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Original Article

# Association Between Serum Uric Acid Levels and Severe Pre-Eclampsia

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## ABSTRACT

***Objective:*** To determine the association of hyperuricemia with severe preeclampsia in pregnancy.
***Study Design:*** Prospective Longitudinal study
***Place and Duration of Study:*** Department of Gynecology, Combined Military Hospital, Multan, Pakistan from Mar 2019 to Jul 2019.
***Methodology:*** A total of 68 women with gestational age 20 weeks, parity 0-5, patients with uricemia level ≥5.5mg/dl has been added in exposed group and patients with uricemia level <5.5mg/dl has been added in non-exposed group. Patients were evaluated by detailed history, clinical examination and BP. All relevant findings were documented on a designed proforma. Severe Preeclampsia was noted from both groups.
***Results:*** Women of 18 to 40 years age were selected with mean age of 29.911± 3.49 years in Group A while 31.558± 3.99 years in Group B. Mean gestational age was 23.264±1.84 weeks in Group A and 24.352±1.99 weeks in Group B. Mean serum uricemia level was 6.961±0.74 mg/dl in Group A and 4.635±0.44 mg/dl in Group B. In group A, severe preeclampsia has been seen in 17(50%) womens as compare to 6(17.6%) womens in group B, ($p$=0.004, R.R=2.8).
***Conclusion:*** This study concluded that the severe pre-eclampsia was associated with hyperuricemic pregnancy.

**Keywords:** Hyperuricemia, Pregnancy, Severe pre-eclampsia.

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## INTRODUCTION

Preeclampsia is a severe condition. It is a complicated condition described by proteinuria (24-hr urinary protein ≥0.3g) usually associated with edema, elevated blood pressure ≥140/90 mmHg, 5th month onwards of gestation in earlier normotensive and nonproteinuric patient.[1] This syndrome usually involve all organ. Gestational hypertension is a communal appearance of preeclampsia. Preeclampsia is related with Hyperuricemia. The relationship between hyperuricemia and pre-eclampsia previously described during 1917.[2] Decreased uric acid clearance due to reduced renal functions, augmented reabsorption and diminished secretion are causes of Hyperuricemia in pregnancy.[3] The pathophysiology of this condition including augmented trophoblastic tissue flaking, endothelial dysfunction, and decreased flow of blood had also been theorized as the primary cause of elevated uric acid in this disorder.[3] Hyperuricemia in pregnancy is not merely a sign of harshness, it does play an uninterrupted role with the pathophysiology of the condition as Hyperuricemia negatively effects vasculature of gravid uterus. It can lead to hypertension by a rise in salt sensitivity and multiplication of vascular muscle fibers and proteins in urine.[4] Other literature stated that elevated uric acid is not a constant element of preeclampsia.[5] Another study revealed minor difference in uric acid level amongst normal and slight preeclamptic women.[6] Due to this debate of diverse studies, generating mutable results, which cannot be isolated on our confined population, consequently I have organized to define the link of hyperuricemia with severe preeclampsia in pregnancy in our confined population.

## METHODOLOGY

This prospective longitudinal study has been conducted in the department of gynecology Combined Military Hospital, Multan from March 2019 to Jul 2019. A total of 68 women with gestational age 20 weeks, parity 0-5, patients with uricemia level ≥5.5mg/dl has been added in exposed group and patients with uricemia level <5.5mg/dl has been added in non-exposed group. Sample size was calculated by using WHO calculator. Technique was Non-probability consecutive sampling technique was used. Patients as per inclusion criteria from outdoor patient department of CMH, Multan were taken under approval of ethical

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committee Ser no 10. Size of the sample was concluded with confidence level= 95% and alpha= 5% (two-sided) with power =80% By taking least expected proportion (severe Preeclampsia) in population 1=50%. and least expected proportion (severe preeclampsia) 2=18%.[7] Predictable sample size n=68 was divided into two groups. 34 patients from Group A or Hyperuricemia group while 34 patients from Group B or normouricemic group. Basic demographics were documented and consent was signed by each patient, ensuring that there was no threat to the patient involved while doing this study.

