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Raised Serum Uric Acid as a Predictor of Perinatal Outcome in Parturient with Pregnancy Induced Hypertension

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ABSTRACT

Objective: To evaluate the association of increased uric acid in pregnancy-induced hypertension with adverse perinatal outcomes.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Departments of Anesthesia, Gynecology & Obstetrics, Combined Military Hospital, Okara Pakistan, from Mar to Sep 2018.

Methodology: After approval of the Hospital Ethical Committee, 106 patients with pregnancy-induced hypertension were included in our study (n=53 in each group). Group-A had patient with raised uric acid, whereas Group-B had normal uric acid. Perinatal outcomes were monitored prospectively.

Results: There was no difference in demographic profile of the two study groups. Raised uric acid was shown to be associated with a higher cesarean mode of delivery (p=0.014); preterm delivery (0.001); intrauterine growth retardation (0.038); and low APGAR at 5mintues (0.008). Raised uric had a sensitivity greater than 65% and specificity greater than 50% for perinatal outcomes.

Conclusion: Raised uric acid is associated with adverse perinatal outcomes in neonates.

Keywords: AGPAR score, Cesarean section, Intrauterine death, Intrauterine growth retardation, Preterm delivery, Raised uric acid, Sensitivity, Specificity.

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INTRODUCTION

Pregnancy-induced hypertension (PIH) and its sequelae cause maternal and neonatal morbidity and mortality. The incidence of pregnancy-induced hypertension is reported between 5-19.4% worldwide.[1,2] Hypertension and its complications are the second cause of maternal mortality, accounting for 15% of maternal deaths in the USA.[3] Maternal complication of pregnancy-induced hypertension include pulmonary oedema; eclampsia; intracranial haemorrhage; acute renal failure; hepatic dysfunction, infarct or subcapsular hematoma; hemolysis elevated liver enzyme and low platelet (HELLP) syndrome, disseminated intravascular coagulopathy or consumption coagulopathy. Fetal complications include placental abruption, premature delivery, intrauterine growth retardation and intrau-terine fetal death.[4,5] Early diagnosis and prompt, effective management can help prevent complications; and improve maternal and neonatal outcomes. Unfortunately, no biomarker or laboratory test predicts PIH's progression to eclampsia, HELLP syndrome or adverse perinatal outcome. Clinical features include increased maternal age, chest pain, dyspnea, decreased oxygen saturation, and reduced platelet count. In addition, increased creatinine and aspartate transaminases concentration are predictive of adverse maternal outcomes.[6,7] Studies have shown that elevated uric acid is a useful biomarker in identifying patients at risk of progression to pre-eclampsia, developing adverse perinatal outcome or both.[8-10] Doppler ultrasound and Fetal Doppler pulsatility index ratio are other tests used for identification of parturient at risk of perinatal complication. Doppler ultrasound, however, requires equipment and expertise for management.[10]

The optimal tool for predicting perinatal outcomes should have high sensitivity and specificity, be readily available and be inexpensive to perform so that parturients at risk of complication from PIH can be referred early to tertiary care centres with facilities to monitor and manage both the mother and neonate. Therefore, our study aimed to evaluate the association of increased uric acid in pregnancy-induced hypertension with adverse perinatal outcomes.

METHODOLOGY

After the approval of the Hospital Ethical Committee (IERC/OBS/18/02), the comparative cross-sectional study was conducted at the Departments of

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Anesthesia and Gynecology & Obstetrics, Combined Military Hospital, Okara Cantonment Pakistan, from March to September 2018. The WHO sample size calculator was used to calculate sample size with predicted cesarean delivery of 32.87% versus 65.35%.[11]

Inclusion Criteria: Parturients of age greater than 18 years and suffering from pregnancy-induced hypertension with singleton pregnancy admitted for delivery were included in our study.

Exclusion Criteria: Parturients with chronic hypertension; pre-existing epileptic disorders; renal, hepatic dysfunction and coagulopathy were excluded from our study.

