International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

A Prospective Study to Evaluate the Role of Uric Acid for Progression to Pre-Eclampsia in Gestational Hypertensive Pregnancy

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ABSTRACT

Background: Preeclampsia is a multiple organ disorder characterized by severe cardiopulmonary, renal, hepatic, and neurologic complications.The elevation of uric acid in preeclamptic women often precedes hypertension and proteinuria, the clinical manifestations used to diagnose the disorder.The purpose of this study was to determine whether maternal serum uric acid concentration, alone or combination with other biomarkers, can predict maternal or perinatal outcomes in women with preeclampsia.

Materials & Methods: A hospital based prospective study was done on 50pregnant women ≥20 weeks of gestation at department of Obstetrics & gynecology in Ananta Institute of Medical sciences, Rajsamand, Rajasthan, India.Blood samples were collected in plain vial and then sent for routine antenatal investigations. Then serum uric acid levels by biochemical testing at lab was estimated. Preeclampsia was diagnosed based on the "ACOG Task Force on Hypertension in Pregnancy 2013".

Results: Our study showed that, out of the 50 patients with an initial presentation of gestational hypertension, 32 patients (64%) progressed to preeclampsia. There were no significant differences in maternal age and history of miscarriage or gestational hypertension. Serum uric acid levels at the initial presentation of gestational hypertension were significantly higher comparing patients who later progressed to preeclampsia vs. those who did not (mean ± s.d.: 5.03±0.77 vs. 4.58±1.02 mg/dl, P < 0.01), whereas the levels of other routinely available lab test biomarkers were very similar.

Conclusion: We concluded that higher serum uric acid levels at the initial presentation of gestational hypertension may indicate heightened risk of progression to preeclampsia.

Keywords: Preeclampsia, Gestational Hypertension, Pregnancy, Hyperuricemia.

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Article History:

Received: 10-09-2020, **Revised:** 22-10-2020, **Accepted:** 28-11-2020

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2020.6.6.001	

INTRODUCTION

Hypertensive disorders are among the commonest medical disorders during pregnancy and a major cause of maternal and perinatal morbidity and mortality worldwide. It accounts for 15% to 20% of maternal deaths in developing and developed countries.[1]

Preeclampsia is a pregnancy-induced syndrome defined by sudden onset hypertension (≥140 systolic/90 diastolic mm Hg) and proteinuria (>300mg/24 h) after 20 weeks of gestation. The incidence of preeclampsia is estimated to be between 2% and 8% of all pregnancies.[2]

Preeclampsia is a multiple organ disorder characterized by severe cardiopulmonary, renal, hepatic, and neurologic complications. The fetus is also affected, and adverse perinatal outcomes include fetal growth restriction, preterm birth, and intrauterine death.

Gestational hypertension with hyperuricemia is associated with excess adverse fetal outcomes like intrauterine growth restrictions, perinatal deaths, intrauterine fetal deaths (IUFD). [1]

Increased uric acid concentration is one of the most pronounced clinical findings in preeclampsia. Hyperuricemia in preeclamptic women is primarily due to a reduction in glomerular filtration rate due to endothelial dysfunction.[3,4] Several studies have reported elevated uric acid concentrations to be positively correlated with adverse maternal and fetal outcomes.[5,6] However, others propose that an increased uric acid level is a poor predictor of maternal and fetal outcomes.[7,8] Experimental studies suggest that uric acid may attenuate trophoblastic invasion and inhibit placental system amino acid intake.[9] Uric acid may be directly involved in the

pathogenesis of preeclampsia by promoting inflammation, oxidative stress and endothelial dysfunction.[10] The elevation of uric acid in preeclamptic women often precedes hypertension and proteinuria, the clinical manifestations used to diagnose the disorder.The purpose of this study was to determine whether maternal serum uric acid concentration, alone or combination with other biomarkers, can predict maternal or perinatal outcomes in women with preeclampsia.

MATERIALS & METHODS

A hospital based prospective study done on 50pregnant women ≥20 weeks of gestation at department of Obstetrics & gynecology in Ananta Institute of Medical sciences, Rajsamand, Rajasthan.

