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THE ROLE OF SERUM URIC ACID LEVEL IN PROGRESSION TO PREECLAMPSIA IN GESTATIONAL HYPERTENSIVE PREGNANCIES

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ABSTRACT

Introduction: Pre-eclampsia, is a pregnancy induced disorder characterized by hypertension and proteinuria. **Aim:** To study the role of serum uric acid level in progression to preeclampsia in gestational hypertensive pregnancies. **Methodology:** The study will be conducted as a hospital-based comparative cross-sectional observational study, taking place at the Department of Obstetrics and Gynaecology, SMS Medical College in Jaipur. It will span from February 2019 to February 2020, with an additional two months allocated for data collection and analysis. This study design allows for the examination of serum uric acid levels among women diagnosed with gestational hypertension and those who subsequently develop preeclampsia. **Result:** It provides a detailed comparison between gestational hypertension with and without pregnancy-induced hypertension. It highlights differences in demographic characteristics (age distribution), clinical parameters (blood pressure, uric acid levels), delivery outcomes (LSCS rates), and neonatal outcomes (birth weight). Additionally, it suggests that serum uric acid levels at presentation might be a valuable predictor for the progression to preeclampsia in women with gestational hypertension. **Conclusion:** In conclusion, 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.

Keywords: Uric acid, preeclampsia, early predictor.

INTRODUCTION

Pre-eclampsia, is a pregnancy induced disorder characterized by hypertension and proteinuria[1].Incidence of pregnancy induced hypertension in India is 5-10% [2]Hypertension during pregnancy is diagnosed when the systolic pressure is 140 mmHg or more, and /or diastolic pressure of 90 mmHg or more, measured on two occasions at least 6 hours apart within 7 days. Throughout history, the primary goal of maternal care has been to ensure that each pregnancy results in the health and well-being of both the mother and the baby. While most pregnancies progress smoothly with minimal medical intervention, it is essential to identify high-risk groups early on. These groups require specialized care plans that cater to the needs of both the mother and her unborn child, who are intricately interconnected patients. Among the high-risk categories, hypertensive disorders of pregnancy are the most common complication. They, along with hemorrhage and infection, are part of a trio of conditions known for significantly contributing to maternal illness and death rates.

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Fortunately, these conditions are largely preventable, and with timely detection, they can be effectively managed.In essence, maternal care throughout history has centered on ensuring optimal outcomes for pregnancies while recognizing and addressing the risks that certain groups face. This approach aims to protect the health of both the mother and her child through early intervention and tailored medical attention.Pre-eclampsia is a progressive, multisystemic disorder characterized by triad of high blood pressure to the extent of 140/90 mm Hg or more, edema and proteinuria, developing after 20 weeks of pregnancy[3].It is one of the most common complications during pregnancy and the leading cause of both maternal and perinatal morbidity and mortality worldwide[4].Incidence of preeclampsia worldwide is around 5-10% of all pregnancies[3] and in developing countries around 4-18%.[5-6] It is much more common in women who are pregnant for the first time[7] and its frequency drops significantly in second pregnancies. Despite active research for many years, the etiology of this disorder remains unknown, although contributory factors including obesity, diabetes, older maternal age and job stress have been observed and studied[8-9]

Aim:

This study aims to contribute to the understanding of how serum uric acid levels may serve as a biomarker for predicting and potentially managing preeclampsia in women with gestational hypertension.

Methodology

The study will be conducted as a hospital-based comparative cross-sectional observational study, taking place at the Department of Obstetrics and Gynaecology, SMS Medical College in Jaipur. It will span from February 2019 to February 2020, with an additional two months allocated for data collection and analysis. This study design allows for the examination of serum uric acid levels among women diagnosed with gestational hypertension and those who subsequently develop preeclampsia. By comparing these groups, the research aims to identify potential cutoff values of serum uric acid that could predict the onset of preeclampsia in gestational hypertensive pregnancies. The findings from this study could contribute valuable insights into early detection and management strategies for improving maternal and fetal outcomes in high-risk pregnancies associated with hypertensive disorders.The study will include women who meet the following inclusion criteria: singleton pregnancy and diagnosed with gestational hypertension. Participants must also provide informed consent to participate in the study. Exclusion criteria will apply to women with other medical disorders of pregnancy and those with abnormal serum creatinine levels (>1.5 mg/dl). By focusing on women with gestational hypertension and ensuring exclusion of those with complicating medical conditions or abnormal renal function, the study aims to investigate the specific role of serum uric acid levels in predicting the progression to preeclampsia in this particular group. This approach will help clarify the relationship between serum uric acid and the development of preeclampsia, potentially leading to improved diagnostic and management strategies for pregnant women at risk for hypertensive disorders.