**Inclusion Criteria**: Pregnant women with age 18-40 years, Gestational age 20 weeks by ultrasound, Parity 0-5, Patients with uricemia ≥5.5mg/dl has been added in Group A or Exposed group and Patients with uricemia <5.5mg/dl has been added in Group B or Non Exposed group.

**Exclusion criteria**: Patients with renal disease, use of drugs affecting uric acid levels, chronic hypertension on medical record, diabetes on medical record and Refused the consent. Severe Preeclampsia was noted as per operational definition.

Patients were evaluated by detailed history, clinical examination and BP. Clinical and laboratory analysis like uricemia levels was noted on a designed proforma. Figures were inspected using IBM-SPSS version 22. Data was assessed to compare proportion of Group A (Hyperuricemia group) and Group B (normouricemic group). Frequencies and percentages were calculated for specified variables as parity, severe preeclampsia. Mean±SD was taken for specified variables as age of the patient, gestational age, and serum uric acid levels. Chi-square test was done to relate both groups taken significant $p \leq 0.05$.

## RESULTS

Total 68 patients, age ranging from 18 to 40 years with mean age of 29.911±3.49 years in Group A while 31.558±3.99 years in Group B were included. Mean gestational age was 23.264±1.84 weeks in Group A and 24.352±1.99 weeks in Group B. Mean uremia level was 6.961±0.74 mg/dl in Group A and 4.635±0.44 mg/dl in Group B displayed inTable-I.

Frequencies and percentages as per parity of patient in both groups are

Displayed in Table-II. Patients with 0-2 number of parity were analyzed separately from patients with 3-5 number of parity in both study groups.

In group A, severe preeclampsia observed in 17(50%) women as compare to 6(17.6%) women in group B, ($p$=0.004, R.R=2.8) as mentioned in Table-III.

**Table-I: Mean Patients as Per the Age of Patient, Gestational age and Serum Uric Acid Levels (n=68)**

| Demographics | | Mean±SD Group A n=34 | Mean±SD Group A n=34 |
|---|---|---|---|
| 1 | Age (years) | 29.911±3.49 | 31.558±3.99 |
| 2 | Gestational age (weeks) | 23.264±1.84 | 24.352±1.99 |
| 3 | Serum uric acid levels (mg/dl) | 6.961±0.74 | 4.635±0.44 |

**Table-II: Frequency of Womens as Per Parity in Both Groups (n=68)**

| Parity | Group A n=34 | Group A n=34 |
|---|---|---|
| 0-2 | 24 (70.6%) | 14 (41.2%) |
| 3-5 | 10 (29.4%) | 20 (58.8%) |
| Total | 34 (100%) | 34 (100%) |

**Table-III: Comparison of Severe Preeclampsia in Both Groups (n=68)**

| Severe Preeclampsia | Group A n=34 | Group A n=34 | $p$-value R.R |
|---|---|---|---|
| Yes | 17(50%) | 6(17.6%) | 0.004 2.8 |
| No | 17(50%) | 28(82.4%) | |
| Total | 34(100%) | 34(100%) | |

## DISCUSSION

Though uricemia does not analyze the progress of preeclampsia, the stringency of uricemia has been detected for relation of mother and fetus diseases and strictness of the kidney lesion, and to be in reverse proportionate to birth weight. Furthermost, surge of the uricemia leads the beginning of proteins in urine and elevated blood pressures, signifying a likely underlying oddity of uric acid. In recent times, as of uricemia's role in vascular injury and in production of oxides, uricemia has been suggested as a feeder in the pathology of preeclampsia. Furthermore, renal vascular disease is frequently observed in persons with preeclampsia and is constant with a uric acid–arbitrated consequence. This can also illuminate why preeclampsia have an augmented probability of evolving elevated blood pressures.

