

## Study of oxidative stress in women with preeclampsia

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### Abstract

**Introduction:** Root cause of preeclampsia is placental ischemia due to impaired trophoblastic invasion in uterine spiral arterioles. Ischemic placenta liberates various inflammatory mediators. Inflammation is associated with development of free radicals leading to vascular endothelial damage. Therefore estimation of oxidative stress can give insight to pathogenesis of disease.

**Objectives:** To compare oxidative stress among women with preeclampsia & normal pregnancy.

**Materials and Method:** Thirty pre-eclamptic women and thirty women with normal pregnancy were included in study as cases and controls respectively. Serum levels of MDA, vitamin C & uric acid were estimated. Data was compared using unpaired student's t-test done by SPSS 17.0 software.

**Results:** Cases were having significantly higher serum MDA levels than controls. There were significantly lower serum levels of vitamin C & uric acid in cases than controls ( $p < 0.05$ ).

**Conclusions:** Significantly increased level of MDA & decreased level of Vitamin C & uric acid in pre-eclamptic mothers suggests that increased oxidative stress and preeclampsia are associated with each other. Elevated oxidative stress is independent risk factor for vascular diseases so it can be used as a biomarker to identify women at risk.

**Keywords:** malondialdehyde, oxidative stress, uric acid, Vitamin C, preeclampsia.

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### Introduction

Incidence of preeclampsia is 6-8% of all pregnancies, 10% of 1<sup>st</sup> pregnancies and 20-25% of women with a history of chronic hypertension.<sup>(1)</sup> Recurrence risk is of 19% for gestational hypertension, 32% for preeclampsia and 46% for preeclampsia superimposed on pre-existing chronic hypertension.<sup>(2)</sup> It is associated with many maternal complications such as preterm labour, antepartum haemorrhage, postpartum haemorrhage, HELLP syndrome & fetal complications such as Intrauterine growth retardation (IUGR).<sup>(3)</sup>

Working group of National High Blood Pressure Education Programme (NHBPEP 2000) have defined hypertensive disorders of pregnancy. Any mother who was previously normotensive and nonproteinuric, develops elevation of blood pressure (BP)  $\geq 140/90$  millimeter of Mercury (mmHg) after 20 weeks of gestation (2 reading, at least 6 hours apart) and proteinuria of  $\geq 300$ mg in 24hours urine sample or  $\geq 1+$  by dipstick method in a random urine sample is defined as preeclampsia.<sup>(4)</sup>

Root cause of preeclampsia is inadequate invasion of trophoblasts into uterine spiral arterioles which causes narrowing of uterine arterioles leading to placental ischemia.<sup>(5)</sup> Placental ischemia induced formation of reactive oxygen species (ROS) leads to depletion of antioxidant capacity of cells.<sup>(6)</sup> Increased level of oxidative stress causes dysfunction in vascular endothelium leading to angiogenic imbalance.<sup>(7)</sup> Thus,

oxidative stress induced endothelial dysfunction becomes causative factor for manifestations and complications of preeclampsia.<sup>(8)</sup>

Present study was done to compare status of oxidative stress parameters in preeclamptic women with that of normal pregnancy.

### Materials and Method

Thirty women with preeclampsia and Thirty healthy pregnant women were included in a cross sectional study done from January 2012 to June 2012. Preeclamptic mothers were taken as cases and healthy pregnant mothers were taken as controls after taking informed consent. Cases & controls were taken from Bapuji Hospital and Chigateri Hospital, Davangere (both these hospitals are attached to teaching institute, J.J.M. Medical College, Davangere). Approval was taken from the ethical and research committee of J.J.M. Medical College, Davangere to conduct the study.

#### **Inclusion criteria for selection of study subjects:**

**Cases:** Thirty diagnosed cases of preeclampsia in age group of 20-45 years.

Pregnant female of  $\geq 20$  weeks of gestation with blood pressure  $\geq 140/90$  mm of Hg noted first time during pregnancy on  $\geq 2$  occasions at least 6 hours apart with proteinuria of  $\geq 1+$  ( $\geq 30$ mg/dl) by dipstick method in a random urine sample was considered as having preeclampsia.<sup>(4)</sup>

**Controls:** Thirty healthy pregnant women of  $\geq 20$  weeks of gestation after matching for age & gestational period.

**Exclusion Criteria:** Women with history of systemic illness, addiction or medication affecting blood antioxidant level were excluded.

