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EVALUATION OF NITRIC OXIDE, URIC ACID AND CREATININE LEVELS IN PRE-ECLAMPSIA

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ABSTRACT

Introduction: Pre-eclampsia is one of the multisystem disorder of pregnancy characterised by high blood pressure and protein in the urine, it is associated with endothelial dysfunction. The aim of the present study was to investigate the relationship between serum and urinary nitric oxide (NO), serum Uric acid and serum and urinary creatinin status between preeclamptic patients and normal control. **Materials and Method:** This study involves 34 normal healthy pregnant subjects & 34 cases of preeclampsia aged between 20 to 35 years attending the Department of Obstretics & Gynecology AJIMS, Mangalore. About 5ml of blood and urine was collected from the subjects used for the biochemical estimations. **Result:** Serum NO concentrations in preeclamptic women were significantly higher when compared to normal pregnant women, whereas a significant decrease was observed in urine NO in preeclamptic woman. Serum uric acid levels increased in preeclampsia patients when compared to normal individuals. Creatinine levels increased in preeclampsia patients in both serum and urine. **Conclusion:** This study might help clinicians to have diagnostic significance for the prediction of severity of the disease. Further experimental and clinical studies are necessary to clarify the pathogenesis of preeclampsia.

KEYWORDS: Preeclampsia, Nitric Oxide, Uric acid, creatinine.

INTRODUCTION

Preeclampsia is one of the major pregnancy complications, it is characterized by high blood pressure and there is sign of damage to other organ system, often the kidneys. Preeclampsia usually begins after 20 weeks of gestation with proteinuria (either ≥300 mg protein per day or a urinary protein/creatinine ratio ≥30 mg/mmol).[1] In a woman whose blood pressure had been normal. Even a slight rise in blood pressure may be a sign of preeclampsia. If left untreated preeclampsia will lead to serious complications for both mother and baby. In India the prevalence of preeclampsia is reported to be 8-10 percent of the pregnancies.[2] Preeclampsia is disease of theories, the exact etiology is not known. Various theories have been proposed to explain the possible etiology like immunological, genetic and oxidative stress theories.[3] The epidemiology of preeclampsia is complicated by differences in definitions and inaccuracy of diagnosis. A single blood-pressure reading of 140/90 mm Hg or above is not uncommon in pregnancy and was reported in nearly 40% of pregnant women in one study.[4] Such a finding carries little risk to the mother or fetus. Persistent hypertension is diagnosed if a high reading is found on two occasions at least 4 h apart. Persistent hypertension occurs in around 12.22% of pregnancies[5-7], depending on the populations and definitions used. The type of hypertension can be further defined on the basis of other clinical signs, particularly proteinuria and abnormalities of coagulation.[8] Blood pressure generally falls in the first and second trimesters; therefore women with high blood pressure before the 20th week of gestation are assumed to have pre-existing hypertension. Preeclampsia is twice as common in primigravid women as in women having second or later pregnancies.[9] However, with a change of partner, the risk in a multiparous woman increases; this effect suggests that prim paternity is important. Particular men seem to have an increased risk of fathering a pre-eclamptic pregnancy.[10] Preeclampsia can be familial, but various groups have studied the genetic basis of this disorder and no persistent results have been obtained with obvious population differences. Hypertension is the most common diagnostic sign, although some women present with convulsions, abdominal pain, or general malaise. Because there are no specific diagnostic investigations, the initial diagnosis of preeclampsia remains clinical. Oxidative Stress and Free radicals, antioxidants, nitric oxide (NO), lipid peroxidation. At early pregnancy stage the uric acid level will fall then it slightly increase, As a consequence of these

observations, obstetricians frequently measure serum uric acid to both help diagnose preeclampsia and to predict maternal and fetal complications.[11] The level of serum uric acid and serum creatinin were significantly elevated in pre-eclamptics. In this study we examine the relationship between the results in serum nitric oxide/creatinine ratio & urine nitric oxide/creatinine ratio and serum uric acid.

