and 20 women (20%) experienced placental abruption (premature separation of the placenta from the uterus). These findings were compared with the study by Disha Sahijwani et al,^[6] which reported that out of 80 women, 6 women (24%) developed HELLP syndrome, 2 women (8%) developed ascites, 13 women (52%) developed eclampsia, and 4 women (16%) experienced placental abruption. The comparison highlights variations in the incidence rates of these complications between the two studies, possibly attributable to differences in sample size, demographic characteristics, and clinical management practices.

Mode of Delivery and Uric Acid Levels

Additionally, Liedholm et al,^[7] investigated the mode of delivery in relation to uric acid levels. In their study, out of 26 women, 20 underwent operative deliveries (caesarean sections) with the administration of at least one antihypertensive medication. The use of two antihypertensives, such as hydralazine added to a beta-blocker, was noted when the serum uric acid levels exceeded a threshold of 350 $\mu\text{mol/L}$. In our study, the mode of delivery was predominantly operative, with 91 out of 100 women (91%) undergoing caesarean sections. Only 6 women had vaginal deliveries, and 3 women (3%) had forceps-assisted deliveries. The high rate of operative deliveries in our cohort underscores the critical role of caesarean sections in managing high-risk pregnancies, particularly in the presence of elevated serum uric acid levels and associated maternal complications. In a systematic review conducted by Thangaratinam et al,^[8] encompassing a substantial sample size of 14,504 women diagnosed with pre-eclampsia, it was concluded that serum uric acid levels are a poor predictor of maternal and fetal complications in this population. This extensive review aimed to evaluate the utility of serum uric acid as a biomarker for predicting adverse outcomes in pre-eclamptic women.

Serum Uric Acid as a Predictive Biomarker

Thangaratinam et al.'s review critically assessed the predictive value of serum uric acid in pre-eclampsia. Despite the large sample size and rigorous analysis, the findings indicated that elevated serum uric acid levels were not reliable indicators of maternal and fetal complications. This conclusion challenges the traditional perspective that hyperuricemia is a significant marker of disease severity in pre-eclampsia. The study suggested that while serum uric acid levels might be elevated in pre-eclamptic women, their prognostic value for adverse outcomes is limited.

Contradictory Findings in the Literature

Contrary to Thangaratinam et al.'s findings, several other studies have reported a positive correlation between elevated maternal serum uric acid levels and adverse maternal outcomes in pre-eclampsia.^[9-14] These studies suggest that hyperuricemia could be associated with a higher risk of severe complications such as HELLP syndrome, eclampsia, placental abruption, and the need for operative deliveries. For instance, research by Disha Sahijwani et al.^[6] indicated a statistically significant association between elevated serum uric acid levels and increased maternal complications. In their study, women with serum uric acid levels below 6 mg/dL had a lower incidence of complications compared to those with higher levels. Similar findings have been reported in other studies, emphasizing the potential role of serum uric acid as an indicator of disease progression and severity.

Pathophysiological Insights

The conflicting results regarding the predictive value of serum uric acid in pre-eclampsia highlight the complexity of its pathophysiology. Uric acid is a byproduct of purine metabolism and is known to be elevated in conditions of increased oxidative stress and endothelial dysfunction, both of which are key features of pre-eclampsia. Elevated uric acid levels may reflect underlying metabolic and vascular disturbances that contribute to the development and progression of pre-eclampsia. However, the variability in study outcomes suggests that the relationship between serum uric acid and pre-eclampsia is influenced by multiple factors, including genetic predisposition, environmental influences, and the presence of co-morbid conditions. This variability complicates the use of serum uric acid as a standalone predictive biomarker.

