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Original Research Article

An Analytical Comparative Assessment of the Association of CRP and Uric Acid with Severity of Preeclampsia

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Abstract

Aim: The aim of the present study was to determine the levels of C-reactive protein and uric acid levels in preeclampsia pregnant.

Methods: A case control study was conducted in 30 diagnosed preeclamptic pregnancy, 30 normal pregnant women of comparable gestational age in 3rd trimester admitted in the dept. of Obstetrics and Gynaecology at NMCH, Patna, India for one year.

Results: Maximum number of PE cases belongs to age group of 31-35 years (60%) and maximum number of control group belongs to age group of 21-25 years (40%). It was also observed that mean age in control group is 25.5±3.6 (years), whereas in study group 29.5±4.2 (Years). In study group, maximum number of patients have severe proteinuria i. e. >+++ (55%), and in control group maximum number of patients have proteinuria of (+) (58%) which is considered as physiologically normal. But, both study and control groups mild proteinuria (++) is observed in 40% and 38% patients respectively. There was a significant difference of proteinuria between study group and control group (p=0.001). The mean values of serum uric acid and CRP levels always remain higher in study group than that of control group. The mean values of both serum uric acid and CRP levels in study group were near to their respective upper limits of normal range. There was a strong positive correlation between serum uric acid and blood pressure (systolic and diastolic) with highly significant. A positive correlation is also observed between serum uric acid and serum CRP level.

Conclusion: Serum uric acid and CRP may be feasible to be used as biomarkers for identifying women at risk of preeclampsia. The aetiology of preeclampsia is not well established but having more information about the condition will help in the monitoring and treatment of the pregnant to ensure her and her baby are well.

Keywords: Preeclampsia, hypertension, C-reactive protein.

Introduction

Preeclampsia (PE), is characterized by hypertension, proteinuria and ischemic end-organ damage. [1] Chronic hypertension with evidence of preeclampsia, is classified as chronic hypertension with superimposed preeclampsia. The occurrence of seizures in women with preeclampsia is

characterized as eclampsia. [2] For preeclampsia with involvement of various systems, several markers have been proposed, like markers for renal and liver function – urea, creatinine, uric acid, aspartate and alanine transaminases, vascular function (prostacyclin, thromboxane, fibronectin, homocysteine, nitric acid, cytokines), coagulation and fibrinolytic systems (tissue plasminogen activators, platelets, fibrinogen, antithrombin III, Von Willebrand factor), oxidative stress and lipids (lipid peroxides, antioxidants, lipoproteins), and placental function (human chorionic gonadotropin, corticotrophin-releasing hormone, placental growth factor, α-fetoprotein, inhibin, activin, and uteroplacental flow (velocity waveform). [3-5]

The value of CRP indicates the severity of endothelial cell injury. Endothelial cell injury is one of the responsible factors for developing or initiating preeclampsia. [6] The CRP assay is simple, quick and affordable. CRP is easily measurable and not too invasive, requiring a simple blood draw for the assay. The half-life of CRP is 19 hours and it is cleared from the bloodstream fairly quickly as preeclampsia resolves. [7]

Serum uric acid levels reflect the circulating xanthine oxidase activity and oxidative stress production. There are studies which demonstrate that the development of preeclampsia is associated with hyperuricemia. [8,9] But yet, the role of uric acid in preeclampsia is less clear. Some studies reported an independent association between uric acid and preeclampsia, but others found prognostic and also diagnostic significance. [10,11]

Uric acid is capable of damaging adult vasculature, and could have similar effects in the placentae of pre-eclamptic women. The placental vasculature lacks autonomic innervation, relying entirely upon locally produced or circulating substances, for hemodynamic control. [12] The primary vasoactive compound responsible, for the maintenance of optimized placental perfusion, is endothelial derived NO. Uric acid decreases eNOS activity limiting NO availability, and up-regulates COX-2 expression, with increased generation, of the potent vasoconstrictor thromboxane. [13] A similar vaso-constrictive effect of uric acid in the placentae of women with preeclampsia would compromise placental perfusion, and could inhibit fetal growth.

