

The clinical utility of serum uric acid measurement in pre-eclampsia

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Summary:

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Background: To evaluate the accuracy of serum uric acid to predict maternal and fetal complications in women with pre-eclampsia.

Design: Prospective study. Setting: Tikrit Teaching Hospital.

Subject and Methods: Fifty normotensive and forty-three pre-eclamptic pregnant women at (20-24) weeks of gestation were the study subject, serum concentrations of uric acid were measured and examine the correlations between serum uric acid level with fetal and maternal complications.

Result: Serum concentration of uric acid in pre-eclamptic women were significantly higher than in gestational age match normotensive pregnant women, and women with pre-eclampsia and elevated uric acid concentration at increased risk of low birth weight, preterm delivery and cesarean, delivery compared with each condition in absence of hyperuricemia.

Conclusion: Hyperuricemia consider a good predictor to select group of pre-eclamptic women with high risk for fetal and maternal complications.

Key words: Pre-eclampsia* uric acid *low birth weight *preterm birth.

Introduction

Hypertensive disorders in pregnancy are common and incidence appears to be increasing.⁽¹⁾

Hypertensive disorder during pregnancy increase maternal and fetal risk. The greatest impact is associated with the pregnancy-specific syndrome, pre-eclampsia.⁽²⁾

Pre-eclampsia conventionally -diagnosed by gestational onset-of hypertension and protein urea, increase prenatal mortality five-fold⁽²⁾ and kill 50,000 women yearly worldwide.⁽³⁾

Gestational hypertension without protein urea has much less of an adverse effect on maternal or fetal outcome, where as the major risk from hypertension that antedates pregnancy is the superimposition of pre-eclampsia.

The importance of differentiating these conditions is reflect in several classification schemes in which gestational hypertension and protein urea is separated from gestational hypertension with out protein urea and hypertension that antedates pregnancy.⁽⁴⁾

These diagnostic criteria currently used to discriminate high risk from low risk with gestational hypertension.

Pre-eclampsia complicates 3-5 % of first pregnancies and 1% of subsequent pregnancies with around 5-10% of cases being severe (5) Pre-eclampsia is characterized by a marked increase in peripheral vascular resistance, where as this decrease during a normal pregnancy. Recently it was hypothesized that a decrease in placental blood flow in early

pregnancy activates endothelial functions in the mid pregnancy period, but this conceivably damages endothelial cells, with subsequent development of pre-eclampsia in mid-to-late pregnancy.

Recently, it has been hypothesized that reduced perfusion of uteroplacental Unit (i.e. reduced blood flow in the spiral artery) might activate endothelial cell functions in early pregnancy⁽⁶⁾

Leading to pre-eclampsia, low birth weight and preterm delivery, in clinical practice, pre-eclampsia is probably more than one disease, with major difference between near term pre-eclampsia with out demonstrable fetal involvement and preterm pre-eclampsia.⁽⁷⁾ Pre-eclampsia associated with increase prenatal morbidity and mortality related to intrauterine growth restriction, premature delivery and prenatal asphyxia.

In addition, the pregnant women is at increase risk for abruption placenta, intracerebral hemorrhage and hepatic and renal failure (8)

Management of pre-eclampsia, delivery to halt the progression of path physiology is responsible for 15% of preterm birth in developed countries. (9)

Pre-eclampsia is one of the largest causes of maternal and fetal mortality and morbidity, hyperuricemia is often associated with pre-eclampsia (10) Serum uric acid was first noted to be associated with increase blood pressure by Frederick Mohamed in the 1870s.(11)

Hyperuricemia is an established marker of severe pre-eclampsia, correlating histologically with the severity of renal lesions, and clinically with adverse fetal outcomes. (12)

In pre-eclampsia, an increase in serum uric acid is also known to occur and hyperuricemia can

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contribute to damage to the vascular wall because of elevated oxidative stress, however it is unclear whether uric acid is itself involve in the reduced placental perfusion in pre-eclampsia. (13)

During normal pregnancy, the serum concentration of uric acid slowly decrease until 16 weeks gestation, for most of the second trimester it remains stable, and then it increase during the third trimester, the variation reflecting increased catabolism and/or production. (14)

Uric acid is the end product of purine catabolism catalyzed by the enzyme xanthine oxidase/dehydrogenase. this bifunctional enzyme in its dehydrogenase form produces uric acid and reduced nicotinamide adenine dinucleotide and, in the oxidase form, produces uric acid and super oxide.

The enzyme is up regulated and the expression of oxidase form increase proportionally with hypoxia, thus increase uric acid production occur in a setting of hypoxia, local acidosis, or increase tissue break down or with reduced renal function and can increase oxidative stress. (15)

In the setting of chronic hypertension, hyperuricemia could identify women with increase the likelihood of having superimposed pre eclampsia (16)

In current study, we used a research data base in which pre-eclampsia had been rigidly diagnosed to ask whether the inclusion of uric acid in diagnosis of pre-eclampsia would be an indicator of outcome; we focused primarily on fetal outcome, gestational age at delivery, and birth weight because these adverse outcomes occur more frequently than severe maternal morbidities.

Subject and Method:

We evaluated data acquired from March 2005 to September 2006 in department of obstetric and gynecology /Tikrit teaching hospital.

Fifty normotensive pregnant women and forty -three pre-eclamptic women, regularly visiting antenatal care unit, participated in the study.