SAMPLE SIZE

Sample size of 80 patients is required at 80% study power and alpha error of 0.05 assuming 63% progression of gestational hypertensive pregnancies into preeclampsia and area under curve (AOC) of 0.66 for serum uric acid level as per results of seed article (American Journal Of Hypertension, 2014, Volume 25 Number 6, page 711-717). It is further enhanced and rounded off to 90 patients as final sample size for present study expecting 10% droupouts/loss to follow up.

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RESULT

Distribution of study population according to maternal age

Age in Yrs	**GH without PIH**		**GH with PIH**		**p-value**
	No	**%**	**No**	**%**	
<20	3	4.84	2	7.14	0.265
20-24	23	37.10	10	35.71	
25-29	30	48.39	15	53.57	
30-34	6	9.68	0	0.00	
≥35	0	0.00	1	3.57	
Total	**62**	**100.00**	**28**	**100.00**	
Mean	25.10		25.38		0.726
SD	3.74		3.37		

The maximum number of subjects i.e. 30 (48.39%) belonged to age group 25-29 years followed by 23(37.10%) subjects belonged to 20-24 yrs in GH without PIH group. The maximum number of subjects i.e. 15 (53.37%) belonged to age group 25-29 years followed by 10(35.71%) subjects belonged to 20-24 yrs in GH without PIH group.The mean age in GH without PIH was 25.10±3.74 years and mean age in GH with PIH was 25.38±3.37 years (p value >0.05). This shows that the age of subjects were comparable in the two groups. This age group reflects the peak of reproductive period.

Distribution of study population according to SBP DBP

SBP in mm of hg	**GH without PIH**	**GH with PIH**	**p-value**
Mean	142.85	147.50	0.03
SD	8.54	10.58	

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Mean	95.12	97.12	0.02
SD	8.24	7.68	

Systolic blood pressure was significantly higher in with PIH (147.50±10.58mm of hg) as compared to without PIH (142.85±10.58mmof hg)Diastolic blood pressure was significantly higher in with PIH (97.12±7.68 mm of hg) as compared to without PIH (95.12±8.24 mm of hg)

Distribution of study population according to uric acid birth weight

Uric acid (mg/dl)	**GH without PIH**	**GH with PIH**	**p-value**
Mean	4.92	6.68	0.001
SD	0.57	0.36	
Mean	2.83	2.21	0.001
SD	0.15	0.16	

Uric acid level was significantly higher in with PIH (6.68±0.36 mg/dl)as compared to without PIH (4.92±0.57 mg/dl).Brith weight level was significantly higher in without PIH (2.83±0.15kg) as compare to with PIH (2.21±0.16kg).

Distribution of study population according to mode of delivery

Mode of delivery	**GH with PIH**		**GH without PIH**		**p-value**
	No	**%**	**No**	**%**	
NVD	10	16.13	18	64.29	0.001
LSCS	52	83.87	10	35.71	

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Total	62	100.00	28	100.00	

83.87% LSCS in with PIH group and 35.71% LSCS in without PIH.

Diagnostic value of uric acid

Area	**Std. Error[a]**	**Asymptotic Sig.[b]**	**95%CL**	
			Lower	**Upper**
1.0	0.0	0.0	1.00	1.00

Receiver-operator characteristic curve showed relatively poor sensitivity and specificity performance (area under the curve= 1.00) of serum uric acid level at the initial presentation of gestational hypertension for predicting the progression to preeclampsia The best cut-off revealed from the curve was 6.18 mg/dl.