Decreased urea clearance due to reduced renal functions, augmented reabsorption and decreased excretion can be the causes of raised uricemia in pregnancy with preeclampsia. In group A (Hyperuricemia), severe preeclampsia was seen in 17(50%) patients as relate to 6(17.6%) women in group

B, ($p$=0.004, R.R=2.8). In a research conducted at Delta Med Col J, associated the average altitudes of uricemia in normotensive patients with preeclampsia, consequences indicated that preeclampsia was related to raised uricemia.[7] Also, another study monitored subjects for 30 days post-delivery and stated uricemia as a consistent interpreter of preeclampsia in pregnancy with elevated blood pressure in pregnancy. They specified uricemia of 309 µm/l as a forecaster of preeclampsia.[8] Idemudia JO similarly demonstrated that uricemia in pregnancy with severe pre-eclampsia was greater relative to the controller group.[9] Tong M along with coworkers presented an elevated uricemia in patients having preeclampsia and rise occurred at the commencement of preeclampsia. Although no major dissimilarity was seen amongst preeclampsia and normal pregnancy concerning the uricemia in the starting 6 months of pregnancy. Tong M convinced that serum uricemia augmented at the commencement of preeclampsia, nevertheless it may not be an interpreter of preeclampsia and must not be measured as an analytical sign.[10] Gadde R stated the rise of uricemia in the start of pregnancy was related to preeclampsia and rise of blood pressure in pregnancy was associated with elevated uricemia.[11] Roberts JM described increase in uricemia in pregnancy with elevated blood pressure was a significant outcome which may lead patient to adversarial maternal and fetal problems. Though patients with gestational hypertension, deprived of added marks of pre-eclampsia had contrary embryonic problems such as small for gestational age and underdevelopment. Here uricemia was dignified at fully developed period as in our set ups.[12] Simsek T presented increased uricemia, xanthine oxidase and Allantoin action and hypertension in women having preeclampsia as opposed to the controller group.[13] Simsek T recommend augmented uricemia, xanthine oxidase and Allantoin action could be documented resulting the demise of placental cells ensuing atypical response of trophoblast in preeclampsia. As a result, presently, clinicians favor the revealed origins for raised uricemia in preeclampsia as a substitute of renal disease ensuing preeclampsia.[14] Balconi SM presented that untill 20 weeks of gestation, the average uricemia in preeclamptic patients and normal pregnancy were parallel. However after that, the average uricemia in preeclamptics was 1.5 times greater than normal women. The rise corresponded to the constant creatinine and uric acid in women and exhibited raised uricemia must be alienated from renal disorders.[15] Conversely, Yang JM related raised uricemia in pregnancy with preeclampsia and inflammatory response of maternal vasculatures, which might be accessible by raised Tumor necrosis factor alpha TNF-alpha and Intercellular adhesion molecule-1.[16,17] Romao M articulated the raised uricemia by inflammatory responses, which was related with the appearance of nod-like intracellular receptors with a pyrin domain NLRP3 gene in pregnancy having preeclampsia.[18]

The main limitations in my study are small sample size and ultrasound technique to know the exact gestational age of fetus. I acknowledge all my fellow authors who participated in completing this study.

## CONCLUSION

Our study concluded that the severe pre-eclampsia was related to Hyperuricemia pregnancy. As measuring uricemia in the pathology department could be simply executed, this gives the impression of diagnosis and prognosis in defining the likelihood of preeclampsia and should be utilized in treatment and management of patients with preeclampsia.

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**Authors' Contribution**

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

AA & MSA: Data acquisition, data analysis, critical review, approval of the final version to be published.

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

ABS: Conception, data acquisition, 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.