**Sample collection:** Women were instructed for 12 hours overnight fasting. 3 ml of venous blood was collected in plain vial using proper aseptic precaution. Serum was separated by centrifugation and used to

measure serum malondialdehyde (MDA), vitamin C and uric acid concentration.

**Sample analysis:** Thiobarbituric acid method<sup>(9)</sup> was used to determine concentration of serum MDA, 2,4-Dinitrophenylhydrazine method<sup>(10)</sup> for serum vitamin C and enzymatic uricase method<sup>(11)</sup> for serum Uric acid.

**Statistical analysis:** Statistical analysis was done by Student's unpaired t-test using SPSS 17.0. The probability value  $< 0.05$  was considered as statistically significant.

## Results

**Table 1: Comparison of parameters among cases & controls**

	Controls (Mean $\pm$ S.D.)	Cases (Mean $\pm$ S.D.)	p value of unpaired student's t test
Period of Gestation (Weeks)	34.26 $\pm$ 1.56	34.14 $\pm$ 3.34	0.53
Age (years)	24.1 $\pm$ 2.52	23.56 $\pm$ 2.67	0.43
Systolic Blood Pressure (mm of Hg)	114.3 $\pm$ 5.64	158.5 $\pm$ 9.24	$< 0.001$
Diastolic Blood Pressure (mm of Hg)	72.31 $\pm$ 4.57	97.04 $\pm$ 7.2	$< 0.001$
Serum MDA (nmol/mL)	3.22 $\pm$ 0.94	6.91 $\pm$ 1.35	$< 0.001$
Serum vitamin C ( $\mu$ IU/ml)	1.1 $\pm$ 0.17	0.6 $\pm$ 0.12	$< 0.001$
Serum Uric acid (mg/dL)	5.83 $\pm$ 1.05	4.52 $\pm$ 0.85	$< 0.05$

Table 1 shows that cases had significantly higher mean levels of systolic & diastolic blood pressure & serum MDA than controls ( $p < 0.001$ ). The mean value of serum Vitamin C ( $p < 0.001$ ) & serum uric acid ( $p < 0.05$ ) were significantly lower in cases than controls. Statistically non-significant difference was found in period of gestation and age of mother among the study groups.

## Discussion

Evidence of knowledge about hypertensive disorders of pregnancy is there in the Hippocratic writings.<sup>(12)</sup> Pathological changes induced by narrowing of uterine spiral arterioles secondary to impaired invasion of trophoblasts is found to be the cause of preeclampsia.<sup>(13)</sup>

We found higher levels of serum MDA in preeclamptic mothers than healthy pregnant mothers. This result is in accordance with studies done by Rafeenia A et al<sup>(14)</sup> & Siddiqui IA et al.<sup>(15)</sup> Many studies have shown association between preeclampsia and oxidative stress.<sup>(6-8,16)</sup> As free radicals in the cell increases, chances of lipid peroxidation of membrane lipid increases. Malondialdehyde (MDA) is liberated as an end product of membrane lipid peroxidation.<sup>(17)</sup> Thus, increased level of MDA signifies elevated oxidative stress in preeclampsia.

We found significantly decreased levels of serum vitamin C and uric acid in cases when compared with controls. Ascorbic acid works as an antioxidant. As

level of oxidative stress increases, increased amount of vitamin C is needed to neutralize free radicals and lipid peroxides.<sup>(18,19)</sup> End product of purine catabolism is Uric acid. It is also involved in antioxidant activity in human plasma.<sup>(20)</sup> Thus, decreased levels of antioxidants such as vitamin C and uric acid along with elevated levels of lipid peroxidation end product MDA suggest more oxidative stress in preeclampsia than normal pregnancy.

Elevation of oxidative stress is associated with many complications in pregnancy.<sup>(21)</sup> Therefore estimation of oxidative stress can be useful tool to assess the mothers at risk. Such mothers can be prescribed diet or supplements rich in antioxidant, life style changes, yoga etc., which can be helpful to them to reduce impact of oxidative stress on ongoing pregnancy.<sup>(22,23)</sup>

## Conclusion

Impaired trophoblastic invasion into uterine spiral arteriole leads to placental ischemia. This increases production of inflammatory mediators. Inflammation causes depletion of antioxidants in preeclamptic mother and elevation of oxidative stress. Serum MDA, vitamin C and uric acid levels can give idea of oxidative stress. Mothers having elevated oxidative stress can be monitored carefully to reduce complications and improve outcome.

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