All women were singleton pregnancy at 20-24 weeks of gestation with out history of smoking, diabetes mellitus, renal disease, collagen disease, antiphospholipid syndrome, or infection as these are known to impact on endothelial functions, and also with out history of previous surgical operations.

Pre-eclampsia diagnosed by systolic blood pressure higher than 140mmHg but not exceeding 160mmHg and/or diastolic blood pressure higher than 90mmHg but not exceeding 110mmHg as well as daily protein urea higher than 300mg but not exceeding 2gm. We investigated

serum concentration of uric acid in all women enrolled in this study in laboratories of Tikrit teaching hospital and considered hyperuricemia if uric acid level > 0.35 mmol/L. (7)

We follow all women enrolled in the study regularly and also examined the correlations between serum uric acid level and several clinical outcomes, gestational age at delivery and birth weight , still birth or neonatal death and cesarean section delivery.

Results:

Ninety-three cases were included in the study; the mean maternal age was 28.7 years range (16 - 38) years.

Thirty-five (37.6%) of the cases were multiparous and fifty-eight (62.4%) were primiparous.

Table (1) the distribution of the study sample by maternal age and parity.

Criteria	No.	%
Age (years)		
<20	13	13.8
20-29	48	51.6
>30	32	34.6
Parity		
Multiparous	35	37.6
Primiparous	58	62.4
Total	51	

Hyperuricemia was diagnosed in 16 (17.3%) women, all of them were had pre-eclampsia, while normal uric acid level was found in 77(82.7%) women as shown in table (2).

Table (2) Uric acid Level in the study groups

	NT		PE		Total	
	No.	%	No.	%	N.	%
Normal uric acid	50	100	27	62.7	77	82.7
Hyperuricemia	0	0	16	37.3	16	17.3
Total	50	100	43	100	93	100

Table (3) Type and mode of delivery in study groups

	Total	NT		PE		PE&HU	
	No.	No.	%	No.	%	No.	%
Term-spontaneous vaginal delivery	30	20	40	8	20	2	12.5
Term induced vaginal delivery	43	26	52	13	48.8	4	25
Term- cesarean section	14	3	6	4	14.3	7	43.7
Preterm-spontaneous vaginal delivery	1	1	2	0	0	0	0
Preterm-induced vaginal	1	0	0	0	0	1	6.3
Preterm-cesarean section	4	0	0	2	7.4	2	12.5
Total	93	50	100	27	100	16	100

Incidence of low birth weight in study groups shown in table (4)

Table (4) Incidence of low birth weight in study groups

	NT		PE		PE&HU		Total	
	No.	%	No.	%	N.	%	No.	%
Average weight	48	96	22	81.5	2	12.5	72	77.5
Low birth weight	2	4	5	18.5	14	87.5	21	22.5
Total	50	100	27	100	16	100	93	100

NT = normotensive
 PE = Pre-eclampsia
 PE = Pre-eclampsia

There were two neonates dead in the first week post delivery and one fetus was intrauterine death and all of them of pre-eclamptic hyperuricemic mother.

Discussion:

Elevated serum uric acid is another component of pre-eclampsia syndrome that was recognized many years ago.

It is one of the most consistent and earliest detectable changes in preeclampsia and has been cited as a better predictor of fetal risk than blood pressure. (18)

In the present study, the serum concentration of uric acid was clearly higher in patients with pre-eclampsia than they were in

gestational age matched normotensive pregnant women as shown in table (2) and there was appositive correlation between blood pressure and serum uric acid suggesting that uric acid might play a role in the increase in peripheral resistance typical of pre-eclampsia and reduction of birth weight , the placenta is abundant source of purines because of its high cell turnover, resulting in high production of uric acid, which is the final product of purine metabolism. (19)

The hyperuricemia of pre-eclampsia has been variably suggested to be associated with lactic acidosis alter renal function, or oxidative stress. The currently favored concept is that increased circulating uric acid is secondary to reduced renal urate clearance, as can be seen with hypovolemia (15)

It was thus suggested that uric acid might lead to restriction of fetal growth by reducing placental blood flow in pre-eclampsia.

Despite the fact that hyperuricemia is not a conventionally used diagnostic criterion for pre-eclampsia and not typically considered a useful aid to management, several observations have suggested that the presence of hyperuricemia may identify a form of pregnancy with increased risk. (19)

Redman- 30 years ago demonstrated an increased risk of fetal death in pre-eclampsia with elevated uric acid. (12)

Likewise, in another study, there was an increase in small for gestational age among gestational hypertensive women with protein uric and no protein uric hyperuricemia. (20)

The data presented indicate that in women with pre-eclampsia, elevated uric acid concentration identified a group of pregnancies at risk of low birth weight, preterm delivery and cesarean delivery compared with each condition in absence of hyperuricemia as shown in table (3)&(4).

The increased incidence of preterm delivery in this study in most instances reflects the severity of disease rather than natural history, because most early deliveries with pre-eclampsia were medically indicated preterm inductions and births.

There is evidence from this study to support the association between prenatal death and high uric acid level in patient with pre-eclampsia. Data from the pre-eclampsia and hyperuricemic women indicating low birth weight and shortened pregnancies support pre-eclampsia as syndrome in which perhaps any two path physiological abnormalities will identify a pregnancy at increased risk.

Conclusion:

There is a significant correlation between elevated serum uric acid values and several clinical outcome measures in pre-eclampsia,

makes it possible to select a group of pre-eclamptic women with high risk for low birth weight, prenatal death, and preterm delivery.

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