Diagnostic Accuracy

Sensitivity	64.29
Specificity	100.00
PPV	100.00
NPV	86.11
Diagnostic accuracy	88.89

The best cut-off revealed from the curve was 6.18 mg/dl, with sensitivity = 64.29%, specificity = 100.00%, positive predictive value = 100.00%, negative predictive value = 86.11%.

Discussion

In our study the maximum number of subjects i.e. 30 (48.39%) belonged to age group 25-29 years followed by 23(37.10%) subjects belonged to 20-24 yrs in GH without PIH group. The maximum number of subjects i.e. 15 (53.37%) belonged to age group 25-29 years followed by 10(35.71%) subjects belonged to 20-24 yrs in GH without PIH group. Mean age in GH without PIH was 25.10±3.74 years and mean age in GH with PIH was 25.38±3.37 years (p value >0.05). This shows that the age of subjects were comparable in the two groups.Meena R et al (2019)[10] shows that almost 58% and 74% participants belonged to <24 years age

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group in case and control group respectively. Mean age of participants were 23.9 years with 3.4 SD and 25.4 years with 4.8 SD in case and control group respectively.

Systolic blood pressure was significantly higher in with PIH (147.50±10.58mm of hg) as compared to without PIH (142.85±10.58mm of hg). Diastolic blood pressure was significantly higher in with PIH (97.12±7.68 mm of hg) as compared to without PIH (95.12±8.24 mm of hg) in our study.Naina K et al (2017)[11]observed that Systolic blood pressure was significantly higher in with PIH (46.23±9.62 mm of hg) as compared to without PIH (140.21±10.12 mm of hg). Diastolic blood pressure was significantly higher in with PIH (96.32±6.21 mm of hg) as compared to without PIH (95.00±8.01 mm of hg).

In our study 83.87% LSCS in with PIH group and 35.71% LSCS in without PIH.Yuquan Wu et al (2012)[12] observed that birth weight was significantly lower in cases (2.19±0.24 kg) as compare to control(2.69±0.24kg).
Uric acid level was significantly higher in with PIH (6.68±0.36 mg/dl) as compared to without PIH (4.92±0.57 mg/dl). Receiver-operator characteristic curve showed relatively poor sensitivity and specificity performance (area under the curve= 1.00) of serum uric acid level at the initial presentation of gestational hypertension for predicting the progression to preeclampsia. The best cut-off revealed from the curve was 6.18 mg/dl, with sensitivity = 64.29%, specificity = 100.00%, positive predictive value = 100.00%, negative predictive value = 86.11%.Which was compatible with Ahmed A et al,[13] found in preeclampsia 7.35 mg/dl as compare to 4.47 mg/dl in control group, Pramanik T et al,[14] in Nepal (2012-2013) [6.27±1.37 vs 4.27±0.61 mg/dl] in pre-eclamptic patients compared to their healthy counterparts and ALZuabidi ZFM et al,[15] in Iraq in preeclampsia was 7.68±0.79 mg/dl as compare to 4.18±1.17 mg/dl in control group.

The associations between higher uric acid levels and preeclampsia,[16-17] or between higher uric acid levels and poorer perinatal outcomes among preeclamptic patients[18,19] have been well documented. More recently, elevated uric acid levels at as early as the 1st trimester of pregnancy have been associated with the development of preeclampsia[20] 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[21].Uric acid levels were not adjusted for gestational age in their analyses. If uric acid levels were not adjusted for gestational age, the effect size was slightly smaller. These findings suggest that serum uric acid level may be a risk marker of progression to preeclampsia among patients with an initial presentation of gestational hypertension, even though most serum uric acid levels were within the normal range. We could not confirm the excellent sensitivity and specificity of serum uric acid in predicting the progression to preeclampsia reported by Bellomo and colleagues[22].The relatively poor sensitivity and specificity in our cohort suggest limited clinical utility of uric acid alone in predicting the progression to preeclampsia. Larger multicenter prospective studies are required to elucidate the clinical utility of uric acid in predicting the progression to preeclampsia and the development of adverse conditions.

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Conclusion

In conclusion, 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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