MATERIAL AND METHODS

SOURCE OF DATA

The study comprises of 34 normal healthy pregnant subjects & 34 cases of preeclampsia aged between 20 to 35 years attending the Department of Obstretics & Gynecology AJIMS Mangalore from the year 2010-2012. Ethical clearance certificate was obtained from the institutional Ethical Committee.

The diagnosis of preeclampsia was based on the definition of American college of Obstetrics & gynecologists.[12]

Inclusion criteria

34 Primi gravida with diagnosed preeclampsia according to A.C.O.G with an age between 20 to 35 years in third trimester and 34 normotensive primigravida women with no protienuria from third trimester and without any age systemic or endocrine disorders and age matched with cases.

Exclusion criteria

Subjects with the history of diabetes, kidney disease, infections, severe anaemia (Hb<6 gm%), history of smoking, history of high blood pressure prior to pregnancy, multigravida & age above 35 yrs will be excluded.

Method of collection of data

Method of sample collection

5ml of fasting blood sample was collected aseptically from the anticubital vein using plain vacutainers from 34 subjects each with and without preeclampsia. Serum was separated and analysed for the levels of serum nitric oxide, creatinine and uric acid**.**

5ml of urine was collected in a clean, dry & sterile container for estimation of urinary nitric oxide and creatinine.

Nitric-Oxide Level was estimated by Using Griess-Reagent Method.[13] Uric acid Determined in serum/ urine by uricase/ POD Method.[14,15] Creatinine was Estimated by Modified Jaffe's Method.[14,15]

RESULTS

Demographical and obstetrical characteristics of the patients and control group were shown in Table 1.

Table 1: Demographical and obstetrical parameters of patients

Demographical and obstetrical Characteristics	Pregnancies	
	Healthy (n=34)	Preeclampsia (n=34)
Age	27±4.47	25.6±4.8
Gestational Weeks	37.20±1.5	32.76±4.09
Systolic blood pressure (mmHg)	120±9.44	150±8.16
Diastolic blood pressure (mmHg)	77.2±4.8	96.8±7.67

Serum Samples

The mean level of serum nitric oxide in normal individuals is 49.88±6.78 and that of Pre-eclempsia patients is 66.77±7.54 'p' value statistically significant ($p<0.0001$). The mean level of serum uric acid in normal individuals is 6.16±1.46 and that of Pre-eclempsia patients is 9.15±1.02 'p' value statistically significant ($p<0.0001$). The mean level of serum creatinine in normal individuals is 0.67±0.11 and that of Pre-eclempsia patients is 0.82±0.153 'p' value statistically significant ($p<0.0001$). (Table 2, Figure 1-3).

Table: 2 Comparison of serum parameters in Normal and Pre-eclempsia patients.

Parameters	Normal Mean±SD	Pre-eclempsia Mean±SD	'P' value
Nitric Oxide (µM/L)	49.88±6.78	66.77±7.54	P<0.0001
Uric acid (mg/dl)	6.16±1.46	9.15±1.02	P<0.0001
Creatinine (mg/dl)	0.67±0.11	0.827±0.15	P<0.0001

$p<0.05$ is statistically significant. Statistical comparison were performed by Student's't' test. Data expressed as Mean±SD.

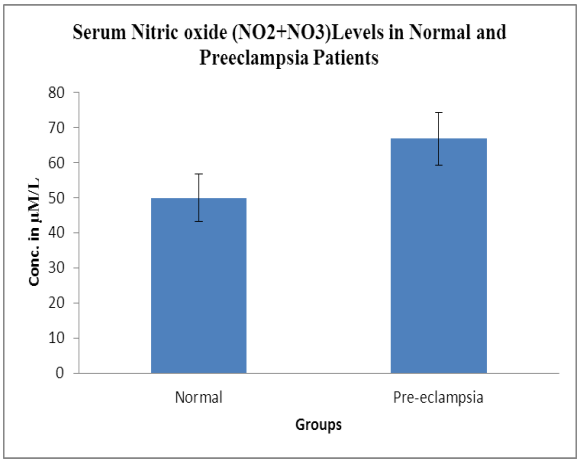

Figure 1: Comparison of serum Nitric oxide (NO_2+NO_3) in normal and preeclampsia patients

