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Review Article

Serum uric acid levels during pregnancy: a predictive marker for hypertensive disorders in antenatal women

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ABSTRACT

Hypertensive disorders of pregnancy i.e., gestational hypertension, preeclampsia and eclampsia, are most common medical disorders of pregnancy and have serious implications on feto-maternal health outcomes. Owing to substantial risk to both mother and baby, one of emerging area of interest is the role of serum uric acid levels as a potential predictor of hypertensive disorders during pregnancy, notably preeclampsia. This comprehensive review focuses on role of serum uric acid levels, as a prescient marker for hypertensive complications in pregnant women. The review included the original research articles studying role of serum uric acid early detection of hypertensive disorders of pregnancy in pregnant women with gestational age >20 weeks. Original articles having primary data of study of predictive markers of hypertensive disorders of pregnancy were reviewed thoroughly for their demographic indicators, serum uric acid level and feto-maternal outcome of pregnancy. All the studies showed a significant high serum uric acid level among pre-eclamptic women compared to normotensive or pregnant women with gestational hypertension. The ROC also showed greater sensitivity and specificity compared to other markers such as serum calcium and serum creatinine. To conclude, this comprehensive review underscores the pivotal role of serum uric acid levels in predicting adverse maternal and fetal outcomes during pregnancy. This valuable insight has the potential to significantly enhance the care and outcomes for pregnant women and their unborn children facing hypertensive disorders.

Keywords: Hypertensive disorders of pregnancy, Preeclampsia, Feto-maternal outcome, Serum uric acid level

INTRODUCTION

Pregnancy is characterized by complex physiological changes that extensively influence maternal and fetal health. During pregnancy, 2-10% pregnancy may be affected by Hypertensive disorders, which are the most common and serious medical disorders.[1] The spectrum of hypertensive illnesses includes gestational hypertension (GH), preeclampsia (PE), and eclampsia. Hypertensive diseases during gestation, particularly preeclampsia, exacerbate significant dangers for maternal-fetal dyads.[1-5] During the ante-natal period, serum Uric Acid level is checked regularly, suggested as a potential precursor for impending hypertension diseases in pregnant women.[1,2,7] Early in pregnancy, uricosuric effects of oestrogen and increased renal blood flow cause serum uric acid levels to drop, frequently to 3 mg/dl or less. Uric acid levels then increase during the third trimester, reaching levels of 4–5 mg/dl by term.[4] The increase in serum uric acid is result of reduced clearance of uric acid due to decrease glomerular filtration clearance, increased tubular reabsorption, and reduced secretion.[8] Among the high-risk group of developing pre-eclampsia (pregnant women with gestational hypertension with Gestational Age >20 weeks and without proteinuria), the increased serum uric acid is the first and earliest laboratory marker of the presentation of pre-eclampsia, it is considered as criterion for pre-eclampsia.[2] Given the importance of hypertensive disorders during pregnancy, the search for reliable biochemical markers that may be used to predict and treat these hypertensive disorders early on becomes crucial.[9-10]

This article comprehensively reviews the available literature studying role of serum uric acid level as a predictive marker for the hypertensive disorder in the pregnancy, in order to help the obstetrician in identifying the pregnant women having potential to develop pre-eclampsia.

METHODS

Study design and data collection

The purpose of this thorough review was to synthesize available information on the use of blood uric acid levels as a predictive marker for hypertensive problems in pregnant women. The relevant articles were searched on electronic database PubMed, published until 2023. The search strategy employed a combination of keywords, such as "serum uric acid," "pregnancy," "hypertensive disorders," and "antenatal," to ensure comprehensive coverage of the literature.

Inclusion criteria

This includes original research articles examining the relationship between serum uric acid levels during pregnancy and hypertensive diseases, Studies providing data on pregnant women at more than 20 weeks gestational period, and studies accessible in English. The extracted data included study characteristics, participant demographics, serum uric acid levels, hypertensive disease outcomes, and other important variables. Mean Serum uric acid levels with standard deviations (SD) were collected across several hypertensive disease groups. Given the heterogeneity among the included studies, the findings of each study were summarized highlighting patterns and trends in the described correlations between serum uric acid levels and hypertensive disorders in antenatal women. The synthesized results were integrated to provide a comprehensive overview of this domain's current state of knowledge. Some definitions have been used across the studies which are given as follows.

