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Serum Uric Acid in Women with Preeclampsia and its Relation to Perinatal and Maternal Outcomes

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Abstract:

Background and objective: Preeclampsia is a dangerous, progressive condition that is linked to maternal and neonatal death and morbidity. The purpose of this study was to determine the association between serum uric acid levels in preeclampsia with maternal and fetal outcomes.

Method: A case-control study was conducted on 300 women delivered at the labour room of Duhok Obstetrics and Gynecology Hospital, from 1st of April 2021 to 1st of April 2022. The study participants were divided into two groups, pregnant women with preeclampsia and normotensive women. The serum uric acid levels of these women were estimated with the impact on fetal and mother outcomes.

Results: There was a highly significant association between preeclamptic and normotensive women in relation to mean serum uric acid (5.862 ±1.416) mg/dL and (3.570 ±0.982) mg/dL respectively. A highly significant association was seen between uric acid test levels and maternal eclamptic fit, HELLP syndrome and admission to intensive care unit. A highly significant association also seen with newborn birth weight, APGAR scores and admission to neonatal intensive care unit.

Conclusion: The current study demonstrates a significant raise in serum uric acid level in preeclamptic women and associated with adverse perinatal and maternal outcomes.

Keywords: Maternal Outcomes, Neonatal Outcomes, Preeclampsia, Uric acid.

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Introduction:

Preeclampsia is a pregnancy related disease that is characterized by raised blood pressure more than 140/90mmHg and proteinuria (0.30gm in 24h) with or without oedema after 20 weeks of gestation in previously normotensive women.[1,2] The incidence of preeclampsia is around 2 to 8 percent of all pregnancies.[3] There are many risk factors that are associated with preeclampsia, they include nulliparity, mother age of 40 years or older, interpregnancy interval of more than 10 years, family history of preeclampsia, multifetal pregnancy, obesity, gestational age at presentation, previous history of preeclampsia or gestational hypertension.[4] Preeclampsia is associated with increased maternal and perinatal morbidity and mortality. It is an obstetric complication that can have detrimental effects on the heart, lungs, kidneys, liver, neurological system, and all of those organs.[1] It has detrimental perinatal effects, including as premature birth, intrauterine growth restriction (IUGR), and intrauterine death, in addition to complications for the mother.[5]One of the sensitive indications of the severity of preeclampsia is the maternal serum uric acid level which is monitored in clinical practice.[6] Uric acid is one of the end products of purine metabolism, which is produced by the enzyme xanthine oxidase from xanthine.[7] Because uric acid is a sign of oxidative stress, tissue damage, and renal failure, a higher amount of uric acid indicates a more serious disease.[8] Reduced glomerular filtration rate (GFR) attributable to endothelial dysfunction is the primary cause of elevated blood uric acid in preeclamptic women.[1]Preeclampsia and its sequelae must be predicted in order to prevent morbidity and mortality in both pregnant women and fetuses. One of the predictions is an increase in serum uric acid levels.[9] It was revealed that raised serum uric acid concentration is a poor predictor of unfavorable outcomes for both the mother and the fetus, but evidence now is there supporting that high concentration of serum uric acid is positively associated with unfavorable results for both.The objective of this study was to compare serum uric acid levels in preeclamptic women to normotensive pregnant women and examine how they related to maternal and fetal outcomes.

Patients and methods:

The was a case control study conducted on a convenient sample of 300 pregnant women delivered at the labour word of Duhok Obstetrics and Gynecology hospital from 1st of April 2021to 1st of April 2022. One hundred and fifty women were preeclamptic women used as cases and the other 150 were normotensive pregnant women regarded as the control group. Inclusion criteria included in the study were: Gestational age more than 28 weeks, age more than 18 years, singleton pregnancy and agreed to participate in the study. Exclusion criteria were gestational age less than 28 weeks, age less than 18 years, multiple pregnancy, chronic hypertension women, women with metabolic disorders, those with diseases that adversely affect serum uric acid levels such as diabetes mellitus, thyroid disorders, renal failure and refused refused to participate in the study.A detailed history was taken from all selected women including general and obstetrics information of age, parity, body weight, gestational age in weeks by using the first trimester ultrasound, socioeconomic status, previous history of preeclampsia and family history of preeclampsia. Laboratory investigations were done and the serum uric acid was measured by modified trender peroxidase method using tribromo-3-hydroxybenzoic acid (TBHB). Normal values of uric acid level in pregnant women