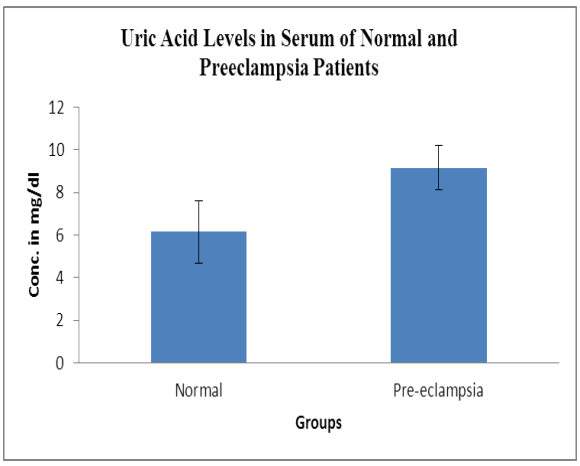

Figure 2: Comparison of serum uric acid levels in normal and preeclampsia patients

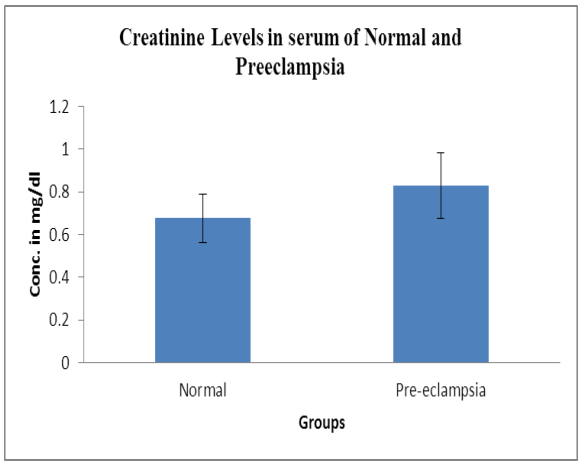

Figure 3: Comparison of serum Creatinine levels in normal and preeclampsia patients

Urine Samples

The mean level of nitric oxide in urine of normal individuals is 645.85±119.84 and that of Preeclampsia patients is 396.08±151.26 'p' value statistically significant (p<0.0001).The mean level of creatinine in urine of normal individuals is 0.85±0.13 and that of Preeclampsia patients is 0.85±0.09 'p' value statistically significant (p<0.0001). (Table 3, Figure 4,5).

Table: 3 Comparison of urine parameters in Normal and Preeclampsia patients.

Parameters	Normal Mean±SD	Preeclampsia Mean±SD	'p' value
Nitric Oxide (µM/L)	645.85±119.84	396.08±151.26	P<0.0001
Creatinine (g/24hr)	0.85±0.13	0.85±0.09	P<0.0001

p<0.05 is statistically significant. Statistical comparison were performed by Student's 't' test. Data expressed as Mean±SD.

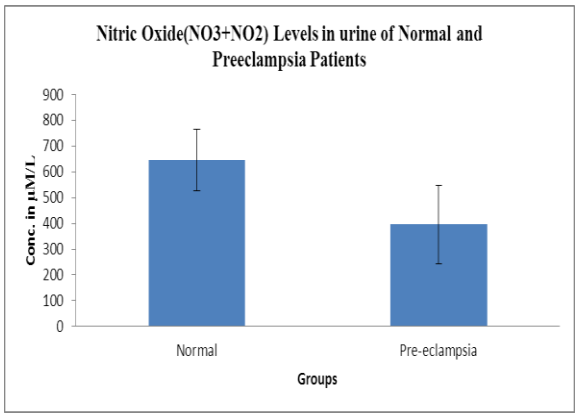

Figure 4: Comparison of urine Nitric oxide (NO_3+NO_2) levels in normal and preeclampsia patients