Gestational hypertension

Blood pressure >140/90 mmHg without proteinuria after 20 weeks of gestation.[11]

Preeclampsia

Multisystem disorder of unknown etiology, characterized by systolic BP>140 mmHg or a diastolic BP>90 mmHg on two or more occasions, 6 hour apart and proteinuria of greater than 300 mg in 24 hours urine specimen after 20 weeks of gestation.[12]

Eclampsia

Convulsion associated with preeclampsia.[12]

Table 1: Demographic particulars of various studies.

Author	Year and site	Aim and objectives	Study design and Sample size	Demographic particulars
Vyakaranam et al[13]	2015, India	To determine serum uric acid and creatinine in hypertensive disorders of pregnancy and correlate with fetal outcome	Prospective cohort study, 30 in each group of normotensive, gestational hypertension and pre-eclampsia, with gestational age>32 weeks.	The parameters were evaluated across three groups: Normotensive Pregnant (NP) (n=31), Gestational Hypertension (GH) (n=30), and Preeclampsia (PE) (n=30). All the participants were age matched. The mean age (±SD) was 23.2±2.9 years for NP, 22.9±3.0 years for GH, and 23.7±3.4 years for PE (p =0.582). Gestation age in weeks was 36.4±3.5 for NP, 36.9±2.9 for GH, and 35.8±2.6 for PE (p=0.373). There was no statistically significant difference in the mean age or gestational age between the three groups.
Asgharnia et al[14]	2017, Iran	To study the relationship between the uric acid level with maternal and neonatal complications in preeclamptic women	Cross sectional study, 160 pre-eclamptic women with GA>28 weeks.	The participants' average age was recorded as 31.18±5.41 years. 23.8% (38 participant) had severe preeclampsia GA was 34,7 weeks.
Niraula et al[5]	2017, Nepal	To measure the blood UA levels in PIH and analyse the serum UA level's diagnostic usefulness in PIH.	Observational cross-sectional study. 45 PIH patients and 45 participants in control group.	The mean age for the pre-eclampsia group women was 26.84 years (±5.20), while the Control group had a mean age of 25.84 years (±4.54).

Continued.

Author	Year and site	Aim and objectives	Study design and Sample size	Demographic particulars
Kumar et al[6]	2019, India	To assess the relationship between maternal serum uric acid and severity of Hypertensive disorders of pregnancy in a rural tertiary care centre	Prospective cohort study, 110	In gestational hypertension (n=35), age distribution: 48.57% below 26-30, 37.14% aged 26-30, 88.57% aged 31-35, and 2.86% aged 36-40. In preeclampsia (n=49), 40.82% aged 20-25 and 26-30, 18.37% aged 31-35. Eclampsia (n=26): 65.38% aged 20-30, 7.69% aged 31-35, none aged 36-40. Gestational Hypertension-28.57% primigravida, Pre-eclampsia-24.49% primigravida, Eclampsia-65.38% primigravida. The majority were multigravida. Gestational Hypertension/Preeclampsia-later weeks prevalent, Eclampsia-higher in the 34-37 weeks category.
Tesfa et al[15]	2022, Ethopia	To evaluate the diagnostic importance of serum uric acid, blood urea and creatinine levels in the prediction of PE.	Unmatched case-control study. 84 each of cases and controls	The average age (with associated standard deviation) for both the case and control groups were 27.98±5.642 and 27.33±4.446, respectively. Regarding body mass index (BMI), no noteworthy distinction in mean values was observed between the cases and controls, which were 24.73±3.931 and 23.61±3.584, respectively, in this study. Mean gestational age in hypertensive and non-hypertensive groups were 35.5 and 37.98 weeks respectively.

Table 2: Comparison of uric acid levels among hypertensive and normal pregnant women.

