

ORIGINAL ARTICLE

Study of Lipid Peroxidation and Antioxidant status in pre-eclampsia in Western U.P, India

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ABSTRACT

Preeclampsia is a hypertensive disorder unique to pregnancy and is one of the most leading cause for maternal and fetal mortality. The present study was aimed to study the lipid peroxidation product, malondialdehyde (MDA) and enzymatic antioxidant, superoxide dismutase (SOD) and non-enzymatic antioxidants, uric acid in pre-eclampsia and normal pregnant women. The study included 60 subjects of age group 18-35 years, attending antenatal clinic of Obstetrics & Gynecology Department, out of which 30 were pre-eclamptic women with gestational age of ≥ 20 weeks. (Case group) and rest 30 were normal pregnant women of same gestational age (Control group). In the pre-eclamptic group, MDA, a lipid peroxidation product was significantly increased, while serum antioxidant SOD was significantly decreased ($P < 0.001$), where as uric acid level increased significantly ($P < 0.001$). Our study showed that increased lipid peroxidation and decreased antioxidant in pre-eclamptic women. So, early attention, intensive management and treatment are essential to improve maternal and fetal outcome.

Key Words: Lipid peroxidation, Antioxidants, Pre-eclampsia, MDA, SOD, Uric acid.

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INTRODUCTION

Pregnancy is a physiological stress in which many changes occur in the milieu interior of the body, more and more stress is being laid on the biochemical changes, which occur in the blood during normal pregnancy becomes exaggerated in complications of pregnancy like pre-eclampsia [1]. Preeclampsia is a hypertensive disorder unique to pregnancy. It is one of the most leading cause for maternal and fetal mortality and it occurs in approximately 0.4% - 2.8% of all pregnancies in developed countries and many more in developing countries, leading to as many as 83,70,000 cases worldwide per year [2]. Preeclampsia is a toxic condition that is characterized by a sudden rise in blood pressure, excessive weight gain, generalized edema, albuminuria, severe headache and visual disturbance. With high blood pressure there is increase in the resistance of blood vessel. Preeclampsia occurs during second and third trimester of pregnancy and it is more common in nulliparous women. It is characterized by 1) BP 140/90 mm Hg or greater at least on two occasions, six or more hours apart 2) Proteinuria 300 mg/24 hours or greater [3].

Without intervention, pre-eclampsia progresses to eclampsia which is characterized by malignant hypertension and epileptic form convulsions requiring emergency caesarian section [4]. Despite considerable research, the cause of pre-eclampsia remains unclear. Maternal symptoms are thought to be secondary to endothelial cell dysfunction [5]. Nowadays, lipid peroxidation has become an acceptable marker in medicine to consider endothelial dysfunction at molecular level. It has been suggested that free radicals are likely promoters of maternal vascular dysfunction [5]. 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 [6].

Cumulative evidences have shown that in preeclampsia, there is an increase in lipid peroxidation and a decrease in antioxidants protection leading to oxidative stress [5,7]. For the aforesaid reasons, the

present study was carried out to study the lipid peroxidation product, malondialdehyde (MDA) and enzymatic antioxidant, superoxide dismutase (SOD) and non-enzymatic antioxidants, uric acid in preeclampsia and normal pregnant women.

MATERIALS AND METHODS

The present study was carried out in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology at Muzaffarnagar Medical College and Hospital, Muzaffarnagar and Dhanvantari Hospital, Meerut, India. Informed consent was taken from all subjects. The study was conducted from March 2014 to February 2015.

Subjects:

A total of 60 study subjects ranging in age from 18-35 years, attending antenatal clinic of Obstetrics & Gynecology Department were enrolled in the present study. Out of 60 subjects, 30 were pre-eclamptic women and 30 were normal pregnant women.

Inclusion Criteria:

Group-I (Cases):-The study includes 30 pre-eclamptic women with gestational age of ≥ 20 weeks. The diagnosis of pre-eclampsia was based on the definition of American College of Obstetrics and Gynecologists⁸. (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).

Group-II (Controls):-30 normal pregnant women of same gestational age without a history of any systemic illness belonging to the same socio-economic status were considered as controls. Subjects with normal pregnancy were normotensive and had no proteinuria.

Exclusion criteria:

Women having renal diseases, liver diseases, cardiovascular disease, severe anemia, diabetes, systemic or endocrine disorders, twin pregnancies, known hypertension, women who are taking medication, or other pre-existing medical conditions which alter study parameters were excluded from the study.

Collection of Blood Sample:

About 3-5 ml of venous blood from all subjects was collected in clean, disposable plastic tubes aseptically from anterior anticubital vein. It was allowed to clot for few minutes and was subjected to centrifugation for 10 minutes at 3000 rpm to separate the serum and kept at -20°C until analysis was carried out.

