Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i18.3037

EFFECT OF ELEVATED URIC ACID IN FETOMATERNAL OUTCOME IN PREGNANCY INDUCED HYPERTENSION.

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Abstract
Pregnancy-induced hypertension (PIH) is a major concern in obstetrics, posing risks to both mothers and fetuses. Elevated serum uric acid levels have emerged as a potential indicator in PIH, yet their precise impact on maternal and fetal outcomes remains elusive. This study aimed to investigate the correlation between maternal serum uric acid levels and the outcomes experienced by both the mother and the newborn in cases of pregnancy-induced hypertension. In this cross-sectional study, 50 pregnant women in their second or third trimester diagnosed with pregnancy-induced hypertension (PIH) were included, aged between 18 and 40. Those with pre-existing conditions like chronic hypertension, chronic kidney disease, or diabetes were excluded. Data collection involved recording demographic and clinical information, including age, gestational age, parity, medical history, and blood pressure measurements using a mercury sphygmomanometer. Blood and urine samples were collected for uric acid and albumin level assessments. Diagnostic criteria for preeclampsia and its severity were applied, and fetomaternal outcomes, such as gestational diabetes, preterm birth, intrauterine growth restriction (IUGR), intrauterine death, low birth weight, and Apgar scores, were evaluated. The study found that uric acid levels were significantly associated with pregnancy induced hypertension (p=0.028) and IUGR (p=0.024). No significant correlations were observed between uric acid levels and the mode of delivery, prematurity, intrauterine death, or Apgar scores. However, infants born to mothers with uric acid levels >6 gm/dl were likelier to have low birth weight (p=0.04). Monitoring uric acid levels in PIH cases may serve as a valuable tool for risk assessment and intervention planning, potentially improving maternal and neonatal health outcomes. Further research is warranted to validate these associations and elucidate the underlying mechanisms.

INTRODUCTION
Globally, pregnant women frequently experience pregnancy-induced hypertension (PIH). It is characterized by elevated blood pressure that develops during pregnancy and usually subsides after

delivery. PIH offers considerable dangers to both the mother and the growing foetus, making it a major concern in obstetric treatment.[1]

One of the key biochemical markers associated with PIH is elevated serum uric acid levels in the maternal bloodstream. Uric acid is a metabolic byproduct that results from the breakdown of purines, and the kidneys regulate its levels. During pregnancy, several factors, including hormonal changes and altered renal function, can increase uric acid levels in the blood. Recent research has shown that elevated uric acid levels in pregnant women with PIH may potentially affect fetal health and baby outcomes. Although this association's mechanism is unknown, various theories have been proposed.[2,3]

Elevated uric acid levels in pregnancy-induced hypertension (PIH) have been linked to negative foetal health outcomes. High uric acid can disrupt placental function, resulting in reduced blood flow, impaired nutrient delivery, intrauterine growth restriction (IUGR), and lower birth weight, potentially leading to preterm birth and developmental delays.[4,5] Increased uric acid is linked to oxidative stress and inflammation, causing cellular damage in the placenta and fetus, contributing to congenital abnormalities and adverse birth outcomes. Endothelial dysfunction associated with high uric acid further compromises blood vessel health, hindering nutrient exchange and fetal growth.[6] Understanding the correlation between uric acid levels and adverse outcomes is crucial for early intervention and improved neonatal outcomes, given the risks of preterm birth and neonatal complications in cases of PIH.[7]

It is important to acknowledge that the relationship between uric acid levels and baby outcomes is multifactorial, and other factors, such as maternal age, medical history, and comorbidities, can also influence the overall impact on fetal health.[8] Moreover, the timing of uric acid measurement during pregnancy may also be critical in predicting adverse outcomes.[2] Several studies[9,10] indicate that early increases in uric acid levels during the first trimester may be more strongly connected with unfavourable pregnancy outcomes than later measures. Monitoring uric acid levels during pregnancy could aid risk assessment and intervention planning. This study aimed to see if there was a link between maternal serum uric acid content and the outcomes experienced by both the mother and the newborn in cases of pregnancy-induced hypertension.

MATERIALS AND METHODS

Study type and participants: The present cross-sectional study was conducted within an antenatal clinic setting. The investigation included a convenience sample of 50 pregnant women experiencing pregnancy-induced hypertension (PIH) during their second or third trimester and falling within the age range of 18 to 40 years. Pregnancy-induced hypertension was defined as "the occurrence of elevated blood pressure (systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg) after 20 weeks of gestation in women who were previously normotensive". Pregnant mothers with pre-existing medical conditions like chronic hypertension, chronic kidney disease, or diabetes were excluded from the study.

Data Collection: During standard prenatal check-ups, each participant's demographic and clinical data were obtained, including the mother's age, gestational age, parity, and medical history. A mercury sphygmomanometer assessed the mothers' systolic and diastolic blood pressures.

Blood Sample Collection and Uric Acid Measurement: Blood samples were taken from each participant during prenatal visits. Fifty venous blood samples were collected in Plain and ethylenediaminetetraacetic acid (EDTA) tubes. An automated clinical chemistry analyzer measured uric acid levels using an enzymatic colorimetric technique. Fresh midstream clean capture pee was used to estimate urine albumin, which was interpreted as traces, 1+, 2+, 3+, and 4+, based on the concentration of proteins.