Author	Uric acid levels	Maternal outcome and Fetal outcome
Vyakaranam et al[13]	Serum uric acid and creatinine concentrations exhibited noteworthy increases in Preeclampsia (PE) (6.26±1.19 and 0.94±0.26 mg/dl) compared to PIH (4.27±1.0 and 0.66±0.19 mg/dl) and Normotensive Pregnant (NP) (4.25±0.8 and 0.63±0.13 mg/dl) groups, respectively (p value <0.001 for both comparisons).	Within the Normotensive Pregnant (NP) cohort, 67% of women had full-term normal vaginal delivery (FTNVD), while the corresponding figures for Pregnancy Induced Hypertension (PIH) and Preeclampsia (PE) groups were 36.7% and 13.4%, respectively. Moreover, fetal birth weight displayed significant diminution in the Preeclampsia group (2.31±0.5 kg) in contrast to the Normotensive (2.74±0.58 kg) and PIH (2.8±0.28 kg) groups.
Asgharnia et al[14]	The average uric acid level among women with severe pre-eclampsia (5.66±1.46) was notably higher compared to those with non-severe pre-eclampsia (5.12±1.29) (p=0.031).	The pregnant women with hepatic dysfunction (n=11) had significantly higher uric acid level (6.27±1.40) compared to remaining 149 women (5.17±1.32) (p=0.009). The uric acid levels of preterm delivery women were higher (5.63+1.38) than those of normal term pregnant women (P value 0.0001). Notably, uric acid levels were significantly different between cases requiring NICU admission (n=32) and non-NICU patients (n=124), with means of 5.74±1.37 and 5.10±1.32, respectively (p=0.016).
Niraula et al[5]	The PIH group showed a mean uric acid level of 5.46 (±1.51), whereas the Control group showed a mean uric acid level of 4.03 (±0.69). A very significant p-value of 0.001 was obtained from the statistical analysis, highlighting the considerable difference in uric acid levels between the two groups. In PIH, serum uric acid demonstrated superior diagnostic efficacy (sensitivity 79.07%, specificity 71.99%) in contrast to creatinine (sensitivity 62.75%, specificity 27.45%).	Not assessed

Continued.

Author	Uric acid levels	Maternal outcome and Fetal outcome
Kumar et al[6]	The average values, along with their standard deviations (SD) for serum uric acid levels, were recorded as follows: 5.47±1.93 mg/dl for individuals with Gestational Hypertension, 6.72±2.51 mg/dl for those with Pre-eclampsia, and 8.71±2.97 mg/dl for the cohort experiencing eclampsia.	75.51% of women with pre-eclampsia and 73.07% with eclampsia were induced either at term or at <37 weeks of gestation. The rate of LSCS percentage among Gestational Hypertension, Pre-eclampsia and eclampsia was 20%, 30% and 46% respectively. Of 110 women with HDP, 34(97.14%) in GH group, 27(55.10%) with PE and one (3.85%) with eclampsia remained stable and healthy in the immediate post-partum period. Remaining patients were managed in high dependency unit or intensive care unit.
Tesfa et al[15]	The uric acid level in hypertensive pregnant women was 6.27±1.85 mg/dl, while the value was 4.47+1.38 mg/dl among normotensive individuals (P value<0.001). Multi-variate logistic regression revealed, that serum Uric acid levels were positively associated with the development of pre-eclampsia among pregnant women with an (B=0.439, p=0.010*) and yielded an odds ratio of 1.551 (95% CI: 1.110-2.166). Urea levels also displayed a significant positive correlation (B=0.353, p<0.001*) with an odds ratio of 1.424 (95% CI: 1.183-1.712). Estimated fetal weight (EFW) exhibited a negative correlation (B=-0.001, p=0.013*) with an odds ratio of 0.999 (95% CI: 0.998-1.000). Other variables, including creatinine levels, gestational age, and body mass index (BMI), did not show significant associations with the outcome (p>0.05).	In the present study, there is a statistically significant difference in the mean values of gestational age and expected fetal weight (EFW) between the cases and controls. The EFW was significantly higher in control group (2927.7±602.05 gm) than cases (2317.4±747.6 gm).

