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Original Article

Serum Uric Acid as a Predictor of Perinatal Outcome in Women with Pre-eclampsia: A prospective Cohort Study

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Abstract

Objective: To assess the connection among elevated serum uric acid (SUA) levels and adverse fetal outcomes in women with pre-eclampsia.

Methods: This Prospective, cohort study was conducted in the Department of Obstetrics & Gynecology, Fauji Foundation Hospital Rawalpindi. Ethical approval was granted by the ERC of the hospital. A total of 60 women (30 exposed and 30 unexposed) of age 18-40 years were included. Patients with already taking medications for hyperuricemia, chronic hypertension, CRF and severe systemic illness like uncontrolled diabetes mellitus type 2, heart diseases were excluded. Group A (exposed) included the females with serum uric acid levels ≥6 mg/dl on presentation while Group B (unexposed) included pregnant females with serum uric acid levels <6 mg/dl . Data was analyzed using SPSS-25.0

Results: The study results indicated that 50.0% of women with serum uric acid level of ≥ 6 mg/dl and pre-eclampsia experienced low birth weight, whereas only 26.67% of women having a SUA level of <600 mg/dl and preeclampsia had this outcome. Additionally, 40.0% of women with pre-eclampsia and high serum uric acid levels had intrauterine growth retardation, compared to 6.67% of those with lower serum uric acid levels. NICU admission was also more common in women with serum uric acid ≥6 mg/dl (23.33%) and pre-eclampsia as compared to those with <600 mg/dl (6.67%). These findings, with a p-value of <0.05 and a relative risk of >1, signify a significant and positive association between elevated serum uric acid levels and adverse outcomes for both the fetus and the mother.

Conclusion: This study concluded that there is a positive association between high serum uric acid levels and adverse feto-maternal outcome.

Keywords: Preeclampsia, Uric acid, Feto-maternal outcome

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Introduction

Pregnancy-related hypertensive disorders, notably gestational hypertension and pre-eclampsia, are significant maternal health issues. These conditions, which impact expectant mothers, are characterized by increased blood pressure levels and, in the case of pre-eclampsia, encompass a multifaceted range of the problems affecting both the mother and the fetus. These complications include visual disturbances, reduced urine output, seizures (eclampsia), red blood cell breakdown (hemolysis), elevated liver enzyme levels, decreased platelet count (thrombocytopenia), fluid accumulation in the lungs (pulmonary edema), and restrictions in fetal growth.[1] Pregnancy-induced hypertension occurs in approximately 12-22% of pregnancies, adding issues to a significant portion of expectant mothers.[2] Swift recognition and effective handling of these conditions are crucial for minimizing their consequences, even though we still have an incomplete understanding of their fundamental pathophysiology. Among these conditions, pre-eclampsia is said to be a major contributor to morbidity and mortality of the mother and fetus. It affects around 2-8% of pregnancies and is linked to numerous complications.[3] Forecasting its onset remains difficult due to

the many contributing factors involved[4], Stimulating a variety of approaches that employ fetal/placental and maternal indicators at various pregnancy stages for predicting this condition.[5] Significantly, an association between elevated serum uric acid levels, a condition known as hyperuricemia, and pre-eclampsia has been established as far back as 1917.[6]

Moreover, theories establish a connection between it and the injury of endothelial cells[7], placenta rejection by immune system,[8] altered vascular activity, atmospheric pollution[9], and other factors. Many research findings have demonstrated a 'positive' connection between heightened uric acid levels and adverse maternal as well as fetal outcomes.[10,11] Nonetheless, some suggest that an elevated uric acid level may not effectively forecast maternal and fetal results.[12,13] Factors that increase the likelihood of developing pre-eclampsia encompass gestational age,[14] age of the mother, her racial background, and a range of medical conditions. First-time pregnant individuals, mothers of advanced age, and women of African descent encounter heightened risks. Factors such as smoking while pregnant, placenta previa, insufficient vitamin D levels, and obesity are also linked to these risks. It's important to note that early-onset and late-onset pre-eclampsia have distinct sets of risk factors and outcomes, with early-onset cases being connected to increased fetal and perinatal mortality rates.[15]

However, its effectiveness as a dependable predictor of negative outcomes for both mothers and fetuses remains a topic of contention, with differing results in existing research. Given the worldwide nature of these investigations, it becomes crucial to evaluate the applicability of hyperuricemia as an indicator of unfavorable fetal outcomes in pre-eclampsia on a regional level. Our study seeks to explore this connection within our specific population, offering valuable local data. These discoveries will empower healthcare professionals with evidence-driven insights to establish systematic screening procedures and efficient management approaches for elevated serum uric acid levels during pregnancy, ultimately leading to a substantial reduction in perinatal health issues and fatalities in our community. Our research adds to the global conversation about this pivotal subject while addressing its implications within our local context.