were regarded as: (2-4.2mg/dL in first trimester, 2.4-4.9mg/dL in second trimester, 3.1-6.3mg/dL in third trimester). [10] Post-delivery examinations of the newborns done including birth weight in grams and categorized as: Extremely low birth weight less than 1000g, very low birth weight 1000g -1500g, moderate low birth weight 1500g-2500g, normal birth weight 2500g-4000g, macrosomia more than 4000g).[11] Extremely low birth weight not included in study because gestational age included in the study was more than 28 weeks, APGAR score was categorized as equal to seven or more and less than seven. Also; admission to neonatal intensive care unit was reported. The following postpartum complications were considered: postpartum hemorrhage defined as: minor postpartum hemorrhage less than1000ml and major postpartum hemorrhage more than 1000, major postpartum hemorrhage subdivided into moderate 1000ml to 2000ml and severe more than 2000ml).[12] Eclamptic fit (a convulsion condition associated with preeclampsia), HELLP syndrome (hemolysis, elevated liver enzymes and low platelet)[13] and admission to ICU or not. The proposal of the research was approved by research protocol ethics committee - Kurdistan Higher Council of Medical Specialties (No.1182 on September 8th, 2021)Data were analyzed using SPSS program version 23 IBM. Numerical data were summarized descriptively as frequency, percentage, mean and standard deviation. Association between categorical variables as uric acid categories with other variables was done by Chi square and Fisher's exact test. The significant cut off level of p-value was set at 0.05.

Results:

The mean age of mothers with preeclampsia was 28.9 ± 6.673 years and of normotensive women was 29.99 ± 6.472 years. Table (1) shows that 36.7% of preeclamptic women had hyperuricemia compared to only 0.7% in normotensive women. The mean serum uric acid level in preeclamptic women was 5.862 and it was 3.57 in normotensives. This difference was statistically very highly significant.

Table (1): Distribution of uric acid levels of preeclampsia and non-preeclampsia mothers.

Uric acid	Pre-eclampsia		Normotensive pregnant women		p-value
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	
Low Normal Hyperuricemia	2 (1.3) 93 (62) 55 (36.7)	5.862 (1.416)	49 (32.7) 100 (66.7) 1 (0.7)	3.570 (0.982)	< 0.001

There was a highly significant association between serum uric acid level and maternal outcomes of eclamptic fits, HELLP syndrome, and admission to ICU as shown in table (2). The association was not significant with mode of delivery, antepartum and postpartum hemorrhage.

Table (2): Association between patients' serum uric acid level and maternal outcomes.

Maternal outcome	Uric Acid			p-value
	Low No. (%)	Normal No. (%)	Hyperuricemia No. (%)	
Mode of delivery				
Vaginal delivery	22 (43.1)	76 (39.4)	22 (39.3)	0.882 (NS)
Cesarean section	29 (56.9)	117 (60.6)	34 (60.7)	
Antepartum hemorrhage				
No	49 (96.1)	186 (96.4)	53 (94.6)	0.834 (NS)
Yes	2 (3.9)	7 (3.6)	3 (5.4)	
PPH				
No	50 (98.1)	174 (90.2)	54 (96.4)	0.416 (NS)
Mild	1 (1.9)	8 (4.2)	0 (0)	
Moderate	0 (0)	10 (5.1)	2 (3.6)	
Severe	0 (0)	1 (0.5)	0 (0)	
Eclamptic fit				
Yes	0 (0)	9 (4.7)	11 (19.6)	<0.001
Not	51 (100)	184 (95.3)	45 (80.4)	
HELLP syndrome				
Yes	0 (0)	5 (2.6)	10 (17.9)	<0.001
Not	51 (100)	188 (97.4)	46 (82.1)	
Admission to ICU				
Yes	0 (0)	10 (5.2)	13 (23.2)	<0.001
Not	51 (100)	183 (94.8)	43 (76.8)	

NS, not significant; ICU, intensive care unit; HELLP syndrome (hemolysis, elevated liver enzymes and low platelet)Regarding neonatal outcomes, there was a highly significant statistical association of maternal serum uric acid level with neonatal birth weight, APGAR score and admission to NICU as seen in table (3).

