



STUDY OF LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN PRE-ECLAMPSIA

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ABSTRACT

Background: Preeclampsia is a pregnancy specific syndrome, a leading cause of maternal- fetal morbidity and mortality. Free radicals lead to lipid peroxidation which is destructive in nature and has been suggested as an etiological factor in preeclampsia.

Methods: The study was conducted in the Dept. of Obstetrics and Gynecology in collaboration with Dept. of Biochemistry at RNT Medical College, Udaipur. Investigations were carried out in 100 women suffering from preeclampsia and compared with 100 normal control group composed of age matched healthy pregnant women.

RESULTS: Serum MDA and uric acid levels were significantly raised ($P < 0.01$) in pre eclamptic women as compared to normal pregnant women. while serum antioxidant vitamin E, vitamin C, and SOD levels were significantly decreased ($P < 0.01$) in pre eclamptic women as compared to normal pregnant women.

Conclusion: These results provide further evidence that excessive lipid peroxidation level and decreases in vitamin E and C levels (which are responsible from antioxidant activity) may contribute to the pathophysiology and pathogenesis of preeclampsia.

KEYWORDS : Preeclampsia, MDA, uric acid, vitamin E, vitamin C and SOD.

INTRODUCTION

Pregnancy is a physiological condition in which women are more prone to oxidative stress, which results due to an imbalance between the pro oxidant-antioxidant levels (Toescu V *et al.* 2002). Oxidative stress results because of the presence of placenta which is rich in mitochondria. Fully developed placenta consumes about 1% of the basal metabolic rate of the pregnant woman. It is also highly vascular and is exposed to high maternal oxygen partial pressure. Pregnancy is characterized by increased basal oxygen consumption and changes in energy substrate use by different organs.

Formerly also known as toxemia, preeclampsia is a condition that pregnant women develop. It is marked by high blood pressure in women who have previously not experienced high blood pressure before; the condition begins after 20 weeks of pregnancy. Preeclamptic women will have a high level of protein in their urine and often also have swelling in the feet, legs, and hands. This condition usually appears late in pregnancy although it can occur earlier.

Pre-eclampsia increases the risk of poor outcomes for both the mother and the baby. Undiagnosed, preeclampsia can lead to eclampsia, a serious condition that can put you and your baby at risk, and in rare cases, cause death. Women with preeclampsia who have seizures are considered to have eclampsia (Obstet. Gynecol Nov 13).

Preeclampsia is a multisystem disorder characterized by hypertension to the extent of 140/ 90 mm Hg or more, proteinuria ($\geq 300\text{mg/day}$) and edema induced by pregnancy after 20th week. Without intervention, preeclampsia may progress to eclampsia. Despite considerable research, the cause of preeclampsia remains unclear. Maternal symptoms are thought to be secondary to endothelial cell dysfunction (Phalak P *et al.* 2013). Nowadays, lipid peroxidation has become an acceptable marker in medicine to consider endothelial dysfunction at molecular level (Patil SB *et al.* 2007). It has been suggested that free radicals are likely promoters of maternal vascular dysfunction (Phalak P *et al.* 2013). Vascular endothelial dysfunction may be caused by

uncontrolled lipid peroxidation. Lipid peroxidation is an oxidative process which occurs at low levels in all cells and tissues. Under normal conditions variety of antioxidant mechanisms serve to control this peroxidative process (Patil SB *et al.* 2007).

Cumulative evidence in recent years has shown that in preeclampsia, there are an increase in lipid peroxidation and a decrease in antioxidants protection leading to oxidative stress (Phalak P *et al.* 2013). For the aforesaid reasons, the present study was conducted to study the lipid peroxidation product, malondialdehyde (MDA) and enzymatic antioxidant SOD and non-enzymatic antioxidants vitamin E and vitamin C, uric acid in pre eclampsia and normal pregnant women.

AIM & OBJECTIVE:

The aim of this study was to evaluate Oxidative stress status in pre eclampsia and normal pregnancies by measuring serum malondialdehyde (MDA) levels, an end product of lipid peroxide. The reinforcement of antioxidant capacity is the body attempt to overcome oxidative stress during pregnancy. In view of these facts, the present study was planned to measuring the plasma antioxidants (Vitamin C and E, SOD and Uric Acid level) to investigate the antioxidants level in pre eclamptic women.

MATERIAL AND METHOD:

The study was conducted in the Dept. of Obstetrics and Gynecology in collaboration with Dept. of Biochemistry at RNT Medical College, Udaipur.

Group A: Study Group n= 100 Pregnant females suffering from pre eclampsia.

Group B: Control Group n= 100 Healthy pregnant females.

INCLUSION CRITERIA:

100 pre eclamptic patients and 100 normotensive pregnant women, within the age range of 20-35 years. All the women were in their third trimester of pregnancy. As for the studying group Subjects with blood pressure $> 140/90\text{mmHg}$, proteinuria and edema were included. Normal pregnant

women, diagnosed on clinical and ultrasonography findings were taken as controls. Patients and controls were matched for gestational age and maternal age.

EXCLUSION CRITERIA:

Elderly primigravid subjects, gestational diabetics, renal diseases, liver diseases, cardiovascular disease, severe anemia, systemic or endocrine disorders, chronic hypertension and multiple gestations were excluded from the study.