Parameters Measured:

The following parameters were estimated in the present study-

1. Serum Malondialdehyde (MDA) by the method described by Nourooz-zadeh J *et al*⁹.
2. Serum Superoxide dismutase (SOD) by method described by Marklund and Marklund¹⁰.
3. Serum Uric acid with the help of CPC TURBO Chem 100 (Fully autoanalyzer).

RESULT

Table No. - 1: Showing biochemical parameters to assess lipid peroxidation and antioxidant status of pre-eclamptic women and normal pregnant women.

Biochemical Parameters	Pre-eclamptic Women (n=30)	Normal Pregnant Women (n=30)	p-value
MDA (nmol/ml)	4.53±0.45	2.83±0.57	<0.001S
SOD (U/ml)	2.14±0.23	3.51±0.31	<0.001S
Uric Acid (mg/dl)	6.92±1.11	4.65±0.58	<0.001S

S=statistically significant

The mean MDA levels in pre-eclamptic women and normal pregnant women are 4.53 ± 0.45 nmol/ml and 2.83 ± 0.57 nmol/ml respectively. MDA is significantly more in pre-eclamptic women compared to normal pregnant women ($P < 0.001$). The mean SOD levels in pre-eclamptic women and normal pregnant women are 2.14 ± 0.23 U/ml and 3.51 ± 0.31 U/ml respectively. There is significant decrease in SOD levels ($P < 0.001$) in pre-eclamptic women as compared to normal pregnant women. The mean uric acid levels in pre-eclamptic women and normal pregnant women are 6.92 ± 1.11 mg/dl and 4.65 ± 0.58 mg/dl respectively. There is significant elevation of uric acid ($P < 0.001$) in study group in comparison to normal pregnant women.

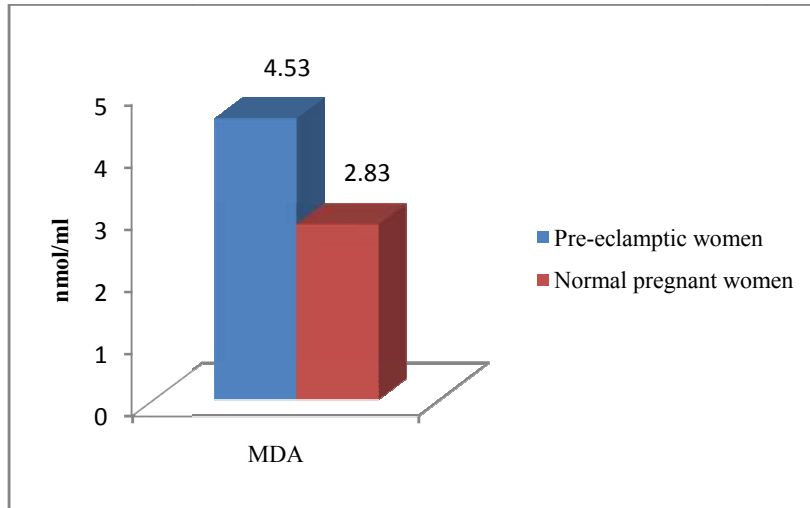


Fig 1: Showing comparison of mean serum MDA level between Pre-eclamptic women and Normal pregnant women.

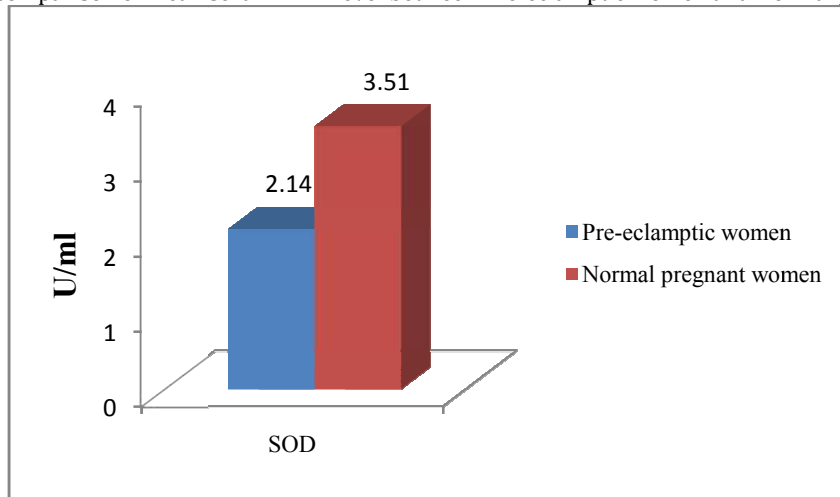


Fig 2: Showing comparison of mean serum SOD level between Pre-eclamptic women and Normal pregnant women.

