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Oxidative Stress (MDA) Levels and Urinary Protein-Creatinine Ratio in Pre-Eclamptic Patients Attending in the Outpatient's Clinic in A Tertiary Care Hospital

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Abstract

Objective: *To evaluate the serum levels of malondialdehyde as marker of lipid peroxidation and to estimate urinary protein-creatinine ratio to evaluate proteinuria.*

Methods: *This was a case-control study. The study was approved by the ethical committee of the institute. The consent was taken from each patient before enrolling in the study.*

The cases comprised of pre-eclampsia patients. The control group consisted of age matched normal pregnant women. Both cases and control were interviewed to obtain the relevant data after taking informed consent. Based on inclusion and exclusion criteria, 30 cases were selected and 30 age matched normal pregnant women were taken as controls.

Results: *There was no significant ($p>0.05$) difference in age, height, weight and BMI between cases and controls. The lipid peroxidation product, MDA was significantly increased in the cases as compared to the controls ($p=0.001$). There was significant difference in the Protein-creatinine ratio between cases and controls. There was significant ($p=0.001$) difference in the Protein-creatinine ratio between non-severe and severe Pre-eclampsia.*

Conclusion: *The protein-creatinine ratio was found to be significant predictor of proteinuria with a reasonable sensitivity and specificity.*

Key words: *Pre-eclampsia, Proteinuria, Sensitivity, Specificity*

INTRODUCTION

Preeclampsia is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation. It is associated with hepatic, neurological, hematological and renal involvement. Rapid development of edema, particularly of the face and hands, along with a rise in blood pressure, often signals the onset of this condition. Jaundice and abnormal liver functions may be present.

The risk of preeclampsia markedly increases in women with previous preeclampsia and in those with either preexisting vascular disease or conditions associated with increased cardiovascular risk, including renal disease, hypertension, diabetes, thrombophilia, and obesity (body mass index >29)[1].

Additionally, occurrence in first-degree relatives increases the risk. Thus preeclampsia also has a hereditary origin, but inheritance does not follow simple Mendelian characteristics and a single "preeclampsia gene" is unlikely. Despite intensive effort, associations with polymorphisms of likely candidate genes, mostly associated with cardiovascular disease, have been weak, inconsistent, or negative[2]. The low blood pressure goal had a greater beneficial effect in persons with higher baseline proteinuria[3].

Women who have had preeclampsia are also at greater risk for cardiovascular disease in later life, and pregnancy, itself a transient state of the metabolic syndrome, is considered to represent a "stress test" that unmasks latent cardiovascular risk[4-5].

Oxidative stress is a normal phenomenon in normotensive pregnancy; however, in preeclampsia, oxidative stress is exaggerated may result in a greater potential for endothelial oxidative damage. It has been reported that higher MDA/total antioxidant capacity (TAC) ratio is indicative of oxidative stress in women with preeclampsia. It has been suggested that uncontrolled lipid peroxidation may play a role in the etiology of the PIH[6].

Creatine is an amino acid derivative involved with cellular energy production, but other beneficial effects of creatine have been identified, including antioxidant actions, stabilization of lipid membranes, and interactions with glutamate and $GABA_A$ receptors that diminish excitotoxi-city[7]. Recent animal experiments demonstrate that when given as a supplement to the mother's diet during pregnancy, creatine protects the fetal brain, diaphragm, and kidney against hypoxic insult at term[8-9].

The present study was conducted to evaluate the serum levels of malondialdehyde as marker of lipid peroxidation and to estimate urinary protein-creatinine ratio to evaluate proteinuria.

MATERIAL AND METHODS

This was a case-control study. The study was approved by the ethical committee of the institute. The consent was taken from each patient before enrolling in the study.

The cases comprised of pre-eclampsia patients. The control group consisted of age matched normal pregnant women. Both cases and control were interviewed to obtain the relevant data after

taking informed consent. Based on inclusion and exclusion criteria, 30 cases were selected and 30 age matched normal pregnant women were taken as controls. The pre eclampsia patients with age group 20-45 years, pregnant >20 weeks of gestation with blood pressure of ≥ 140/90mm of Hg were included in the study. The pregnant women with primary hypertension, diabetes mellitus, gestational diabetes and smokers were excluded from the study. The controls were 30 age matched healthy pregnant women of 20 weeks of gestation or more without any major illness and who are not on any medication.

Collection of Blood

5ml of venous blood was collected from the subjects and the control group under all aseptic condition. The plasma was used for analysis of malondialdehyde.

Collection of Urine Sample

First mid stream urine sample was collected without any preservative.

Urine samples were analysed for protein by pyragallol method and creatinine by Jaffes method without delay. Urinary protein creatinine ratio was then calculated.