Subjects also had to be nonsmokers, non alcoholics, not suffering from any acute infections and none were taking aspirin or receiving vitamin E therapy.

Sample Collection:

10 ml of venous blood was drawn and collected in plain and EDTA vials.

Analysis of Blood for various analytical parameters:

1. MDA (Buege & Aust, 1978)
2. Vitamin C (Natelson, 1971)
3. Vitamin E (Natelson, 1971)
4. Uric Acid (Bulger and Johns, 1941)
5. SOD (Wooliams et al. 1983)

STATISTICAL ANALYSIS:

The comparisons between two groups were analyzed by student's t-test. All parameters were given as mean ± standard deviation. The criterion for significance was p<0.01. Data analysis was performed with the statistical package for the social sciences version 16.00 (SPSS, Chicago, Ielinois USA).

RESULTS

Table 1: Showing Mean ± SD of serum MDA, Uric acid, Vitamin E, Vitamin C and SOD in normal pregnant and pre eclamptic women

Parameters	Normal Pregnant Women (n=100)	Pre eclamptic Women (n=100)	p- value
Malondialdehyde (nmol/ml)	5.60 ± 0.79	8.30 ± 0.97	p<0.01
Uric acid (mg/dl)	5.01 ± 0.20	7.49 ± 0.77	p<0.01
Vitamin E (mg/dl)	0.95 ± 0.26	0.49 ± 0.18	p<0.01
Vitamin C (mg/dl)	0.98 ± 0.26	0.53 ± 0.15	p<0.01
Superoxide dismutase (U/ml)	4.00 ± 0.59	3.03 ± 0.63	p<0.01

Serum MDA and uric acid were significantly increased (P<0.01) in the pre eclamptic women as compared to the normal pregnant women. Antioxidants such as vitamin E, vitamin C and SOD were significantly decreased (P<0.01) in pre eclamptic women when compared to normal pregnant women. (Table1)

DISCUSSION

Free radicals by their unstable and transient nature are difficult to measure directly, hence their tendency to cause lipid peroxidation has been used as an indirect measure (Patil SB et al. 2007).

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 (Phalak P et al. 2013).

Markers of lipid peroxidation (MDA) are increased during the progression of normal pregnancy. In the present study, we have observed that MDA levels have been significantly

increased (p <0.01) in preeclamptic women as compared to normal pregnant women. These findings corroborate with other authors who have seen increase in MDA (Sheena PS. 2012 and Ghate J et al. 2011).

The mean serum uric acid level in preeclampsia has been significantly increased (P<0.01) when compared to normal pregnant women. These findings are consistent with other studies (Bargale A et al. 2011 and Satya P et al. 2012). Serum uric acid is one of the parameters used in early diagnosis of pre eclampsia. An elevated level of uric acid reflects the degree of placental cell destruction as well as severity of preeclampsia (Bargale A et al. 2011).

There has been a significant decrease (P< 0.01) in vitamin E in cases as compared to pregnant women. Many studies have observed that levels of antioxidants such as vitamin E, vitamin C, and other antioxidants are reduced in the serum of pre eclamptic women (Bargale A et al. 2011 and Rao GM et al. 2005). Antioxidant vitamins have been reported to have an important function in regulating blood pressure (Dehghan MH et al. 2006). Decrease in vitamin E in preeclampsia 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 preeclampsia (Phalak P et al. 2013).

Several studies have demonstrated decreased serum levels of vitamin C in preeclamptic patients (P< 0.01) (Kashinakunti SV et al. 2010). Reduced ascorbate is quite effective in protecting plasma lipids and susceptible molecules from peroxidation. Plasma ascorbate level decreases gradually throughout normal pregnancy. Decrease in ascorbate concentration in preeclampsia relative to normal pregnancy are seen and the present values also agree with the same (Rao GM et al. 2005).

Significant decrease (P<0.01) in serum SOD level has been found in the present study in preeclampsia as compared to normal pregnant women and non pregnant women. Other studies also reveal similar findings (Howlader ZH et al. 2009). SOD is an important antioxidant enzyme, which is capable of preventing excessive superoxide accumulation and may contribute to the continuation of pregnancy. A significantly reduced SOD activity in preeclampsia may be due to increased attack of free radicals and thus resulted in low production of SOD (Bargale AB et al. 2011 and Sarkar P et al. 2013).

The endothelial disturbing factors like lipid peroxides, uric acid and depletion of antioxidants could be possible causes in the pathogenesis of preeclampsia. This association may be significant in understanding the pathological process of preeclampsia and may help in developing strategies for prevention and early diagnosis of preeclampsia (Phalak P et al. 2013).

Thus, estimation of MDA, uric acid, vitamin E and vitamin C levels may have a predictive role in the assessment of the extent of endothelial damage in preeclampsia and may help in preventing or foreseeing complications in pre eclampsia. As oxidative stress can provoke endothelial dysfunction, pregnant and pre eclamptic subjects should be supplemented with antioxidants to prevent overwhelming effect of oxidative stress.

CONCLUSION

The results of this study confirm the hypothesis that hyperuricemia is correlated with pre eclampsia being indirect risk factors for placental vasculopathy predating clinical preeclampsia.

Thus it can be concluded that hyperuricemia can be used as

biomarker for identifying women at risk of preeclampsia and its complications with adverse effects.

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