DISCUSSION

Numerous researchers have studied the intricate relationship between uric acid levels and the various complications experienced by pregnant women. However, based on the search criteria used, five original articles were selected for thorough review. The findings of which have been described in the result section. For early diagnosis of preeclampsia and eclampsia, several biochemical markers have been studied such as serum uric acid, serum calcium, serum creatine etc. However, most of the studies have shown superior correlation between serum uric acid level and hypertensive disorders of pregnancy, compared to other biochemical markers. The Indian study by Vyakaranam S et al studied levels of serum uric acid and creatinine among three groups i.e, normotensive, gestational hypertension, and pre-eclampsia. Serum Uric level was significantly higher in pre-eclamptic women. However, no difference in serum uric acid level was found in between normotensive and gestational hypertension group. A threshold value of 4.9 mg/dl for blood uric acid in pre-eclamptic women showed 86.7% sensitivity and 83.9% specificity in ROC analysis. The author of this study discovered a substantial negative connection between uric acid and foetal birth weight in PE. In comparison to GH and NP, the mean foetal weight in PE was substantially lower at 2.31±0.5 kg. Preeclamptic women also had high blood creatinine levels, although their specificity and sensitivity were lower than their serum uric acid levels.[13]

Asgharnia and colleagues conducted an insightful cross-sectional analysis encompassing 160 women diagnosed with preeclampsia beyond the 28-week gestational threshold. On univariate level analysis serum Uric acid level was significantly higher among women with hepatic dysfunction, pre-term labour and NICU admission of neonates. Logistic regression analysis showed a 1.74-fold increased risk of hepatic dysfunction with 1 mg/dl increase of serum uric acid level. Preterm labour risk was also increased by 1.54-fold with 1 mg/dl increase in serum uric acid.[14]

According to Kumar and Singh's study, elevated levels of uric acid in the mother's blood were linked to a worsening of the condition and a general poor prognosis for both the mother and the foetus. The mean blood uric acid levels in women with severe pre-eclampsia and eclampsia were 7.88±3.11 and 8.79±3, respectively, which was highly significant than the normotensive and gestational hypertension patients. Compared to multigravida (34.61%), primigravida (65.38%) had eclampsia more frequently. LSCS percentage in gestational hypertension, pre-eclampsia and eclampsia was 20%, 30.6% and 46.1% respectively, while primary LSCS was 14%, 10% and 34% respectively. Among all pregnant women with Hypertensive disorders, women with postpartum morbidity had higher mean serum uric acid (8.43+3.06) compared to women without morbidity (5.53+1.5). A significant correlation was also seen in poor perinatal outcome and maternal serum uric acid.[6]

E. Tesfa at al conducted a hospital-based case-control study, and studied the relationships between maternal uric acid, urea, and creatinine levels with the occurrence of preeclampsia. Maternal blood uric acid and BUN concentration were found to be 1.55 and 1.42 times higher in preeclamptic women than in normotensive pregnant women, respectively. When compared to normal controls, the maternal serum creatinine levels in PE were 12.94 times higher; however, this difference was not statistically significant. With the cut-values of serum uric acid level 5.25 mg/dl, the areas of uric acid under the ROC curve were 0.785 with the sensitivity and specificity of 69% and 73.8%, respectively.[15]

Niyonzima et al contributed a cross-sectional study investigating the correlation between uric acid levels and blood pressure in 80 pregnant women of different gestational trimesters. The study found a robust positive correlation between uric acid levels and systolic/diastolic blood pressure, highlighting the interplay between uric acid and blood pressure in pregnancy. However, this study has maximum patients registered from first trimester. The trimester wise hypertension data and serum uric level has not been analysed in the study.[16]

CONCLUSION

In conclusion, the comprehensive review delves into the intricate relationship between serum uric acid levels and hypertensive disorders during pregnancy. All the studies showed that serum uric levels were associated with hyper disorders of pregnancy, especially pre-eclampsia and eclampsia. There has been a positive correlation between these two factors. The studies examined here signify the pivotal role serum uric acid levels play as a predictive marker for adverse maternal and fetal outcomes.

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