Inclusion Criteria

- Women with singleton pregnancy with gestational hypertension.
- Patients giving consent to participate in study.

Exclusion Criteria

- Medical disorders of pregnancy.
- Abnormal high serum creatinine level (>1.5mg/dl).

Methods

All eligible pregnant women (n= 50) fulfilling inclusion criteria were explained about nature and purpose of the study. Blood samples were collected in plain vial and then sent for routine antenatal investigations (complete blood count, liver function test, renal function test, ABO Rh, viral markers).

Then serum uric acid levels by biochemical testing at lab were estimated. Concurrently, using all aseptic precautions, 5mL of venous blood was drawn for measurement of serum uric acid levels. The normal values used for reference in the 3rd trimester ranged between 3.1 and 6.3mg/dL.[11]

Preeclampsia was diagnosed based on the "ACOG Task Force on Hypertension in Pregnancy 2013"[12] as follows: women known to be normotensive who developed a systolic BP≥140mm Hg or diastolic BP≥90mm Hg on 2 occasions at least 4 hours apart after the 20th week of gestation and proteinuria ≥300mg/24 h urine collection or a protein/ creatinine ratio ≥0.3. In the absence of proteinuria, preeclampsia was diagnosed as hypertension with new-onset thrombocytopenia, elevated liver transaminase levels, renal insufficiency, pulmonary edema, and/or now-onset cerebral or visual disturbances.

Statistical Analysis

For continuous variables, differences between 2 groups were analyzed by a Student t test. Categorical variables were analyzed using the Pearson Chi square test or Fisher exact test, as appropriate.

Table 1: Characteristics of 50 singleton pregnant women with an initial presentation of gestational hypertension (GH) with vs. without the progression to preeclampsia (PE)

Characteristics	GH only (N=18)	GH-PE (N=32)	p-value
Maternal age	29.3±5.12	30.18±5.97	>0.05
Age≥35 yrs	4 (22.22%)	8 (25%)	>0.05
Primiparity	12 (66.66%)	20 (62.5%)	>0.05
BMI (kg/m²)	22.8±3.67	26.2±6.3	<0.05*
History of miscarrige	6 (33.33%)	13 (40.62%)	>0.05
History of preeclampsia	1 (5.55%)	4 (12.5%)	>0.05
Gestational age (weeks)	37.56±2.13	31.23±3.97	<0.01*
Systolic B.P (mmHg)	146±8	144±7	<0.05*
Diastolic B.P (mmHg)	87±7	85±8	<0.05*
Serum creatinine (mg/dl)	0.65±0.11	0.67±0.13	0.18
Serum uric acid (mg/dl)	4.58±1.02	5.03±0.77	<0.01*
Caesarean section delivery	4 (22.22%)	14 (43.75%)	<0.01*
Labor induction delivery	10 (55.5%)	17 (53.12%)	>0.05

GH= Gestational hypertension, GH-PE= Gestational hypertension with preeclampsia

Table 2: Crude and adjusted odds ratios* of the progression from gestational hypertension (n = 50) to preeclampsia (n = 32)

	Preeclampsia	
	Crude OR (95%CI)	**Adjusted OR (95%CI)**
Serum uric acid at GH onset per SD increase*	3.40 (1.50, 3.82)*	2.32 (1.44, 3.75)*
Gestational age at GH onset (weeks)	0.46 (0.38, 0.55)*	0.49 (0.40, 0.62)*
Primiparous	0.87 (0.50, 1.50)	1.08 (0.34, 3.28)
Obesity	8.34 (1.92, 36.3)*	5.40 (0.77, 39.7)

CI, confidence interval; GA, gestational age; GH, gestational hypertension; OR, odds ratio

RESULTS

Our study showed that, out of the 50 patients with an initial presentation of gestational hypertension, 32 patients (64%) progressed to preeclampsia. Comparing patients who progressed to preeclampsia vs. those who did not, the proportion of obese women was higher, the onset of gestational hypertension was earlier (mean gestational age: 31 vs. 37 weeks, P < 0.01), but systolic and diastolic BP were slightly lower at the onset of gestational hypertension (Table 1).