Statistical Analysis

The results are presented in mean±SD. The Unpaired t-test was used to compare the study parameters between cases and controls. The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

There was no significant (p>0.05) difference in age, height, weight and BMI between cases and controls (Table-1).

The lipid peroxidation product, MDA was significantly increased in the cases as compared to the controls (P=0.001) (Table-2).

There was significant difference in the Protein-creatinine ratio between cases and controls (Table-3).

There was significant (p=0.001) difference in the Protein-creatinine ratio between non-severe and severe Pre-eclampsia (Table-4).

Table-1: Age and anthropometric distribution of cases and controls

	Cases (n=30)	Controls (n=30)	p-value
Age in years	31.30±5.67	30.34±7.68	0.25
Height in ms	1.53±0.11	1.52±0.14	0.26
Weight in kg	47.45±11.23	49.34±12.24	0.24
BMI	25.45±4.50	24.35±6.78	0.27

Table-2: Comparison of MDA levels in cases & control

	MDA (Mean) nmol/ml
Cases (n=30)	6.71±0.71
Control (n=30)	2.72±0.31
p-value[1]	0.001*

[1]Unpaired t-test, *Significant

Table-3: Comparison of protein –creatinine ratio in cases & control

	Protein-creatinine ratio
Cases (n=30)	0.57±0.09
Control (n=30)	0.23±0.03
p-value[1]	0.001*

[1]Unpaired t-test, *Significant

Table-4: Comparison of MDA levels in non-severe & severe Pre-eclampsia

Cases	MDA (Mean) nmol/ml
Non-severe (B.P.140/90-160/110 mmHg)	0.59±0.11
Severe (B.P.≥ 160/110 mmHg)	0.66±0.13
p-value[1]	0.001*

[1]Unpaired t-test, *Significant

DISCUSSION

In normal pregnancy, progressive trophoblastic invasion transforms the high resistance uteroplacental spiral arteries into low resistance circulation i.e. there is remodeling of the spiral arteries. Pre-eclampsia is associated with inadequate and shallow trophoblastic invasion of these spiral arteries resulting in high resistance, low flow uteroplacental circulation which causes placental ischemia and hypoxia[10].

It has been proposed that the poorly perfused placenta secondary to defective placental invasion may be the origin of blood borne material(s) that directly or indirectly activate the maternal endothelial cell setting up a vicious cycle of endothelial dysfunction and vascular damage[11]. Free radicals have emerged as the likely promoters of maternal vascular malfunction[12]. One of the important consequences of free radical formation is lipid peroxidation which is reaction of oxidative deterioration of polyunsaturated fatty acids involving direct reaction of oxygen and lipid to form lipid peroxides. Lipid peroxidation is particularly damaging because it proceed as selfperpetuating chain reaction[13]. In present study, the MDA levels were significantly increased in cases as compared to controls. Thus the antioxidant defense available within the cell and extracellularly should be adequate to protect against the oxidative damage.

In the present study, there was significant difference in the Protein-creatinine ratio between cases and controls and there was significant (p=0.001) difference in the Protein-creatinine ratio between non-severe and severe pre-eclampsia. Sandvik et al[14] reported almost similar findings in which the median urinary ACR in follow-up urine samples was 0.53 mg/mmol for women with and 0.50 mg/mmol for women without preeclampsia (P=0.54). Only one woman (1%) with previous preeclampsia had urinary ACR >2.5 mg/mmol in two of three urine samples. Preeclampsia was not associated with urinary ACR above the 75th percentile. Women with preeclampsia did not have significantly higher eGFR than women without preeclampsia (107.9 versus 104.9 ml/min per 1.73 m(2); P=0.12), but preterm preeclampsia was significantly associated with eGFR above the 75th percentile (P=0.03). Aggarwal et al[15] assessed the diagnostic accuracy of random urine

protein-creatinine ratio for the prediction of significant proteinuria in patients with preeclampsia. 155 pregnant patients diagnosed to have hypertension in late pregnancy were instructed to collect urine during a 24-hour period. Protein-creatinine ratio was evaluated in a random urinary specimen. Out of these, 120 patients fulfilled the inclusion criteria. The predictive value of the random urinary protein-creatinine ratio for the diagnosis of significant proteinuria was estimated by using a 300-mg protein level within the collected 24-hour urine as the gold standard. 104 patients (86.67%) had significant proteinuria. There was significant association between 24-hour protein excretion and the random urine protein-creatinine ratio (r(s)=0.596, p< 0.01). With a cut-off protein-creatinine ratio greater than 1.14 as a predictor of significant proteinuria, sensitivity and specificity were 72% and 75%, respectively. The positive predictive value was 94.9% and negative predictive value was 29.2%.

CONCLUSION

The protein-creatinine ratio was found to be significant predictor of proteinuria with a reasonable sensitivity and specificity.

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