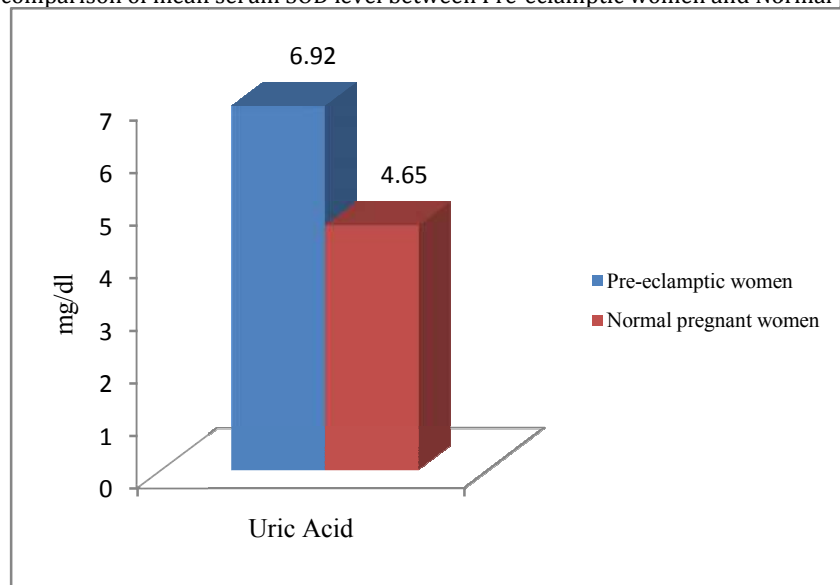


Fig 3: Showing comparison of mean serum Uric acid level between Pre-eclamptic women and Normal pregnant women.

DISCUSSION

The present study evaluated the oxidative stress by analyzing the pro-oxidants and antioxidant. Lipid peroxidation (MDA) was considered as a marker for pro-oxidant where as superoxide dismutase (SOD) and uric acid were considered as antioxidants.

The pathophysiology of pre-eclampsia is poorly understood. Free radicals and other damaging reactive oxygen species, such as the superoxide anions are in oxidative metabolic processes; their activation is thought to increase during preeclampsia [1]. 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 [6]. 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 [5,7].

In the present study, serum MDA level was significantly increased in preeclampsia compared to normal pregnant women. Similar findings were observed by Kashinakunti et al [1], Sheena [11], Dave et al [3], Phalak et al [5] and Sayyed et al [7], suggesting that lipid peroxidation is an important factor in the pathogenesis of preeclampsia. Increased activation of neutrophils, macrophages and T cells along with exaggerated placental response resulting in elevated formation of reactive oxygen species like superoxide radical, hydroxy radical which will cause increase in lipid peroxidation damage to vascular endothelium, membranes of cells and organelles which is evidenced by elevation of MDA level [11].

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 preeclampsia [5,7].

The levels of serum SOD were found to be significantly decreased in patients of pre-eclampsia compared to normal pregnant women. Similar results were observed by Dave et al [3], Sheena [11], Sayyed et al [7], who found that antioxidant activity was markedly reduced in pre-eclampsia. The excessive generation of free radicals inactivates the enzymes system in the body leading to decreased SOD activity observed in present study.

In the present study, mean serum uric acid level in preeclampsia has been significantly increased compared to normal pregnant women. These findings are consistent with previous studies done by Kashinakunti et al [1] and Sayyed et al [7]. An elevated level of uric acid reflects the degree of placental cell destruction as well as severity of pre-eclampsia [12]. Uric acid is a marker of oxidative stress, tissue injury and renal dysfunction. Abnormal trophoblast invasion is reported in preeclampsia, because of which placenta receives less blood supply from uteroplacental artery. Subsequently placenta becomes hypoxic. This hypoxia causes placental tissue breakdown and provides additional source of purines. Placenta and damaged placental tissues are the rich sources of purines for generation of uric acid by xanthine oxidase [12]. This may lead to decrease in the renal tubular excretion. Altered renal handling of urate clearance may be due to renal dysfunction and increased xanthine oxidase activity [13]. Thus hyperuricemia in pre-eclampsia is primarily due to decreased renal clearance and increased tubular reabsorption of uric acid, because of the reduction in glomerular filtration rate [7]. Thus it has important role in vascular damage and oxidative stress. Hyperuricemia may also reflect impaired endothelial integrity and contribute to the pathogenesis of preeclampsia. Hence early estimation of serum uric acid might reduce systemic complications and maternal deaths due to preeclampsia [12]. 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 pre-eclampsia [5, 7].

CONCLUSION

The present study has shown a significant increase in serum MDA level, the indicator of lipid peroxidation in pre-eclamptic women, suggesting that lipid peroxidation plays a role in the pathogenesis of pre-eclampsia. In pre-eclamptic women, antioxidants may be utilized to greater extent to counteract free radicals mediated cellular changes, resulting in the reduction of antioxidant levels. Early attention, intensive management and treatment may be essential to improve maternal and fetal outcome as well as in preventing impending complications in pre-eclamptic women. However, further studies with adequate sample size are needed for proper conclusion.

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