One hundred and six (53 in each group) consecutive parturients with pregnancy-induced hypertension were divided into two groups by convenience sampling. Group-A had serum uric acid greater than 6 mg/dL, whereas Group-B had uric acid levels less than 6mg/dL. Informed consent was taken. After a detailed history and examination, all the baseline investigations (Blood complete picture, urine for proteins, liver and renal function test and coagulation profile) were sent. The decision for vaginal or cesarean delivery was based on obstetric history and examination. Serum uric acid levels were also repeated at admission. All the patients were followed till discharge from the hospital. The adverse perinatal outcomes were recorded. The maternal outcome studied was the mode of delivery. The perinatal adverse outcome studied were intrauterine growth retardation, intrauterine death, preterm birth and low APGAR (<7) score at 5 minutes. This data and the demographic data were recorded on a pre-determined form.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Independent sample t-test was applied to find the mean differences among the groups. Chisquare test was applied to find out the association. The *p*-value lower than or up to 0.05 was considered as significant. The relative risk (RR) was calculated to see the strength of the association between serum uric acid and adverse perinatal outcomes. RR> 1 was considered significant.

RESULT

A total of 106 patients were included in our study. The mean age was 25.50±4.33 years. The comparison between the two groups was shown in Table-I. Most of the parturients in Group-A, 24(22.6%), underwent lower segment cesarean section due to obstetrics reasons versus 12(11.3%) in Group-B; *p*=0.014 and Relative Risk 2.8 (95%CI: 1.2-6.5). The comparison of neonatal outcomes was shown in Table-II. The comparison of raised uric acid as a diagnostic tool for perinatal outcomes was shown in Table-III.

Table-I: Comparison of Demographic Profile of Study Groups (n=106)

Variables	Group -A (n=53) (Mean±SD)	Group-B (n=53) ((Mean±SD)	*p*-value
Age (years)	25.79±4.42	25.30±4.27	0.714
Body Mass Index	24.94±4.57	24.57±4.65	0.710
Gestational age	31.43±1.60	31.62±1.71	0.868
Parity	2.32±0.89	2.32±0.85	0.679
	n(%)	**n(%)**	
Living			
Rural	15(14.2%)	17(16%)	0.672
Urban	38(35.8%)	36(24%)	
Gestational diabetes mellitus			
Yes	16(15.1%)	11(10.4%)	0.265
No	37(34.9%)	42(39.6%)	

Table-II: Comparison of Neonatal Outcomes in the Study Groups (n=106)

Variables		Group-A (n=53)	Group-B (n=53)	*p*-value	RR (95%CI)
APGAR score at 5 minutes	>7	9(8.5%)	1(0.9%)	0.008	10.6 (1.2-87.2)
	<7	44(41.5%)	52(49.1%)		
Intrauterine growth retardation	Yes	10(9.4%)	3(2.8%)	0.038	3.87 (1.0-14.9)
	No	43(40.6%)	50(47.2%)		
Intra-uterine demise	Yes	11(10.4%)	5(4.7%)	0.104	2.5 (0.8-7.8)
	No	42(39.6%)	48(45.3%)		
Preterm delivery	Yes	20(18.9%)	5(4.7%)	0.001	5.8 (1.9-17.0)
	No	33(31.1%)	48(45.3%)		

Table-III: Raised uric acid as Diagnostic Tool for Perinatal Outcomes (n=106)

Variables	Sensitivity	Specificity	Negative Predictive value	Positive Predictive Value
Low apgar score	90% (59.5-98.2)	45.8% (36.2-55.7)	97.7% (88.4-99.6)	14.7% (7.9-25.7)
Preterm delivery	80% (60.8-91.1)	59.2% (48.3-69.3)	90.5% (79.7-95.9)	37.7% (25.9-51.2)
Intrauterine growth retardation	76.9% (49.7-91.8)	53.76% (43.6-63.5)	94.3% (84.6-98.1)	18.9% (10.6-31.4)
Intrauterine demise	68.8% (44.4-85.8)	53.3% (43.1-63.3)	90.6% (46.2-64.8)	20.7% (12-33.5)

