

Evaluation of Oxidative Stress and Antioxidant Defence in Subjects of Preeclampsia

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Abstract

Objectives To evaluate the parameters of oxidative stress and anti oxidant defense in preeclampsia and thereby find any etiological correlation.

Methods Study was carried out on pregnant and non pregnant women attending or admitted in the Obstetrics and Gynecology Department of SSG Hospital, Baroda between 1st June 2007 to 31st May 2008. Each serum sample from different groups was evaluated for malondialdehyde (MDA), a product of lipid peroxidation process as a marker for oxidative stress and reduced Glutathione, Superoxide Dismutase, and Catalase for antioxidant enzyme activity and a comparison drawn and analyzed using *t*-test and χ^2 test.

Results The levels of MDA (a lipid peroxidation product) increased significantly in pregnancy compared to non-pregnant females and further significantly increased in preeclampsia compared to normal pregnant females. The superoxide dismutase levels, catalase levels and vit-E levels were found to be increased in preeclamptic females as compared to normal pregnant females.

Conclusion Preeclampsia is found to be a condition with markedly increased oxidative stress as is evidenced by highly significantly increased levels of MDA, a marker of lipid peroxidation. Levels of antioxidant enzymes, viz. reduced glutathione, superoxide dismutase, catalase and vitamin E have been found to be increased in preeclampsia as

compared to normal pregnant females. This may be a compensatory mechanism for handling the increased oxidative stress.

Keywords Oxidative stress · Antioxidants · Preeclampsia

Introduction

Preeclampsia is a pregnancy specific condition characterized by hypertension and proteinuria that remits after delivery. It is a characteristic multisystem disorder of pregnancy, one of the most common complications of pregnancy and is a leading cause of maternal and perinatal morbidity and mortality [1]. The etiology of preeclampsia is still unknown. The hypotheses currently accepted are the placental ischemia hypothesis, genetic hypothesis, the immune maladaptation hypothesis and hypothesis of the imbalance between free oxygen radicals and scavengers in favour of oxidants. Cumulative evidence in recent years has shown that a biochemical imbalance in preeclampsia occurs with an increase of oxidative stress and lipoperoxidation and at the same time, a deficient antioxidant protection. Lipid peroxides, as products of an altered oxidative stress, are involved in endothelial cell injury, vasoconstriction and imbalance between thromboxane and prostacyclin [2]. This study was done to assess various parameters of oxidative stress and antioxidant defense in normal pregnancy and in preeclampsia and comparing with non-pregnant females and post partum females.

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Subjects and Methods

The study was carried out over a period of 1 year starting from 1st June 2007 to 31st May 2008. Women were placed in following 3 groups:

- Group A—Non-pregnant normotensive—50 patients (normal women of peak childbearing age 19–35).
- Group B—Pregnant women without preeclampsia between 32 and 36 weeks of gestation presenting immediately following the ‘cases’—50 patients
- Group C—Antenatal subjects of gestational age between 32 and 36 weeks with mild/severe preeclampsia. This group constitutes ‘cases’—50 patients (Blood pressure—>140/90 mmHg, with proteinuria, with or without pathological oedema)

Those who had diabetes mellitus, chronic hypertension, hepatitis, medical disorders like renal disease, thyroid disease, collagen vascular disease, hemoglobin <8 g%, BMI >30, patients treated for PCOS in past and eclampsia were excluded from the study.

Blood sample (5 ml) was collected in EDTA bulb from pregnant and non pregnant women with all aseptic precautions by the qualified staff of O.G Department, S.S.G. Hospital, Baroda. All blood samples were preserved in refrigerator and the prooxidants and antioxidant parameters were estimated using Spectrophotometer within 48 h of collection of the blood samples.

Observations and Results

Malondialdehyde (mg/dl)

Malondialdehyde, an indicator of lipid peroxidation and oxidative stress, was calculated in all the subjects and mean calculated. It was found to be highly significantly increased in normal pregnancy compared to nonpregnant females. The levels further showed a highly significant increase in preeclampsia than normal pregnancy. Concentration in preeclampsia was found to be a little less than two times than non pregnant females. Post partum the level was found to be decreasing again (Table 1).