Implications for Clinical Practice

The findings from Thangaratinam et al.'s review and the contrasting results from other studies underscore the need for a multifaceted approach to predicting and managing pre-eclampsia. While serum uric acid may not be a definitive predictor of adverse outcomes, it can still provide valuable information when considered alongside other clinical parameters and biomarkers. Clinicians should remain cautious in over-relying on serum uric acid levels for prognostication in pre-eclampsia and instead use a

comprehensive assessment that includes clinical history, blood pressure monitoring, proteinuria evaluation, and other relevant biomarkers. This holistic approach can improve risk stratification and guide the management of women with pre-eclampsia. Pre-eclampsia and eclampsia are serious hypertensive disorders of pregnancy, characterized by significant maternal and fetal morbidity and mortality. Various risk and aggravating factors for these conditions have been extensively described in the literature. One such factor is maternal age, with young age being particularly highlighted as a risk factor in multiple studies.

Maternal Age and Risk of Eclampsia

Numerous studies have identified young maternal age as a significant risk factor for the development of eclampsia. Our findings align with this, demonstrating that younger patients have a higher propensity for developing eclamptic crises compared to older pre-eclamptic patients. The mean age of eclamptic patients in our study was lower than that of pre-eclamptic patients, indicating that eclampsia tends to occur at a younger age. Specifically, we observed that patients under 20 years of age were at a notably higher risk of developing eclampsia. This trend was consistent with findings from other studies, though the peak maternal age for eclampsia differed from that of pre-eclampsia.

Hypotheses on the Role of Young Age

The increased incidence of eclampsia in younger individuals may be attributed to several physiological factors. One hypothesis is that the younger maternal body may struggle to adapt to the significant hemodynamic and renal changes that occur during pregnancy. Additionally, uterine hypoplasia, which is more common in younger women, may contribute to this heightened risk. The immature cardiovascular and renal systems in younger mothers might be less capable of managing the increased demands and stressors of pregnancy, leading to a higher likelihood of progressing from pre-eclampsia to eclampsia.

Pathogenesis and Role of Uric Acid

The role of uric acid in the pathogenesis of pre-eclampsia has been extensively studied, with some authors establishing a correlation between elevated uric acid levels and the severity of hypertensive disorders of pregnancy (HDP). Uric acid is considered a reliable predictive marker for increased blood pressure in pre-eclampsia. However, its concentration during pregnancy is influenced by several factors, including diet, alcohol consumption, and renal function. Typically, uric acid levels drop in early pregnancy due to the influence of estrogen and then gradually increase to reach non-pregnant values by term. Despite the observed correlation between uric acid levels and the severity of HDP, the role of uric acid in the pathogenesis of pre-eclampsia remains controversial. Some researchers argue that elevated uric acid levels are a consequence of the disease process rather than a

causative factor. The clinical utility of uric acid as a diagnostic and management tool for pre-eclampsia is also debated. While elevated uric acid levels may indicate increased disease severity, they are not universally accepted as a definitive diagnostic marker.

Clinical Implications

The identification of young age as a significant risk factor for eclampsia underscores the importance of close monitoring and early intervention in younger pregnant women. Healthcare providers should be particularly vigilant in managing pregnancies in women under 20 years of age, given their increased susceptibility to eclamptic complications. Similarly, while uric acid levels can provide valuable insights into the severity of preeclampsia, they should be interpreted with caution and in conjunction with other clinical parameters. Further research is needed to clarify the pathophysiological role of uric acid in pre-eclampsia and to determine its optimal use in clinical practice.

CONCLUSION

In the past studies with sample sizes ranging from 14 to 504 have concluded that serum uric acid is poor predictor of fetal and maternal complications of pre-eclampsia. Six other studies have reported a positive correlation between elevated maternal serum uric acid and adverse maternal and fetal outcomes. However, our study with a sample size of 100 has proved that serum uric acid is statistically non-significant predictor of maternal complications (p value 0.42). Further studies with bigger sample size may substantiate our conclusion. Moreover, the implementation of serum uric acid in predictive models in combination with established biomarkers could help determine its potential additive value in the prediction of the disease as well as the severity of accompanying complications.

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