

THE STUDY OF OXIDATIVE STRESS IN NORMAL PREGNANCY AND PREECLAMPSIA

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ABSTRACT

Stress may occur in normal pregnancy and Pre-eclampsia. In normal pregnancy, stress occurs as result of high metabolic demand. Pre-eclampsia may be caused by placental oxidative stress. Aims to compare oxidative stress level in normal pregnancy and preeclampsia. This was the cross sectional study done on 100 women attending the antenatal clinic, SRG Hospital & Medical college, Jhalawar. Hundred women were divided into two groups. Of the 100 women, 50 have pre-eclampsia and 50 have normal pregnancy. Malondialdehyde (MDA) level were measured by Beuge et al method. Statistical analysis used: unpaired t test using Graph Pad prism 5 software. Serum MDA levels Value in the preeclampsia patient were significantly higher compared that in patients with the normal pregnancy. Preeclampsia patient are exposed higher level oxidative stress compared to that normal pregnancy.

INTRODUCTION

Oxidative stress is essentially an imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants. There is escape of free radicals from mitochondrial electron transport chain. These act on membrane lipoproteins & polyunsaturated fatty acids and produce lipid peroxidation products. Of the many biological targets of oxidative stress, lipids are the most involved class of biomolecules. Lipid oxidation gives rise to a number of secondary products. Malondialdehyde (MDA) is one such product which may be used to assess the stress.

Stress may occur in normal pregnancy and Pre-eclampsia. In normal pregnancy, stress occurs as result of high metabolic demand. Pre-eclampsia is a pregnancy-specific condition characterised by hypertension and

proteinuria that remits after delivery [1]. Although its exact etiology is unknown, maternal symptoms are thought to be secondary to endothelial cell dysfunction [2]. It has been suggested that free radicals are likely promoters of maternal vascular malfunction, as reactive oxygen species, particularly superoxide anions, evoke endothelial cell activation [3]. Markers of lipid peroxidation have been noted to be increased in the plasma of women with preeclampsia [4]. Some studies, however, have not found raised levels of oxidative stress marker in pre-eclampsia. [5]. In the present study, we had made an attempt to assess the stress level in pre-eclamptic and normal pregnant women. To assess the stress malondialdehyde (MDA) has been used as it is the principal and most studied product of polyunsaturated fatty acid peroxidation. This aldehyde is a highly toxic molecule and should be considered as more than just a marker of lipid peroxidation.

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SUBJECTS AND METHODS

This was the cross sectional study done on 100 women attending the antenatal clinic, SRG Hospital &

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Medical college, Jhalawar. Written informed consent were obtained from the patient attending antenatal clinic. History and examination was done by gynaecologist. Subjects with history of abortion, recent surgery, diabetes, hypertension & other chronic ailments were excluded from the study.

Hundred women were divided into two groups. Of the 100 women, 50 have pre-eclampsia (i.e., high blood pressure [BP] and proteinuria) and 50 have normal pregnancy. Pre-eclampsia is defined as systolic and diastolic BP greater than 140 mm Hg and 90 mm Hg, respectively, with significant proteinuria (N300 mg per 24 h); mild pre-eclampsia is defined as diastolic BP less than 110 mm Hg, with significant proteinuria; and severe preeclampsia as diastolic BP greater than 110mm Hg, or massive proteinuria (N2 g/24 h), or serum creatinine level greater than 1.2 mg/dL, or when other signs and symptoms of severe pre-eclampsia such as persistent headache, visual disturbances, persistent epigastric pain, and/or thrombocytopenia were present [1]. Detailed patient history and physical examination to be done. Blood pressure is measured in the left arm with a sphygmomanometer. Urinalysis is done for proteinuria. A total of 10 mL of venous blood was taken for all routine investigations, out of which 0.5ml blood send for MDA levels for our study. All blood samples will be drawn into tubes free of endotoxins and anticoagulant.

In the present study, patient with mild preeclampsia were only included in study. Malondialdehyde Serum MDA levels was

estimated by the method of Beuge et al [6] using thiobarbituric acid (TBA). The acid reacts with MDA to form a stable pink color with maximum absorption at 535 nm. According to this method, 375 mg of TBA was dissolved in 2 mL of 0.25 N chlorhydric acid (HCl), followed by 15 g of trichloroacetic acid (TCA) for a total volume of 100mL. The solution was heated in a water bath at 50 8C to dissolve TBA properly. Then, 1 mL of serum was combined with 2 mL of TCA—TBA—HCl and mixed thoroughly. The solution was heated for 15 min in a boiling water bath. After cooling, the flocculant precipitate was removed by centrifugation. Sample absorbance was then determined at 535 nm against a blank that contained all reagents except the serum sample. Serum MDA concentration was expressed as nmol/mL.

Permission was obtained from institution ethics committee.