Table 1 Mean malondialdehyde concentration in the 3 study groups

	A	B	C
Mean	5.19	6.91	8.1
±SEM	±0.12*	±0.33*	±0.51*

* $P < 0.001$

Reduced Glutathione

The levels of reduced Glutathione as an antioxidant marker was assessed in 3 groups i.e. A, B and C. It was found that the concentration was highly significantly decreased in normal pregnancy as compared to non pregnant females. In preeclampsia, it was marginally increased (Table 2).

Superoxide Dismutase

Its level was found to be increased in normal pregnancy as compared to non pregnant females which was statistically highly significant ($P < 0.001$). In preeclampsia, the level was further increased from normal pregnancy, being statistically highly significant ($P < 0.001$) (Table 3).

Catalase

Blood levels of catalase was found to be decreased significantly in normotensive pregnant women (465.02 ± 24.2) as compared to normal non pregnant women (511.01 ± 22.2). Although this levels were significantly increased in mild preeclamptic patients (499.89 ± 14.5) as compared to normal pregnant women (Table 4).

Discussion and Analysis

Lipid peroxidation has been blamed to be the main causative factor for oxidative stress in preeclampsia. Free radicals

Table 2 Reduced glutathione levels in 3 study groups

	A	B	C
Mean	40.23	33.91	34.12
±SEM	±2.09*	±2.52*	±1.22*

* $P < 0.001$

Table 3 Mean SOD concentration in the 3 study groups

	A	B	C
Mean	100.1	115.41	121
±SEM	±4.51*	±6.51*	±5.59*

* $P < 0.001$

Table 4 Mean catalase concentration in the 3 study groups

	A	B	C
Mean	511.01	465.02	499.89
±SEM	±22.2*	±24.2*	±14.5*

* $P < 0.001$

initiate lipid peroxidation by attacking polyunsaturated fatty acids in cell membranes [3]. Uncontrolled peroxidation of fatty acids and cholesterol alter membrane fluidity and permeability as lipid peroxides are toxic compounds that damage endothelial cells, increase peripheral vasoconstriction and increase thromboxane synthesis and decrease prostacyclin synthesis [4]. Once steady state levels of blood lipid peroxides begin to rise, the stage would be set for self-perpetuating chain-reaction processes to take place. Endothelial contact with lipid peroxides would allow peroxidative damage of endothelial cell membrane lipids. This could ultimately reduce the ability of the endothelium to act as a permeability barrier to plasma components. Exposure of the vascular endothelium to lipid peroxides would begin to shut off production of prostacyclin, increasing the propensity for vasoconstriction and platelet aggregation [2] (133).

In this study, we found that the levels of malondialdehyde (a lipid peroxidation product) increased significantly in pregnancy compared to non-pregnant females and further significantly increased in preeclampsia compared to normal pregnant females. This increase signifies the excessive ongoing lipid peroxidation in preeclampsia and this may well be a marker of oxidative stress. This result correlates well with numerous studies undertaken at many institutes. In India, studies conducted by Adiga, Patil et al. [5] and Krishna Menon S [6] at different institutes showed significant elevations in the levels of malondialdehyde in preeclampsia compared to normal pregnancy and non-pregnant females. Outside India also, various studies like those by Elesá Llusla [7], Madazli R et al., and Chamy et al. [8] have all found significantly increased MDA levels in preeclampsia as compared to normal pregnancy and also in pregnancy as such compared to non-pregnant females.

Studies on antioxidant status in preeclampsia have revealed mixed outcomes. Some show decrease in antioxidant enzymes (due to consumption) and some show increase in antioxidant enzymes (as a compensatory mechanism). In this study, we found decrease in reduced Glutathione levels compared to non-pregnant females.

The superoxide dismutase levels, catalase levels and vitamin E levels were found to be increased in preeclamptic females as compared to normal pregnant females. Increase in superoxide dismutase was also found in study by Sharma et al. [9] conducted at AIIMS, India and by Krishna Menon et al. [6]. Their elevation may be an adaptive response to counter the effect of increased oxidative stress. Reduced glutathione was found to be decreased in preeclamptic females in studies at Turkey and study by Kaur G et al. [10] in India. The latter study also showed significant elevation in Vitamin E levels as compared to normal pregnancy.

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