

“Role of lipid peroxidation and antioxidant status in pathogenesis of Pre-eclampsia.”

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ABSTRACT:

Introduction: In India, the incidence of pre-eclampsia is reported to be 8-10% of the pregnancies. The present study was planned to determine the role of lipid peroxidation and antioxidant function in the development of pre-eclampsia.

Material & Methods : The study comprised of 30 normal pregnant women and 30 pre-eclamptic women in their third trimester of pregnancy. The following estimations were done: Serum Malondialdehyde (MDA), Serum Vitamin E.

Results : The levels of serum MDA were significantly increased in cases as compared to normal pregnant women and vitamin E levels were significantly decreased in cases as compared to controls.

Conclusion: Increased levels of lipid peroxidation product (MDA) and decreased levels of antioxidant (Vitamin E) in women with pre-eclampsia suggest that oxidative stress play a key role in the genesis of endothelial dysfunction and expression of pre-eclampsia.

Key words: Malondialdehyde (MDA), Vitamin E, Oxidative stress, Pre-eclampsia.

INTRODUCTION:

In India, the incidence of pre-eclampsia is reported to be 8-10% of the pregnancies[1]. It contributes significantly to maternal and fetal mortality and morbidity. Pre-eclampsia is a multisystem disorder characterized by hypertension to the extent of 140/90 mm Hg or more, proteinuria (≥ 300 mg/day) and edema induced by pregnancy after 20th week[2]. Without intervention, pre-eclampsia progresses to eclampsia which is characterized by malignant hypertension and epileptiform convulsions requiring emergency caesarian section[3]. Despite considerable research, the cause of pre-eclampsia remains unclear. Maternal symptoms are thought to be secondary to endothelial cell dysfunction[4]. It has been suggested that free radicals are likely promoters of maternal vascular malfunction, as reactive oxygen species evoke endothelial

cell dysfunction[5]. Normally, lipid peroxidation occurs at low levels in all cells and tissues. In health, oxidation by free radicals and neutralization by antioxidants remain in balance. Cumulative evidences in recent years have shown that in pre-eclampsia, there is an increase in lipid peroxidation and a decrease in antioxidants protection leading to oxidative stress. For the aforesaid reasons, the present study was conducted to study the lipid peroxidation product, malondialdehyde (MDA) and lipophilic antioxidant, vitamin E in cases of preeclampsia and normal healthy pregnant women.

MATERIALS AND METHODS : The present study was carried out in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology, B. J. Medical College and Sasson General

Hospitals, Pune. Informed consent was taken from all individual subjects inducted into the study. The study comprised of 30 normal healthy pregnant women and 30 pre-eclampsia cases attending antenatal OPD in their third trimester of pregnancy. The diagnosis of pre-eclampsia was based on the definition of American College of Obstetrics and Gynecologists [6].(A) Systolic blood pressure greater than 140 mm Hg or a rise of at least 30 mmHg or (B) Diastolic blood pressure greater than 90 mm Hg or a rise of at least 15 mmHg (manifested on two occasions at least 6 hours apart) and (C) Proteinuria of 300 mg or greater in 24 hours urine collection or protein concentration of 1 gm/L (on two occasions of at least 6 hours apart). Fasting blood sample (8ml) was collected by venipuncture and the following parameters were estimated in both cases and controls (2.1) Serum Malondialdehyde(MDA) level, a lipid peroxidation product(Beuge and Aust Method) [7] (2.2) Serum Vitamin E level, an antioxidant (Baker and Frank Method) [8].Data were statistically analyzed by unpaired T test and expressed in terms of 'P' value.

RESULT: The lipid peroxidation product, MDA was significantly increased in the cases as compared to the controls ($P < 0.0001$) (Table I). Vitamin E was significantly decreased in cases as compared to controls ($P < 0.0001$) (Table II).

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 [9]. 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[10]. Free radicals have emerged as the likely promoters of maternal vascular malfunction [11]. 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 proceeds as self-perpetuating chain reaction[12]. In present study, we observed that MDA levels were significantly increased in cases as compared to controls. In view of its potentially destructive character, uncontrolled lipid peroxidation has been suggested as an etiological factor in pre-eclampsia. Lipid peroxidation products are the candidate factors that may mediate disturbance of the maternal vascular endothelium. These products may inhibit prostacyclin synthesis and stimulate smooth muscle contraction resulting in widespread vasospasm, a prominent feature of pre-eclampsia. There was a significant decrease in Vitamin E in cases as compared to controls. Many studies observed that levels of antioxidants such as vitamin C, vitamin E, and other antioxidants are reduced in sera and placenta of pre-eclamptic women.[3,13].Decrease in Vitamin E in pre-eclampsia could be due to its increased consumption to counteract free radical mediated changes and also due to decreased absorption from gut as a result of vasoconstriction in pre-eclampsia[14]. Thus the antioxidant defense available within the cell and extracellularly should be adequate to protect against the oxidative damage.

However the balance can be lost because of the overproduction of free radicals by exposure to sources that overwhelm the antioxidant defenses, or by inadequate intake of nutrients that contribute to the oxidative stress in pre-eclampsia [15]. The placentally derived endothelial disturbing factors like lipid peroxides could be a possible cause in the pathogenesis of pre-eclampsia[16].

This association may be significant in understanding the

pathological process of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia. Thus, estimation of MDA levels, vitamin E may have a predictive role in the assessment of the extent of endothelial damage in pre-eclampsia and may help patient by preventing or foreseeing the effects of complications in pre-eclampsia. As oxidative stress can provoke endothelial dysfunction, the pregnant subjects should be supplemented with antioxidants to prevent overwhelming of oxidative stress.

Tables & contents:

Table I: Levels of serum MDA in cases and controls

STUDY GROUP	SAMPLE SIZE (N)	MDA (MEAN±SD)
Patients	30	6.74±0.75**
Controls	30	2.74±0.33

**p<0.001 highly significant

Table II: Levels of serum Vitamin E in cases and controls:

STUDY GROUP	SAMPLE SIZE (N)	VITAMIN E MEAN±SD
Patients	30	0.6±0.15**
Controls	30	1.06±0.25

**p<0.001 highly significant

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Date of Submission: 02 January 2013
Date of Provisional acceptance: 09 January 2013
Date of Final acceptance: 16 February 2013
Date of Publication: 05 March 2013
Source of Support: Nil Conflict of Interest: Nil