There were no significant differences in maternal age and history of miscarriage or gestational hypertension. Serum uric acid levels at the initial presentation of gestational hypertension were significantly higher comparing patients who later progressed to preeclampsia vs. those who did not (mean ± s.d.: 5.03±0.77 vs. 4.58±1.02 mg/dl, P < 0.01), whereas the levels of other routinely available lab test biomarkers were very similar.

Among the routinely available clinical and lab test variables, only gestational age and serum uric acid level at the onset of gestational hypertension were significantly associated with the progression to preeclampsia, and the development of adverse maternal/infant conditions in logistic regression models adjusting for potential confounders (Table 2). Each s.d. increase in serum uric acid level at the onset of gestational hypertension was associated with 2.3-fold higher odds of progression to preeclampsia (aOR 2.32 (95% CI 1.44–3.75)), while each week delay in the onset of gestational hypertension was associated with about 50% reduction in the odds of progression to preeclampsia (aOR 0.49 (0.40–0.62)).

DISCUSSION

Uric acid is the end product of purine metabolism and is synthesized by the enzyme xanthine oxidase. The etiology of hyperuricemia in preeclampsia is associated with oxidative stress and renal function impairment as a result of placental ischemia and reduced maternal glomerular filtration rate.[13] One probable mechanism is that the placenta may be affected by uric acid production associated with the levels and activity of xanthine oxidase/dehydrogenase.[14]

Our study showed that, out of the 50 patients with an initial presentation of gestational hypertension, 32 patients (64%) progressed to preeclampsia. Comparing patients who progressed to preeclampsia vs. those who did not, the proportion of obese women was higher, the onset of gestational hypertension was earlier (mean gestational age: 31 vs. 37 weeks, P < 0.01), but systolic and diastolic BP were slightly lower at the onset of gestational hypertension. Similar results founded by Yuquan Wu et al[15]prevalence of 63%progressed to preeclampsia.

Our results confirm that early onset of gestational hypertension is associated with an increased risk of progression to preeclampsia.[16,17] The lower odds of progression to preeclampsia among patients with later onset of gestational hypertension may be partly due to a shorter duration to delivery. Current practice is in favor of elective delivery in term hypertensive pregnancies to avoid the risk of developing preeclampsia. Maternal obesity and history of preeclampsia were not associated with progression to preeclampsia.

More recently, elevated uric acid levels at as early as the 1st trimester of pregnancy have been associated with the development of preeclampsia.[18] Only one recent study has examined the association between uric acid and progression to preeclampsia among patients with an initial presentation of gestational hypertension—Bellomo and colleagues reported that each 1mg/dl increase in serum uric acid level at the onset of gestational hypertension was associated with a large aOR of 7.1 (3.2, 15.7) for the progression to preeclampsia (effective n = 163; 45% progressed to preeclampsia) in a prospective cohort.[6] Uric acid levels were not adjusted for gestational age in their analyses.

Recent studies suggest more complex roles of uric acid in hypertensive pregnancy.[19,20]

Roberts and colleagues reported that even in the absence of proteinuria, hyperurincemia in gestational hypertensive patients was associated with adverse birth outcomes (preterm or small-for-gestational-age) relative to normotensive pregnancies.[20] Koopmans and colleagues recently linked higher uric acid levels to the development of eclampsia in gestational hypertensive and preeclamptic pregnancies.[21]

Uric acid concentration is not necessarily considered a criterion for diagnosing preeclampsia or used in management decisions regarding hypertensive women in clinics. If clinicians were aware of uric acid levels, it may have affected the timing of delivery for some women as well as fetal growth.[22]

CONCLUSION

We concluded that higher serum uric acid levels at the initial presentation of gestational hypertension may indicate heightened risk of progression to preeclampsia and development of adverse maternal/ infant conditions.

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Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Shabdika Kulshreshtha, Ganesh Gupta. A Prospective Study to Evaluate the Role of Uric Acid for Progression to Pre-Eclampsia in Gestational Hypertensive Pregnancy. Int J Med Res Prof. 2020 Nov; 6(6): 1-4. DOI:10.21276/ijmrp.2020.6.6.001