Methods

A Prospective, cohort study was conducted from 15th December 2020 to 14th June 2021 after approval from ethical review committee, total number of 60 pregnant women (30 exposed and 30 unexposed) who were presented to the Inpatients Department of Obstetrics & Gynecology of Fauji Foundation Hospital, Rawalpindi, fulfilling the inclusion criteria were selected. Informed consent was taken from each woman. All women were followed till delivery by the researcher herself and final outcome i.e. low birth weight, IUGR and NICU admission (yes/no) was noted as defined in operational definition. This all data (age, gestational age, parity, place of living (rural/urban), BMI, education level (illiterate/primary/middle/matric & above), uric acid levels and outcome i.e. low birth weight, IUGR and NICU admission (yes/no)) was recorded on a self-designed proforma. All women of 18 to 40 years age, with singleton pregnancy (assessed on USG) of gestational age >24 weeks (assessed on LMP), excluding women with chronic hypertension, chronic renal disease or severe systemic illness.

The data was subjected to statistical analysis utilizing SPSS version 25.0. The following variables were analyzed: age, gestational age, BMI, and uric acid levels, and they were presented as mean and standard deviation. Additionally, other variables, including parity (primiparous/ multiparous), place of living (rural/urban), education level (illiterate/primary/middle/matric & above), and outcomes such as low birth weight, intrauterine growth restriction (IUGR), and neonatal intensive care unit (NICU) admission (yes/no) were examined. In examining the correlation between uric acid levels and adverse fetal outcomes, particularly in women diagnosed with pre-eclampsia, a Chi-Square test was employed, with a significance threshold established at $P \leq 0.05$.The relative risk (RR) was also calculated to measure the strength of the association, and $RR > 1$ was considered significant, indicating an elevated risk. The study controlled for potential effect modifiers, including age, gestational age, parity, body mass index, place of living (rural/urban), and educational level (illiterate/primary/middle/matric & above) through stratification. Post-stratification chi-square tests were employed to assess their impact on the outcome. Again, a significance level of $P \leq 0.05$ was applied, and RR was calculated, with $RR > 1$ indicating significance in this context.

Results

The demographic characteristics of the study population are displayed in table 1.

The study results indicated that 50.0% of women with serum uric acid level of ≥6 mg/dl and pre-eclampsia experienced low birth weight, whereas only 26.67% of women having a serum uric acid level of <600 mg/dl and preeclampsia had this outcome. Additionally, 40.0% of women with pre-eclampsia and high serum uric acid levels had intrauterine growth retardation, compared to 6.67% of those with lower serum uric acid levels. NICU admission was also more common in women with serum uric acid ≥6 mg/dl (23.33%) and pre-eclampsia as compared to those with <600 mg/dl (6.67%). These

findings, with a p-value of <0.05 and a relative risk of >1, signify a significant and positive association between elevated serum uric acid levels and adverse outcomes for both the fetus and the mother. The results are shown in table 2.

Table 1: *Distribution of patients according to education level*

Education level	Exposed (n=30)		Unexposed (n=30)		Total (n=60)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
Illiterate	02	6.67	04	13.33	06	10.0
Primary	11	36.67	07	23.33	18	30.0
Middle	10	33.33	08	26.67	18	30.0
Matric	07	23.33	11	36.67	18	30.0

Table 2: *Association between raised serum uric acid levels and adverse fetal outcome in women with pre-eclampsia*

Adverse feto-maternal outcome	Exposed (n=30)		Unexposed (n=30)		P-value	RR
	Yes	No	Yes	No		
LBW	15	15	08	22	0.019	2.00
	(50.0%)	(50.0%)	(26.67%)	(73.33%)		
IUGR	12	18	02	28	0.034	4.91
	(40.0%)	(60.0%)	(6.67%)	(93.33%)		
NICU admission	07	23	02	28	0.117	2.20
	(23.33%)	(76.67%)	(6.67%)	(93.33%)		

Stratification of LBW with respect to age, gestational age, parity, body mass index, place of living and educational level is shown in table 3.