Pre-eclampsia is a potential harmful situation during antenatal period that culminates in events increasing maternal and fetal morbidity and mortality. In many instances, the situation defies the treatment once it is fully developed. Early diagnosis or recognition of the onset of Pre-eclamptic changes can help curb and control the situation, limiting the undesirable results. The aim of the present study was to determine the levels of C-reactive protein and uric acid levels in preeclampsia pregnant and to determine severity by the association among CRP, uric acid concentration, BMI and blood pressure.

Materials and Methods

A case control study was conducted in 30 diagnosed preeclamptic pregnancy, 30 normal pregnant women of comparable gestational age in 3rd trimester admitted in the department of obstetrics and Gynaecology at NMCH, Patna, India for one year.

Diagnosis of Preeclampsia

systolic blood pressure greater than 140 MMHG or a rise of at least 30 MMHG;) diastolic blood pressure greater than 90 MMHG or a rise of at least 15 MMHG (measured on two occasions at least 6 hours apart); proteinuria of 300 mg or more in 24 hours urine collection or protein concentration of 1 gm/l (on two occasions of at least 6 hours apart), or ≥2+ in mild preeclampsia and >3+ in severe preeclampsia by dipstick method. Those patients whose 24 hours urine sample examination revealed single plus (+), two

plus (++) and three plus (+++) by dipstick method were categorised as severe preeclampsia.

Blood samples were collected from all of the patients for serum uric acid by fully automated analyzer (HUMASTAR, USA). C- reactive protein estimated by Nyco Card CRP reader. Statistical formulae like chi-square test, independent sample t-test, pearson's correlation were used wherever found suitable and necessary, and accordingly interpretations were made. Statistical Software Using SPSS-16 Version was used.

Results

Table 1: Distribution of patients according to age

Age groups	Preeclampsia (n=30)	Normal Pregnant (n=30)
21-25	6 (20)	12 (40)
26-30	6 (20)	11 (36.66)
31-35	18 (60)	9 (30)
Mean age	29.5±4.2	25.5±3.6

Maximum number of PE cases belongs to age group of 31-35 years (60%) and maximum number of control group belongs to age group of 21-25 years (40%). It was also observed that mean age in control group is 25.5±3.6 (years), whereas in study group 29.5±4.2 (Years).

Table 2: Demographics, CRP and uric acid levels in Study and control groups

Demographic/clinical parameters	Preeclampsia (n=30)	Normal Pregnant (n=30)	p Value
Maternal age (years)	29.2±4.8	25.3±3.7	p=0.07
Gestational age (week)	32.6±2.4	33.6±3.4	p=0.09
Body mass index (kg/m2+)	24.8±2.5	22.5±2.1	p=0.07
Systolic blood pressure (mmHg)	165.25±26.50	119.25± 10.24	p=0.001
Diastolic blood pressure (mmHg)	103.25±14.52	77.62±7.27	p=0.001
Serum uric acid (mg/dl)	5.39±1.76 mg%	3.72±1.29 mg%	p=0.001
C-reactive protein (mg/L)	8.26±6.9 mg/l	6.22±4.29 mg/l	p=0.08
Proteinuria >+++ ++ +	55% 40%	38% 58%	p=0.001

In study group, maximum number of patients have severe proteinuria i. e. >+++ (55%), and in control group maximum number of patients have proteinuria of (+) (58%) which was considered as physiologically normal. But, both study and control groups mild proteinuria (++) is observed in 40% and 38% patients respectively. There was a significant difference of proteinuria between study group and control group (p=0.001). It was observed that the mean ± SD of systolic as well as diastolic blood pressure levels in preeclamptic pregnants (165.25±26.50 MMHG, 103.25±14.52 MMHG) are much higher than that of normal pregnant women (119.25±10.24 MMHG, 77.62±7.27 MMHG). This difference was found to be very highly significant (p=0.001). It was observed that CRP level in study group was 8.26±6.9 and 6.22±4.29 in control group. It was observed that mean serum uric acid level in study group was 5.39±1.76 mg%, which is higher than control group i. e. 3.72±1.29 mg% and the difference shows statistical significant (p=0.001). The mean serum CRP level in study group was higher (8.26±6.9 mg/l) than that of control group (6.22±4.29 mg/l) without statistical significant (p=0.08). The mean values of serum uric acid and CRP levels always remain higher in study group than that of control group. The mean values of both serum uric acid and CRP levels in study group were near to their respective upper

limits of normal range. There was a strong positive correlation between serum uric acid and blood pressure (systolic and diastolic) with highly significant. A positive correlation is also observed between serum uric acid and serum CRP level.