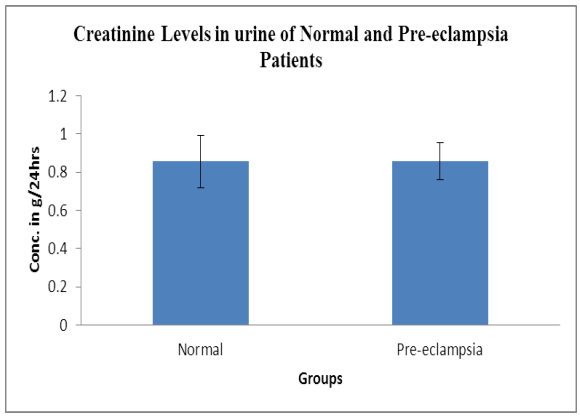

Figure 5: Comparison of urine creatinine levels in normal and pre-eclampsia patients

Table: 4 Relationship between serum nitric oxide/creatinine ratio and urine nitric oxide/creatinine ratio in Control and Study group.

	Serum NO/ Creatinine ratio	Urine NO/ Creatinine ratio	'p' value
Normal	49.88:0.67	645.85:0.85	p<0.0001
Preeclampsia	66.77:0.82	396.088:0.85	p<0.0001

p<0.05 is statistically significant. Statistical comparison were performed by Student's 't' test.

In the present study it was found that serum nitric oxide/creatinine ratio between the study group and the control was statistically significant p<0.001. The ratio was increased in the preeclamptic patients as compared to normal patients. It also showed that urine nitric oxide/creatinine ratio between the study group and the control was statistically significant p<0.001. The ratio was more in normal subjects as compared to the preeclamptic subjects.

DISCUSSION

Preeclampsia is a complex multisystem disorder seen exclusively in the human species. Worldwide, it is a leading cause of maternal and fetal morbidity and mortality. Reduced perfusion as a result of abnormal placentation is thought to lead to ischemia reperfusion injury to the placenta. Placental oxidative stress, which results from the ischemia reperfusion injury, is increasingly reported to be involved in the etiopathogenesis of gestational hypertension/preeclampsia and associated with impaired glucose tolerance.[16]

The role of NO in preeclampsia is still uncertain. Lyall et al.,[17] found that there was no significant difference in maternal serum nitrite concentrations between a control group and a preeclamptic group. Cameron et al.,[18] demonstrated that the plasma or urinary nitrate (or nitrite) level was increased during preeclampsia compared to normal gestation. In the study, serum NO concentrations in preeclamptic women were significantly higher when compared to normal pregnant women, whereas a significant decrease was observed in urine NO in preeclampsia woman. Markedly decreased NO concentrations in urine of preeclamptic women, suggest that NO biosynthesis is decreased in preeclampsia regardless of serum ferritin levels. Because NO is apotent relaxant of vascular smooth muscle, these results suggest that reduced NO production may have an adverse effect on placental hemodynamic function in preeclampsia, and could be involved in the pathogenesis of this important obstetric complication.[19]

Serum uric acid levels increased in preeclampsia patients when compared to normal individuals. In the present study we observed increased levels of creatinine in both serum and urine in preeclampsia patients. The rise in uric acid in pre-eclampsia is reflection of kidney damage, but a sign of antioxidative response, possibly related to the pathogenesis of pre-eclampsia.[20]

CONCLUSION

Serum NO concentrations in preeclamptic women were significantly higher when compared to normal pregnant women, whereas a significant decrease was observed in urine NO in preeclampsia woman. Serum uric acid levels increased in preeclampsia patients when compared to normal individuals. Creatinine levels increased in preeclampsia patients in both serum and urine.

This study might help clinicians to have diagnostic significance for the prediction of severity of the disease. Further experimental and clinical studies are necessary to clarify the pathogenesis of preeclampsia.

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