Table 3: *Stratification of LBW with respect to age, gestational age, parity, body mass index, place of living and educational level*

		Exposed (n=30) LBW		Unexposed (n=30) LBW		P-value	RR
		Yes	No	Yes	No		
Age (years)	**18-30**	12 (57.14%)	09 (42.86%)	08 (33.33%)	16 (66.67%)	0.118	1.71
	31-40	03 (33.33%)	06 (66.67%)	00 (0.0%)	06 (100.0%)	0.266	4.90
Gestational age	**25-32**	13 (50.0%)	13 (50.0%)	07 (29.17%)	17 (70.83%)	0.149	1.71
	>32	02 (2.0%)	02 (2.0%)	01 (16.67%)	05 (83.33%)	0.291	3.00
Parity	**0-2**	08 (44.44%)	10 (55.56%)	07 (36.84%)	12 (63.16%)	0.639	1.21
	3-4	07 (58.33%)	05 (41.67%)	01 (9.09%)	10 (90.91%)	0.059	6.42
BMI (kg/m^2)	**≤30**	14 (53.85%)	12 (46.15%)	08 (28.57%)	20 (71.43%)	0.069	1.88
	>30	01 (25.0%)	03 (75.0%)	00 (0.0%)	02 (100.0%)	0.687	1.80
Place of living	**Rural**	06 (66.67%)	03 (33.33%)	01 (11.11%)	08 (88.89%)	0.065	6.00
	Urban	09 (42.86%)	12 (57.14%)	07 (23.33%)	14 (66.67%)	0.528	1.29
Education level	**Illiterate**	01 (50.0%)	01 (50.0%)	01 (25.0%)	03 (75.0%)	0.535	2.00
	Primary	04 (36.36%)	07 (63.64%)	01 (14.29%)	06 (85.71%)	0.354	2.55
	Middle	05 (50.0%)	05 (50.0%)	02 (25.0%)	06 (75.0%)	0.315	2.00
	Matric	05 (71.43%)	02 (28.57%)	04 (36.36%)	07 (63.64%)	0.147	1.96

The results indicating Stratification of IUGR with respect to age, gestational age, parity, body mass index, gestational diabetes mellitus, place of living, socio-economic status and educational level are displayed in table 4.

Stratification of NICU admission with respect to age, gestational age, parity, body mass index, gestational diabetes mellitus, place of living, socioeconomic status and educational level is shown in table 5.

Table 4: *Stratification of IUGR with respect to age, gestational age, parity, body mass index, gestational diabetes mellitus, place of living, socioeconomic status and educational level*

		Exposed (n=30)		Unexposed (n=30)		P-value	RR
		IUGR		IUGR			
		Yes	No	Yes	No		
Age (years)	**18-30**	09 (42.86%)	12 (57.14%)	01 (4.17%)	23 (95.83%)	0.021	10.3
	31-40	03 (33.33%)	06 (66.67%)	01 (16.67%)	05 (83.33%)	0.499	2.00
Gestational age	**25-32**	10 (38.46%)	16 (61.54%)	01 (4.17%)	23 (95.83%)	0.028	9.23
	>32	02 (50.0%)	02 (50.0%)	01 (16.67%)	05 (83.33%)	0.291	3.00
Parity	**0-2**	06 (33.33%)	12 (66.67%)	01 (5.26%)	18 (94.74%)	0.073	6.33
	3-4	06 (50.0%)	06 (50.0%)	01 (9.09%)	10 (90.91%)	0.087	5.50
BMI (kg/m^2)	**≤30**	12 (46.15%)	14 (53.85%)	07 (7.14%)	26 (92.86%)	0.050	2.18
	>30	00 (0.0%)	04 (100.0%)	00 (0.0%)	02 (100.0%)	0.784	0.60
Place of living	**Rural**	04 (44.44%)	05 (55.56%)	00 (0.0%)	09 (100.0%)	0.122	9.00
	Urban	08 (38.10%)	13 (61.90%)	02 (9.52%)	19 (90.48%)	0.057	4.00
Education level	**Illiterate**	02 (100.0%)	00 (0.0%)	01 (25.0%)	03 (75.0%)	0.109	4.00
	Primary	06 (54.55%)	05 (45.0%)	00 (0.0%)	07 (100.0%)	0.122	8.67
	Middle	**03 (30.0%)**	07 (70.0%)	01 (12.50%)	07 (87.50%)	0.406	2.40
	Matric	01 (14.29%)	06 (85.71%)	00 (0.0%)	11 (100.0%)	0.337	4.50