Statistical analysis was done using unpaired t test using Graph Pad prism 5 software. P value < 0.05 was considered to be statistically significant.

RESULTS

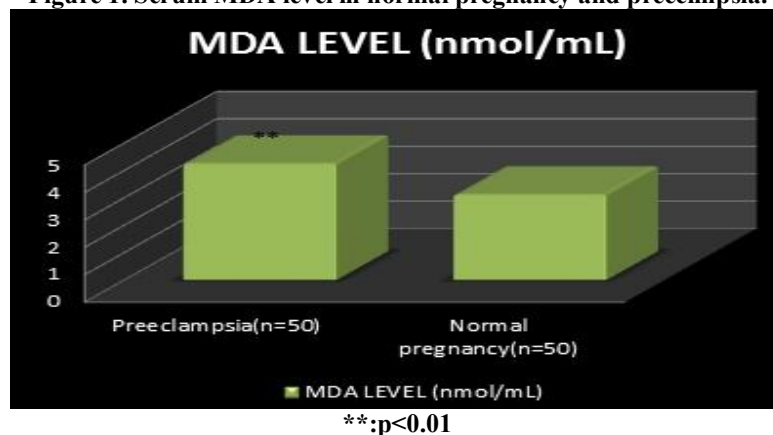
General characteristic of the patient is shown in table 1. There was no significant difference between two groups. Out of 50 pre-eclampsia patient, 10 were primipara and rest were multipara. Out of 50 normal pregnancy, 19 were primipara and rest were multipara. Malondialdehyde Serum MDA levels comparison is shown in figure 1. There was the significant difference between two groups. Value in the preeclampsia patient were significantly higher.

Table 1. Anthropometric parameters of the subjects

Parameters	Preeclampsia (n=50)	Normal pregnancy (n=50)
Age (yrs)	24.120±2.56	25.41±3.01
Height(cms)	165.22±12.64	169.78±13.55
Weight (kg)	64.780±5.54	65.58±5.14
BMI (kg/m ²)	24.136±2.34	24.880±2.335

No significant difference

Figure 1. Serum MDA level in normal pregnancy and preeclmipsia.



DISCUSSION

In the present study, we expected more oxidative stress in preeclampsia patients. We also got the similar result as per our expectation. Saikumar P et al [7] also found similar result comparable to us, however he had done study in various trimester and he found high level second trimester.

The female reproductive system is a complex multiorgan system which require an optimal biological environment. Aerobic metabolism utilizing oxygen is essential for reproductive homeostasis. Aerobic metabolism is associated with the generation of prooxidant molecules called ROS including hydroxyl radical, superoxide anion, hydrogen peroxide, and nitric oxide. The balance between the prooxidants and antioxidants maintain the cellular homeostasis, whenever there is an imbalance in this equilibrium leading to enhanced steady-state level a state of oxidative stress is initiated. Free radicals are key signal molecules modulating reproductive functions by the influence of the endometrial and fallopian tube function, maturation of oocytes, sperm, implantation of the preembryo and early embryo development [8].

Pregnancy is a state of oxidative stress arising from the increased metabolic activity in the placenta and reduced scavenging power of antioxidants [9]. During the gestation, the oxygenation of the utero-placental unit changes continuously. In Early pregnancy, they are exposed to low oxygen tension but in late pregnancy they are exposed to high oxygen tension [10]. In Preeclampsia, trophoblast invasion and maternofetal barrier are abnormal. This results in oxidative stress and decreased antioxidants. In normal pregnancy, there is hyperlipaemia and in preeclampsia, there is further elevation of serum triglycerides and serum free fatty acid. Increased lipid peroxidation has been reported in preeclampsia. Factors

playing role in this are Nicotinamide adenine dinucleotide phosphate oxidase enzyme, Hyperhomocysteinaemia, and altered eicosanoid synthesis.[11] All these factors leads to lipid peroxidation, this results in primary lipid peroxidation product such as lipid hydroperoxides and secondary products such as MDA and lipid peroxides. Their level had been shown to correlate with diastolic blood pressure. Level of antioxidant also play significant role. Serum levels of Vitamin E, beta carotene, Serum coenzyme Q10 and tocopherol levels, ascorbic acid level were significantly reduced in pre-eclampsia patients.[12]

CONCLUSION

Thus all these factors may lead to increased MDA level as seen in our study. To conclude, preeclampsia is associated increased level MDA and thus with increased stress. However we recommend multiple studies with large sample size, and in various degrees of severity of preeclampsia. We also recommend various studies with antioxidative agents.

Limitation of the study

In the present study, we had only included MDA level as a marker of oxidative stress. We should also take into account other parameters for oxidative stress. We had only compared mild Pre-eclampsia patient with subjects with normal pregnancy. We should have included patient with moderate and severe pre-eclampsia. So further studies are recommended keeping all these factors in mind.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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