Table (3): The relationship between patient serum uric acid levels and newborn outcomes

Neonatal outcome	Uric Acid			p value
	Low No. (%)	Normal No. (%)	Hyperuricemia No. (%)	
Birth weight				
Very Low birth weight (1 - < 1.5 kg)	0 (0)	2 (1.1)	5 (9.8)	<0.001
Low birth weight (1.5- <2.5 kg)	2 (3.9)	26 (13.9)	19 (37.3)	
Normal birth weight (2.5 - 4 kg)	46 (90.2)	154 (82.8)	23 (45.1)	
Macrosomia (More than 4 kg)	3 (5.9)	4 (2.2)	4 (7.8)	
APGAR Score				
< 7	2 (3.9)	35 (18.8)	18 (35.3)	<0.001
> 7	49 (96.1)	151 (81.2)	33 (64.7)	
Congenital anomalies				
No	50 (98)	183 (98.4)	50 (98)	0.977 (NS)
Yes	1 (2)	3 (1.6)	1 (2)	
Admission to NICU				
Yes	6 (11.8)	44 (23.7)	21 (41.2)	0.002
No	45 (88.2)	142 (76.3)	30 (58.8)	

NS, not significant; NICU, neonatal intensive care unit

Discussion:

Increased serum uric acid levels may indicate an increased risk for preeclampsia in pregnant women and unfavorable maternal/fetal conditions in those with early-stage gestational hypertension[14]. Preeclampsia in the early preterm stage is closely linked to numerous kidney diseases in later life.[15] The study found that the mean serum uric acid is higher in preeclamptic pregnant women compared to normotensive women. This finding is supported by the study done by Bainbridge SA in 2008 confirming that hyperuricemia is a common finding in preeclamptic pregnancies[16]. The same finding of high serum uric acid in preeclampsia was repeated in different studies done on the same issue[17,18]. Regarding the serum uric acid and fetal outcomes, in this study revealed that highly significant association between uric acid level among preeclampsia and non-preeclamptic mothers with their babies' birth weight, APGAR score and admission to NICU as p-value less than 0.001, while no significant association with a congenital anomaly. It was found that compared to 26% of normouricemic patients, 34.5% of hyperuricemic preeclamptic patients had low birth weights.[19] This showed that elevated serum uric acid is likely to lead to decreased placental function, which may induce LBW. In term of intrauterine death, in present study 9% of hyperuricemic preeclamptic patients delivered a dead baby parallel to the study done by Akter[20], and to a study done in Erbil by Jwan Zangana that revealed a significant association between high serum uric acid and intrauterine death[21]. Regarding admission to NICU, in our study 38%of hyperurecemic preeclamptic patients' babies were admitted to NICU, which is consistent with the study done in Erbil by Zangana. In this study 32% of hyperurecemic preeclamptic patients the APGAR score was <7 in 5minutes and it is inconsistent with a study done in India by Priya and the one done in Erbil [21,22]. In the present study the association between patient serum uric acid level and maternal outcomes shows a highly significant association between uric acid levels among both preeclamptic and non-preeclamptic mothers and their eclamptic fit, HELP syndrome and mothers admission to ICU with a p-value less than 0.001 ,while no association with the other maternal outcomes. Only 15.3% of preeclamptic women were admitted to the ICU in this research, compared to 16% of patients in the Murphy et al study and only 5.6% of preeclamptic women in the Saadat et al study. In our study, neither antepartum nor postpartum bleeding in the participants on either arm reached statistical significance and this result concurs with other studies.[23]

Conclusions:

The level of serum uric acid is significantly increased in women with preeclampsia in comparison to normotensive women. A highly significant association was seen between uric acid level and fetal outcomes of birth weight, APGAR score and admission to NICU. The association was highly significant also with maternal outcomes of eclamptic fit, HELLP syndrome and admission to ICU.

Conflict of interest:

The authors declare no conflict of interest.

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