## REFERENCES

1. English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. Integr Blood Press Control 2015; 8: 7–12.
2. Siemons JM, Bogert LJF. The uric acid content of maternal and fetal blood. J Biol Chem 1917; 32: 63–67.
3. Yalamati P, Bhongir AV, Betha K, Verma R, Dandge S. Relationship of serum uric acid, serum creatinine and serum cystatin C with maternal and fetal outcomes in rural Indian pregnant women. Int J Reprod Contracept Obstet Gynecol 2015; 4(5): 1505–1510.
4. Jin M, Yang F, Yang I. Uric acid, hyperuricemia and vascular diseases. Front Biosci 2012; 17: 656–669.

5. Niraula A, Lamsal M, Majhi S, Khan SA, Basnet P. Significance of serum uric acid in pregnancy induced hypertension. Journal of the national medical association 2017; 109(3): 198-202.
6. Anusha T, Sankaranarayana t. Study of serum calcium, magnesium, uric acid and liver enzymes in pregnancy induced hypertension. Journal of Evolution of Medical and Dental Sciences 2018; 7(11): 1347-53.
7. Sultana R AS, Sultana N, Karim SM F, Atia F. Association of Serum Uric Acid with Preeclampsia: A Case Control Study. Delta Med Col J 2013; 1: 46–50.
8. Le TM, Nguyen LH, Phan NL, Le DD, Nguyen HV, Truong VQ, et al. Maternal serum uric acid concentration and pregnancy outcomes in women with pre-eclampsia/eclampsia. International Journal of Gynecology & Obstetrics 2019; 144(1): 21-26.
9. Enaruna NO, Idemudia JO, Aikoriogie PI. Serum lipid profile and uric acid levels in preeclampsia in University of Benin Teaching Hospital. Niger Med J 2014; 55: 423–427.
10. Chen Q LS, Tong M, Wei J, Shen F, Zhao J, Zhao M. Serum uric acid may not be involved in the development of preeclampsia. J Hum Hypertens 2016; 30: 136–140.
11. Gadde R, Doddaiah DC, Rangappa SS. Relationship between Mean Arterial Pressure, Uric Acid and Calcium with Xanthine Oxidase Activity and Fetal Outcome in Normotensive and Preeclampsia in a Nested Study. Open Journal of Obstetrics and Gynecology 2018; 8(14): 1532.
12. Hawkins TL, Roberts JM, Mangos GJ, Davis GK, Roberts LM, Brown MA. Plasma uric acid remains a marker of poor outcome in hypertensive pregnancy: a retrospective cohort study. BJOG 2012; 119: 484–492.
13. Elmas O AY, Simsek T. The relationship between hypertension and plasma allantoin, uric acid, xanthine oxidase activity and nitrite, and their predictive capacity in severe preeclampsia. J Obstet Gynaecol 2016; 36: 34–38.
14. Masoura S, Makedou K, Theodoridis T, Kourtis A, Zepiridis L, Athanasiadis A. The involvement of uric acid in the pathogenesis of preeclampsia. Curr Hypertens Rev. 2015; 11: 110–115.
15. Corominas AI, Balconi SM, Palermo M, Maskin B, Damiano AE. Serum uric acid levels and risk of developing preeclampsia. Medicina 2014; 74: 462–471.
16. Zhao J ZD, Yang JM, Wang M, Zhang XT, Sun L, Yun XG, et al. Maternal serum uric acid concentration is associated with the expression of tumour necrosis factor-alpha and intercellular adhesion molecule-1 in patients with preeclampsia. J Hum Hypertens 2016; 30: 456–462.
17. Asgharnia M, Mirblouk F, Kazemi S, Pourmarzi D, Keivani MM, Heirati SF, et al. Maternal serum uric acid level and maternal and neonatal complications in preeclamptic women: A cross-sectional study. International Journal of Reproductive BioMedicine 2017; 15(9): 583.
18. Matias ML, Romao M, Weel IC, Ribeiro VR, Nunes PR, Borges VT, et al. Endogenous and Uric Acid-Induced Activation of NLRP3 Inflammasome in Pregnant Women with Preeclampsia. PloS One 2015; 10: e0129095.


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