Discussion

Preeclampsia (PE) develops in 4-5% of human pregnancies. It is characterized by an elevated blood pressure, more than 140/90 mm of Hg, on two separate occasions, taken six hours apart , within a period of one week , and evidence of proteinuria, which develops after 20 weeks of gestation. PE is a complication of pregnancy, constituting a major cause of maternal and foetal morbidity, and mortality. Several aetiologies have been implicated in the development of preeclampsia, including abnormal trophoblast invasion of uterine blood vessels, and immunological intolerance between feto-placental and maternal tissues. Endothelial cell dysfunction and inflammation are considered to have a role in the pathophysiology of PE.

It was speculated that circulating xanthine dehydrogenase/xanthine oxidase (XO) can bind to endothelium and lead to local oxidative injury. [14] Hyperuricemia is a common finding in pre-eclamptic pregnancies. The cause of hyperuricemia in preeclampsia has been attributed to either a decreased excretion or to an increased production of uric acid. Decreased uric acid clearance, reflected by altered tubular function has been documented, while in 1990 fay proposed an increased breakdown of purines in the placenta as a possible explanation for the overproduction of uric acid. [15]

In the current study, maximum number of patients shows severe proteinuria in PE cases. Mild proteinuria is observed in 40% and 38% in both case and control groups. This difference is statistically significant (p=0.001). The triad of severe preeclampsia is often described as a combination of hypertension, edema and proteinuria. Proteinuria is the last sign to develop. [16,17] Although salt and water retention are common features of preeclampsia; salt and water do not cause the condition and are not an essential part of it. In the current study, the mean blood pressure (mmHg) is significantly higher in preeclampsia compared with normal controls. This is comparable to the findings of Powers RW et al and Baksu A et al. [18,19]

In the current study, the level of serum uric acid is significantly higher in the study group than in the controls. During pregnancy maternal serum uric acid levels initially falls, with a subsequent rise to prepregnancy levels near term. [20] Elevated serum uric acid levels due to decreased renal urate excretion are frequently found in women with preeclampsia. [21] Soluble uric acid impairs nitric oxide generation in endothelial cells inducing endothelial dysfunction. [22] Besides the reduced clearance hyperuricemia in pre-eclampsia may be due to increased uric acid production caused by trophoblast breakdown, cytokine release and ischemia. Uric acid can promote endothelial dysfunction, damage and inflammation, which leads to oxidation. It has also been reported that rise in uric acid level in preeclampsia is secondary to placental damage leading to purine catabolism and production of uric acid. In our study, the increased uric acid level in PE cases shows positive correlation with serum CRP level.

In the current study, the serum CRP levels are higher in preeclamptic pregnants than the normal pregnant women. A positive correlation is found between serum CRP level and blood pressure without significant difference. Positive correlation observed between serum uric acid and serum CRP with significant difference. Findings by Ingec M et al. [23] it had been reported that rise in uric acid level in

preeclampsia is secondary to placental damage leading to purine catabolism and production of uric acid. Elevated serum uric acid levels due to decreased renal urate excretion are frequently found in women with preeclampsia. Uric acid is capable of damaging adult vasculature, and could have similar effects in the placentae of pre-eclamptic women. [24] Increased CRP value may be superimposed infection along with preeclampsia which was latent or undiagnosed during taking of blood sample.

Early diagnosis or recognition of the onset of pre-eclamptic changes can help curb and control the situation, limiting the undesirable results.

Conclusion

Increased levels of uric acid and CRP levels in preeclamptic pregnants need to be confirmed in a designed strategy in which uric acid and CRP level can be measured before the development of preeclampsia or early in pregnancy in order to identify and monitor the patients at risk of preeclampsia and thus to provide the best prenatal care for these women and their babies.

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