Discussion

In the earlier scholarly discussions, previous studies and literature regarding hypertensive disorders during pregnancy, specifically pre-eclampsia and its connection to hyperuricemia, have been examined. Pre-eclampsia, a condition affecting 2-8% of pregnancies, has traditionally been associated with hyperuricemia, which was initially seen as a diagnostic indicator for this ailment.[16] Nonetheless, its diagnostic importance diminished as proteinuria became more prominent in the evaluation of maternal hypertensive kidney damage. In recent times, there has been a shift in thinking, indicating that hyperuricemia may not just be an indicator but could potentially play an active role in the development of pre-eclampsia.[17] It is hypothesized that this elevated uric acid level stems from heightened production.[18,19] Maternal renal impairment, along with tissue ischemia and acidosis, are factors to consider. Apart from its association with pregnancy, hyperuricemia has been linked in epidemiological studies to various conditions such as hypertension, metabolic syndrome, coronary artery disease, cerebrovascular disease, vascular dementia, and chronic kidney disease.[20]

In the current study, we explore the connection between

Table 5: *Stratification of NICU admission with respect to age, gestational age, parity, body mass index, gestational diabetes mellitus, place of living, socioeconomic status and educational level*

		Exposed (n=30)		Unexposed (n=30)		P-value	RR
		NICU admission		NICU admission			
		Yes	No	Yes	No		
Age (years)	18-30	06 (28.57%)	15 (71.43%)	02 (8.33%)	22 (91.67%)	0.106	3.43
	31-40	01 (11.11%)	08 (88.89%)	00 (0.0%)	06 (100.0%)	0.634	2.10
Gestational age	25-32	05 (8.93%)	21 (91.07%)	02 (8.33%)	22 (91.67%)	0.288	2.31
	>32	02 (50.0%)	02 (50.0%)	00 (0.0%)	06 (100.0%)	0.175	7.00
Parity	0-2	04 (22.22%)	14 (77.78%)	01 (5.26%)	18 (94.74%)	0.178	4.22
	3-4	03 (25.0%)	09 (75.0%)	01 (9.09%)	10 (90.91%)	0.347	2.75
BMI (kg/m^2)	≤30	07 (26.92%)	19 (73.08%)	02 (7.14%)	26 (92.86%)	0.079	3.77
	>30	00 (0.0%)	04 (100.0%)	00 (0.0%)	02 (100.0%)	0.784	0.60
Place of living	Rural	01 (11.11%)	08 (88.89%)	01 (11.11%)	08 (88.89%)	1.00	1.00
	Urban	06 (28.57%)	15 (&1.43%)	01 (4.55%)	21 (95.45%)	0.076	6.29
Education level	Illiterate	01 (50.0%)	01 (50.0%)	00 (0.0%)	04 (100.0%)	0.271	5.00
	Primary	02 (18.18%)	09 (81.82%)	00 (0.0%)	07 (100.0%)	0.416	3.33
	Middle	03 (30.0%)	07 (70.0%)	00 (0.0%)	08 (100.0%)	0.227	5.73
	Matric	01 (14.29%)	06 (85.71%)	02 (18.18%)	09 (81.82%)	0.830	0.79

serum uric acid levels and unfavorable outcomes for both the fetus and mother in pre-eclamptic women. Our research uncovered a noteworthy association between high serum uric acid levels (≥6 mg/dl) and a substantially increased risk of low birth weight, intrauterine growth retardation (IUGR), and neonatal intensive care unit (NICU) admissions. These findings align with prior studies that have also established a positive link between raised uric acid quantities and adverse fetal results. What's particularly noteworthy is that our study underscores that hyperuricemia is a risk factor independent of proteinuria, underscoring the significance of SUA (serum uric acid) as a potential prognosticator of complications in pre-eclampsia. These discoveries contribute to the growing body of evidence highlighting the clinical importance of measuring uric acid levels when evaluating the well-being of both mother and fetus in pre-eclamptic pregnancies. Nevertheless, it is important to acknowledge that further research with larger sample sizes is warranted to bolster these conclusions.

Conclusion

This study concluded that there is a positive association between high serum uric acid levels and adverse feto-maternal outcome.

Ethical Approval: The IRB/EC approved this study via letter no. 415/FFH/RWP dated 07-09-2024.

Conflict of Interest: None

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