

International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
© Gynaecology Journal
www.gynaecologyjournal.com
2018; 2(1): 78-80
Received: 16-11-2017
Accepted: 17-12-2017

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Association of C - reactive protein and uric acid with severity of preeclampsia attending to teaching hospital

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Abstract

Introduction: Preeclampsia (PE) is one of the main causes of maternal and fetal mortality and morbidity. It is a chief source of morbidity and mortality worldwide. PE is associated with an inflammatory state and with oxidative stress, in maternal circulation. Measuring the CRP and uric acid concentration in preeclamptic women could help in understanding the best course of action for the pregnant woman and the foetus, especially if there is an association between CRP levels and severity of preeclampsia.

Objective: 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.

Method: This was a case-control study was conducted at Dept. of obstetrics and gynecology, Narayana medical college Hospital, including pregnant women. 25 PE cases and matched normal pregnant in third trimester were enrolled, clinical history and blood was collected to to assess CRP and Uric acid levels.

Results: The serum CRP and uric acid levels were found significantly higher in PE cases than normal pregnant. Uric acid and CRP levels were 5.39 ± 1.76 mg% and 8.26 ± 6.9 mg/l respectively in the study group (cases) compared with 3.72 ± 1.29 mg% and 6.22 ± 4.29 mg/l in controls. There was a positive correlation between CRP and mean arterial pressure and also between CRP and uric acid.

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 a human specific pregnancy and multisystem disorder, which may cause maternal and neonatal morbidity and mortality. The global incidence of preeclampsia has been estimated at 5-14% of all pregnancies [1, 2]. In India the incidence of preeclampsia is reported to be 8-10% of the pregnancies [3]. It is 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. The specific cause for this syndrome remains unclear, despite the intense investigation. It has been reported that an altered lipid profile [4]. Leukocyte activation [5]. Enhanced inflammatory response [6]. And oxidative stress [7]. In maternal circulation, are frequently associated with development of this disorder.

Among all these factors, though immunologic factors have long been considered to be key players in preeclampsia, the endothelial cell dysfunction and inflammation are considered to have a crucial role in pathophysiological mechanism of preeclampsia [8].

An inflammatory response is usually accompanied by increasing concentrations of proinflammatory cytokines, acute-phase proteins and may involve leukocyte activation. It has been suggested that elevated levels of CRP, in accordance with its proposed function, may reflect the inflammatory response characteristics of preeclampsia. The Value of CRP Level Reflects the Severity of endothelial cell injury which is one of the responsible factors for developing or initiating preeclampsia.

It is speculated that circulating xanthine dehydrogenase/xanthine oxidase (XO) can bind to endothelium and lead to local oxidative injury [9]. Hyperuricemia is a common finding in preeclamptic 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 [10].

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The present study was conducted 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.

Material and Method

A case control study was conducted in 25 diagnosed preeclamptic pregnancy, 25 normal pregnant women of comparable gestational age in 3rd trimester admitted in the dept. of obstetrics and gynaecology.

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 $\geq 2+$ 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 NycoCard 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.

Results

Maximum number of PE cases belong to age group of 31-35 years (50%) and maximum number of control group belong to age group of 21-25 years (40%). It is 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 (+) (55.7%) which is considered as physiologically normal. But, both study and control groups mild proteinuria (++) is observed in 40.5% and 38.5% patients respectively. There is a significant difference of proteinuria between study group and control group ($p=0.001$).

The comparison of mean \pm SD (MMHG) of blood pressure between the study groups and controls. It was observed that the mean \pm SD of systolic as well as diastolic blood pressure levels in preeclamptic pregnant (165.25 \pm 26.50 MMHG, 103.25 \pm 14.52 MMHG) are much higher than that of normal pregnant women (119.25 \pm 10.24 MMHG, 77.62 \pm 7.27 MMHG). This difference is found to be very highly significant ($p=0.001$).

It is observed that uric acid level are within normal range in 62.5% of study group (preeclamptic group) and 92.5% patients of control group, whereas it was above the upper limit of normal range (i. e. >5.7 mg%) in 37.5% of study group and 7.5% patients in control group. CRP level observed within normal range in 55.6% patients of study group and 72.5% patients of control group. Whereas it is above the upper limit of normal range (i.e. >8.2 mg/l) in 44.4% patients of study group and 27.5% patients of control group.

It was observed that mean serum uric acid level in study group is 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 is 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 is 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.

Table 1: Demographics, CRP and uric acid levels in Study and control groups

| Demographic/clinical parameters | Preeclampsia (n=25) | Normal Pregnant (n=25) | p Value |
|--------------------------------------|---------------------|------------------------|-------------|
| Maternal age (years) | 29.5 \pm 4.2 | 25.5 \pm 3.6 | $p=0.06$ |
| Gestational age (week) | 32.6 \pm 2.8 | 33.5 \pm 3.9 | $p=0.08$ |
| Body mass index (kg/m ² + | 24.8 \pm 2.5 | 22.5 \pm 2.1 | $p=0.07$ |
| Systolic blood pressure (mmHg) | 165.25 \pm 26.50 | 119.25 \pm 10.24 | $p=0.001^*$ |
| Diastolic blood pressure (mmHg) | 103.25 \pm 14.52 | 77.62 \pm 7.27 | $p=0.001^*$ |
| Serum uric acid (mg/dl) | 5.39 \pm 1.76 mg% | 3.72 \pm 1.29 mg% | $p=0.001^*$ |
| C-reactive protein (mg/L) | 8.26 \pm 6.9 mg/l | 6.22 \pm 4.29 mg/l | $p=0.08$ |
| Proteinuria $>+++$ $+++$ | 55% 40.5% | 38.5% 57.7% | $p=0.001^*$ |

Significant difference.

Discussion

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 fetoplacental and maternal tissues. In the current study, the body weight of PE pregnant (59.58 \pm 7.52 kg) shows higher than that of the normal pregnant women (56.92 \pm 74 kg) without significant difference. Whereas, by Rajkovic A *et al.* the weights of the preeclamptic women were more than that of the normal pregnant controls with significant difference [11]. In the current study, maximum number of patients shows severe proteinuria in PE cases. Mild proteinuria is observed in 40.5% and 38.5% 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 [12, 13]. 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* [14, 15].

In the current study, the level of serum uric acid is significantly higher in the study group than in the controls. In study group, 37.5% women have uric acid level more than upper limit of

normal range (>5.7mg %). During pregnancy maternal serum uric acid levels initially falls, with a subsequent rise to prepregnancy levels near term ^[16]. Elevated serum uric acid levels due to decreased renal urate excretion are frequently found in women with preeclampsia ^[17]. Soluble uric acid impairs nitric oxide generation in endothelial cells inducing endothelial dysfunction ^[18]. 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. This is supported by the findings of Ingec M *et al* ^[19], where it has been reported that increase in uric acid level in preeclampsia is secondary to placental damage leading to purine catabolism and production of uric acid. A positive correlation is found between the serum uric acid level and blood pressure.

In the current study, the serum CRP levels are higher in preeclamptic pregnant 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* ^[19]. 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 placenta of pre-eclamptic women.

In the current study, PE case group, 44.4% women have CRP level more than upper limit of normal range (>8.2mg/L). It is also found that in few preeclamptic patients, the CRP value is >10mg/L and in these PE pregnant. 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 pregnant 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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