DISCUSSION

The role of raised serum uric acid on the development of arterial hypertension was first described in 1879. Later, it is associated with renal arteriosclerosis, ischemic stroke, atrial fibrillation and chronic heart

failure.[10-12] The effect of hyperuricemia on coronary artery disease was reported to be stronger in women as compared to men.[13] Elevated serum uric at lower gestational age has also been shown to be associated with increased risk of progression of PIH to pre-eclampsia.[14] It may even precede hypertension and proteinuria in the preeclamptic parturient. Abnormal renal function increased tissue breakdown acidosis and increased xanthine oxidase/dehydrogenase enzyme is postulated to be causes of hyperuricemia. Increased tissue breakdown in maternal, fetal and placental tissue may result in increased uric acid production and increased Xanthane Oxide production resulting in hyperuricemia. No definitive information is available on the effect of uric acid on the placenta, and a few hypotheses have been presented in studies. Uric acid has been shown to inhibit proliferation by 50% and migration by 75% of human umbilical vein endothelial cells. In addition, uric acid reduces the production of nitrous oxide in endothelial cells, which are speculated to prevent the remodelling of maternal spiral arterioles resulting in the compromise of oxygen and nutrients to the fetus. Furthermore, the localized elevation of xanthine oxide in invasive cytoblastic cells of a placenta may occur. All of the above may be further attenuated by the vasoconstrictive effect of uric acid on placental vasculature resulting in fetal compromise.[15]

Our study showed that elevated uric acid levels were associated with worse neonatal outcomes. A study by Enaruna *et al.* has reported that raised uric acid was associated with low birth weight in 76.9% versus 23.1% (p=0.041) in the parturient with normal uric acid levels.[16] Similarly, maternal mean arterial blood pressure was reported to be greater than 120 mmHg in 77.3% of parturients versus 22.7% with normal values (p=0.001). However, their Control Group was a normotensive parturient. They also reported that lipid profile abnormalities were not observed in their study population.

Bellomo *et al.* have reported 87.7% sensitivity and 93.3% specificity of uric acid as a predictor for the development of pre-eclampsia. They also reported its sensitivity and specificity of>70% for delivering small gestationalage infants.[17] However, they used 309 µmole/L versus 356 µmole/L in our study. Le *et al.* studied 205 parturients. Using serum uric acid cut-off value at 393 µg/litre, they reported that hyperuricemia was associated with increased risk of preterm birth (OR 6.367, 95% CI 3.009–13.084), low Apgar scores (OR 5.514, 95% CI 1.877–16.198), intrauterine growth restriction (OR 7.188, 95% CI 3.592–14.382) and neonatal death (OR 7.818, 95% CI 1.614–37.867). These findings correlate with our results. They reported no relationship between raised uric acid and fetal demise or delivery mode.[18]

Other authors have compared uric acid quantitatively on maternal and perinatal outcomes. Ryu *et al.* compared 65 parturients with preeclampsia and 75 parturients with normotensive.[19] They reported that the demographic profile was comparable, but serum uric acid was significantly higher in the pre-eclampsia group, 5.8 mg/dL (4.7-6.6) versus 3.9 mg/dL (3.1-4.6). It was shown to have a positive correlation with maternal higher systolic blood pressure (p=0.014), raised serum creatinine level (p<.001) & proteinuria (p=.014).

Serum uric acid can be easily performed and is economical. It can be used as a screening test to predict pregnancy at risk of development of perinatal complications.

LIMITATIONS OF STUDY

Our study had certain limitations. we did not study the correlation between raised uric acid with maternal outcomes.

CONCLUSION

Raised uric acid is associated with adverse perinatal outcomes like intrauterine growth retardation, intrauterine demise, low birth weight, low APGAR scores and perinatal death.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SZ: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AA & SM: Data acquisition, data analysis, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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