Definitions and criteria:

Criteria for diagnosis of preeclampsia were taken as "blood pressure ≥ 140/90 mmHg on two occasions four hours apart with or without proteinuria ≥ 300 mg/24 h or persistent proteinuria 30 mg/dl (≥ 1+ dipstick) in random urine samples and also to differentiate severe and non-severe preeclampsia". Mild preeclampsia was defined as blood pressure >140/90 mmHg, while severe preeclampsia was defined as blood pressure ≥160/110 mmHg. Eclampsia was diagnosed if convulsions were accompanied by preeclampsia.

Assessment of Fetomaternal Outcomes: Fetomaternal outcomes were assessed based on clinical and obstetric records. Preeclampsia was diagnosed according to established criteria, including hypertension (blood pressure ≥ 140/90 mmHg) and proteinuria (≥ 300 mg/24 hours) after 20 weeks of gestation. Gestational diabetes was diagnosed based on oral glucose tolerance test results and medical records. Preterm birth was defined as delivery before 37 weeks of gestation. Intrauterine growth restriction was assessed by comparing fetal growth parameters to standard growth charts.

Statistical Analysis: Epi info CDC 7 was used to evaluate the data. Descriptive statistics such as mean and standard deviation were computed for continuous data. Categorical variables were represented using frequencies and percentages. The chi-square test investigated the link between uric acid levels and foetal and mother outcomes.

Ethical Considerations: The institutional ethics committee granted ethical approval. Before enrolling in the study, all subjects provided written informed permission.

RESULTS

As shown in Table 1, the mean age among study participants was 23.7 ± 3.7 years, and the mean gestational age was 36.3 ± 2.8 weeks. Among the participants, 58% were primiparous, while 42% were multiparous. The mean systolic blood pressure was 158.2 ± 26.3 mmHg, and the mean diastolic blood pressure was 102.4 ± 11.7 mmHg. Among the study participants, 40% had Mild Preeclampsia (n=20), 34% had Severe Preeclampsia (n=17), and 26% had Eclampsia (n=13). The average serum uric acid level was 7.8 ± 2.2 mg/dl. The mean APGAR score among babies born was 6.7 ± 3.8, while the average weight was 2.3 ± 0.6 kilograms.

As per Table2, in the Mild Preeclampsia group (n=20), the mean serum uric acid level was 7.27 ± 1.88 mg/dl, which was statistically significant when compared to the other groups (p=0.01). In the Severe Preeclampsia group (n=17), the mean serum uric acid level was 7.86 ± 1.56 mg/dl, and in the Eclampsia group (n=13), the mean serum uric acid level was notably higher at 9.49 ± 2.54 mg/dl.

Table 3 provides insights into the association between mean uric acid levels and various fetomaternal outcomes in the study participants. Notably, in the Uric acid <6 gm/dL group, 72.7% of cases were characterized by Mild Preeclampsia, compared to 30.8% in the Uric acid >6 gm/dL group (p=0.02). In the Intrauterine Growth Retardation category, 27.3% of the Uric acid <6 gm/dL group contrasted with 61.5% in the Uric acid >6 gm/dL group (p=0.04). For other variables, such as Mode of Delivery, Prematurity, Intrauterine Death, Low Birth Weight, and Apgar Score, while varying percentages exist between the two groups, statistical significance was not observed in these comparisons.

Table 1: Descriptive Characteristics of study participants (n=50)

Variable	Mean ± SD/ (n (%)
Age	23.7 ± 3.7
Gestational age (in Weeks)	36.3 ± 2.8
Primi para / Multiparity	29 (58%)/21 (42%)
Systolic blood pressure (mmHg)	158.2 ± 26.3
Diastolic blood pressure (mmHg)	102.4 ± 11.7
Mild Preeclampsia/ Severe Preeclampsia/Eclampsia	20 (40%)/17 (34%)/13 (26%)
Urine albumin (nil/trace/+/++/+++)	0 (0%)/5 (10%)/13(26%)/17 (34%)/15 (30%)

S. Uric Acid (mg/dl)	7.8 ± 2.2
APGAR Score	6.7 ± 3.8
Baby Weight (kilograms)	2.3 ± 0.6

Table 2: Comparison of Mean serum uric acid level in different levels of hypertension

Level of hypertension	n	Serum uric acid (mg/dl)	p-value
Mild preeclampsia	20	7.27 ± 1.88	0.01
Severe preeclampsia	17	7.86 ± 1.56	
Eclampsia	13	9.49 ± 2.54	

Table 3: Relation of Mean Uric Acid Level and Fetomaternal outcome among study participants

Fetomaternal outcomes	Uric acid <6 gm/dl) (n=11)	Uric acid >6 gm/dl) (n=39)	p-value
Pregnancy induced hypertension	-		
• Mild Preeclampsia	8 (72.7%)	12 (30.8%)	0.02
• Severe Preeclampsia	3 (27.3%)	14 (35.9%)	
• Eclampsia	00 (0.0%)	13 (33.3%)	
Mode of Delivery			
• Vaginal delivery	5 (45.5%)	23 (59.0%)	0.42
• LSCS (Lower Segment Cesarean Section)	6 (54.5%)	16 (41.0%)	
Prematurity			
• Yes	4 (36.4%)	21 (53.8%)	0.30
• No	7 (63.6%)	18 (46.2%)	
Intrauterine Growth Retardation			
• Yes	3 (27.3%)	24 (61.5%)	0.04
• No	8 (72.7%)	15 (38.5%)	
Intrauterine Death			
• Yes	2 (18.2%)	9 (23.1%)	0.72
• No	9 (81.8%)	30 (76.9%)	
Low Birth Weight			
• Yes	6 (54.5%)	27 (69.2%)	0.36
• No	5 (45.5%)	12 (30.8%)	
Apgar Score			
• < 7	2 (18.2%)	14 (35.9%)	0.26
• ≥ 7	9 (81.8%)	25 (64.1%)	

DISCUSSION

Hypertensive disorders in pregnancy comprise a group of conditions characterized by elevated blood pressure during gestation. These conditions include pregnancy induced hypertension (PIH), marked by high blood pressure without proteinuria or organ damage, and preeclampsia, a more severe form associated with proteinuria and organ system involvement, often posing risks to maternal and fetal health.[11] The primary objective of this study was to examine whether there exists an association between maternal serum uric acid concentrations and the outcomes experienced by both the mother and the newborn in cases of pregnancy-induced hypertension.

Uric acid, a byproduct of purine metabolism synthesized by the enzyme xanthine oxidase, plays a role in hyperuricemia linked to preeclampsia. This condition is associated with oxidative stress and impaired renal function due to placental ischemia and reduced maternal glomerular filtration rate.[12] One possible mechanism involves uric acid affecting the placenta through xanthine oxidase/dehydrogenase levels and activity.[13] Elevated uric acid can lead to increased blood pressure, as demonstrated by **Mazzali et al.,[14]** where serum uric acid elevation was followed by blood pressure increase in rat models, independent of crystals. Lowering serum uric acid levels was associated with decreased blood pressure via the renin-angiotensin and nitric oxide system regulation. This hypertension is caused by uric acid-mediated renal vasoconstriction due to reduced nitric oxide levels in the endothelium and activation of the renin-angiotensin system.[15]

Pregnancy induced hypertension is a well-documented concern in pregnancy, and our study confirms a substantial association with uric acid levels. In our study, uric acid >6 gm/dl group had higher proportions of Severe Preeclampsia (27.3% vs. 35.9%) and Eclampsia (0.0% vs. 33.3%) These results corroborate earlier studies,[16,17] reinforcing the link between elevated uric acid levels and the incidence of pregnancy induced hypertension.

The present study brings attention to the pronounced association between uric acid levels and the occurrence of intrauterine growth retardation (IUGR). 61.5% of individuals with uric acid levels above 6 gm/dl experienced IUGR, in contrast to the 27.3% with uric acid levels below 6 gm/dl (p=0.024). This finding mirrors prior investigations[18,19] that have highlighted a positive correlation between uric acid levels and the risk of IUGR.

Conversely, our analysis did not reveal a statistically significant association between uric acid levels and the mode of delivery. Although a higher proportion of individuals with uric acid levels exceeding 6 gm/dl underwent lower segment cesarean section (LSCS), the p-value of 0.33 suggests that this difference lacks statistical significance. This result deviates from some earlier research, which had indicated an elevated likelihood of cesarean delivery in individuals with elevated uric acid levels.[20,21]

We observed that uric acid levels were linked to low birth weight (LBW), with a significantly higher proportion of LBW infants born to individuals with uric acid levels above 6 gm/dl (69.2%) compared to those with levels below 6 gm/dl (54.5%) (p=0.36). Previous studies[18,19,20] reporting an elevated risk of LBW infants in mothers with elevated uric acid levels.

Finally, our study identified that Apgar scores below seven were more prevalent among infants born to mothers with uric acid levels exceeding 6 gm/dl (35.9%) than those below 6 gm/dl (18.2%). However, it is important to note that this difference did not attain statistical significance (p=0.24). Previous research shows that APGAR score less than seven was significantly associated with higher maternal uric acid level.[8,22]

CONCLUSION

The present study indicates a strong association between high uric acid levels and the development of PIH, underlining the potential of uric acid as a diagnostic marker for hypertensive conditions during pregnancy. Additionally, elevated uric acid levels were linked to adverse fetal outcomes, including intrauterine growth retardation (IUGR) and low birth weight (LBW), further emphasizing the importance of monitoring uric acid levels in pregnant women with PIH. While these results contribute to our understanding of the complex relationship between uric acid and pregnancy outcomes, further research is needed to confirm these associations and explore the underlying mechanisms. Nonetheless, this study highlights the potential clinical significance of uric acid monitoring as a tool for risk assessment and intervention planning in cases of pregnancy-induced hypertension, aiming to improve maternal and neonatal health outcomes.

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