ORIGINAL ARTICLE

Study of Lipid Peroxidation and Antioxidant Status in Preeclampsia

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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 aetiological factor in preeclampsia. *Aims and Objectives*: To determine the role oxidative stress and level of antioxidants in preeclampsia by estimation of malondialdehyde (MDA) (index of lipid peroxidation) and antioxidants such as uric acid, vitamin C, vitamin E and superoxide dismutase (SOD) in preeclampsia. *Material and Methods*: In present study 40 non pregnant women, 40 normal pregnant women and 40 preeclamptic women aged between 18-35 years were enrolled. Clinically diagnosed preeclamptic women were compared with normal pregnant women of same gestational age and serum was analyzed for serum malondialdehyde (MDA), uric acid, vitamin E and vitamin C and SOD. Statistical analysis was done by ANOVA followed by Tukey's multiple comparison. *Results*: Serum MDA and uric acid levels were significantly raised ($P<0.01$) in preeclamptic women as compared to normal pregnant women and non pregnant women while serum antioxidant vitamin E, vitamin C, and SOD levels were significantly decreased ($P<0.01$) in preeclamptic women and normal pregnant women as compared to non pregnant women. *Conclusion*: Increased levels of lipid peroxidation product (MDA) and depletion of antioxidants such as vitamin E, vitamin C and SOD except uric acid in women with preeclampsia may suggest that oxidative stress plays a key role in the genesis of endothelial dysfunction and expression of preeclampsia. Adjuvant supplementation of these antioxidants except uric acid to the diet may minimize further progression of preeclampsia.

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

Introduction:

Preeclampsia is a multisystem disorder characterized by hypertension to the extent of 140/90 mm Hg or more, proteinuria (≥300mg/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 [1].

Nowadays, lipid peroxidation has become an acceptable marker in medicine to consider endothelial dysfunction at molecular level [2]. It has been suggested that free radicals are likely promoters of maternal vascular dysfunction [1]. 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 [2].

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 [1]. 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 preeclampsia and normal pregnant women.

Material and Methods:

The present study was carried out in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology at Bhausaheb Sardesai Rural Hospital & MIMER Medical College Talegaon, Dabhade Pune from January 2011 to March 2013. The study was approved by Institutional Ethical Committee. A total of 120 study subjects ranging in age from 18-35 years, attending antenatal clinic of Obstetrics & Gynecology Department were enrolled. Out of 120 subjects, 40 normal non pregnant women, 40 normal pregnant women and 40 preeclamptic women were selected. Sample size was decided based on power of calculation.

Inclusion Criteria:

Clinically diagnosed preeclamptic women with gestational age of 20 ≥ weeks and normal pregnant women in the same gestational age and normal non pregnant women were enrolled.

Exclusion Criteria:

Women having twin pregnancies, known hypertension, renal diseases, liver diseases, cardiovascular disease, severe anemia, diabetes, systemic or endocrine disorders, women who are taking medication, or other pre-existing medical conditions which alter study parameters were excluded from the study. On admission, 10ml fasting venous blood sample was collected under aseptic conditions with a written informed consent from each subject and separated serum was used for the estimation of malondialdehyde [3], uric acid [4], vitamin E [5], vitamin C [6] and superoxide dismutase [7] activity.

Statistical Analysis:

Data was analyzed by Analysis of Variances (ANOVA) followed by Tukey's multiple comparisons and expressed in terms of 'P' value. $P<0.05$ was considered as statistically significant.

Results:

Serum MDA and uric acid were significantly increased ($P<0.01$) in the preeclamptic women as compared to the normal pregnant women. Antioxidants such as vitamin E, vitamin C and SOD were significantly decreased ($P<0.01$) in preeclamptic women when compared to normal pregnant women as well as non pregnant women (Table 1). Mean and confidence interval of serum MDA, uric acid, vitamin E, vitamin C and SOD in normal non pregnant women, normal pregnant women and preeclamptic women are depicted in Graph No.1, 2, 3, 4 and 5 respectively.

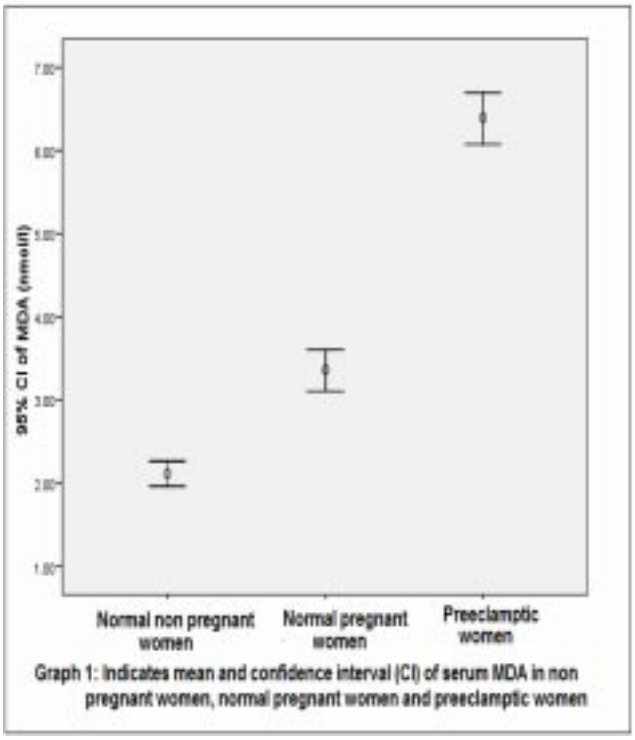
Discussion:

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 [2]. One of the important consequences of free radical formation is lipid peroxidation which is reaction of oxidative deterioration of polyunsaturated

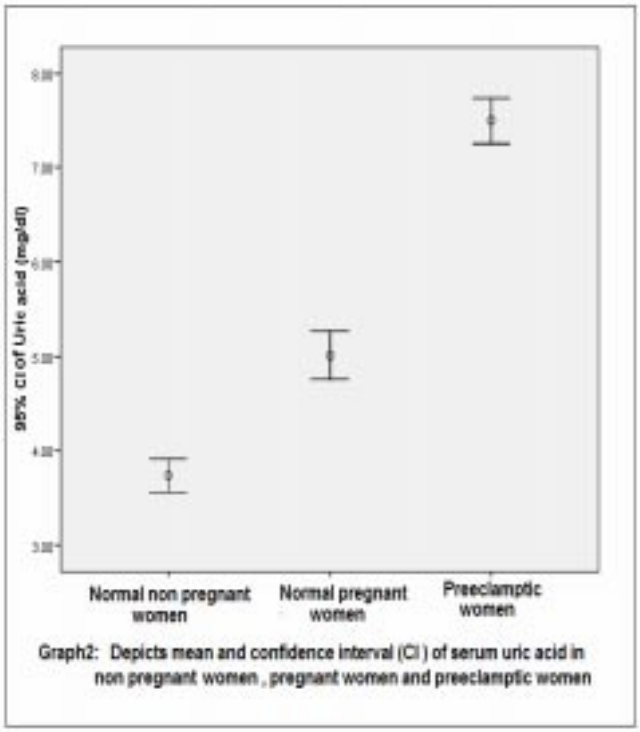
Table 1: Showing the Mean ± SD of serum MDA, Uric acid, Vitamin E, Vitamin C and SOD in non pregnant women, normal pregnant women and preeclamptic women

Parameters	Non Pregnant Women (n=40)	Normal Pregnant Women (n=40)	Preeclamptic Women(n=40)
Malondialdehyde (nmol/ml)	2.11 ± 0.46	5.60 ± 0.79**	8.30 ± 0.97** †
Uric acid (mg/dl)	3.73 ± 0.55	5.01 ± 820**	7.49 ± 0.77**†
Vitamin E (mg/dl)	1.40 ± 0.29	0.95 ± 0.26 **	0.49 ± 0.18**†
Vitamin C (mg/dl)	1.50 ± 0.30	0.98 ± 0.26 **	0.53 ± 0.15**†
Superoxide dismutase (U/ml)	5.19 ± 0.93	4.00 ± 0.59**	3.03 ± 0.63 **†

***As compared to non pregnant women, Tukey's multiple comparison (P<0.01)*
† As compared to normal pregnant women, Tukey's multiple comparison (P<0.01)



Graph 1: Indicates mean and confidence interval (CI) of serum MDA in non pregnant women, normal pregnant women and preeclamptic women

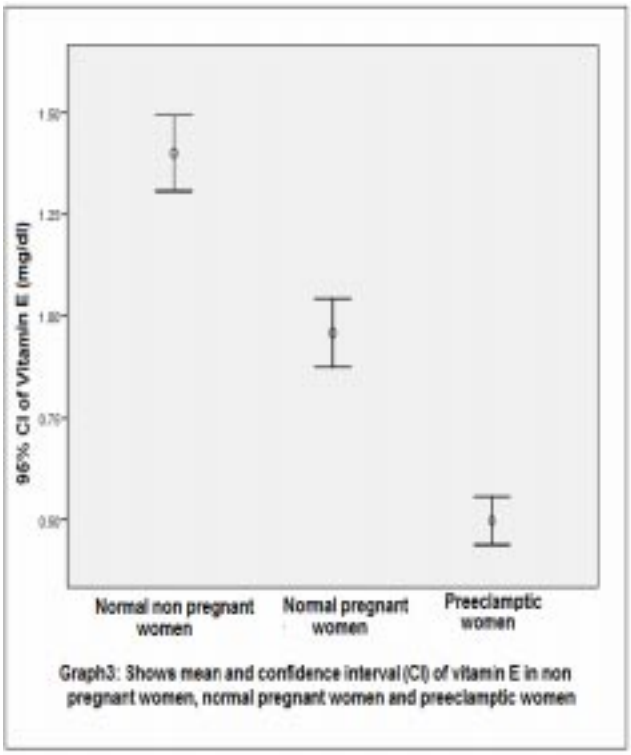


Graph2: Depicts mean and confidence interval (CI) of serum uric acid in non pregnant women , pregnant women and preeclamptic women

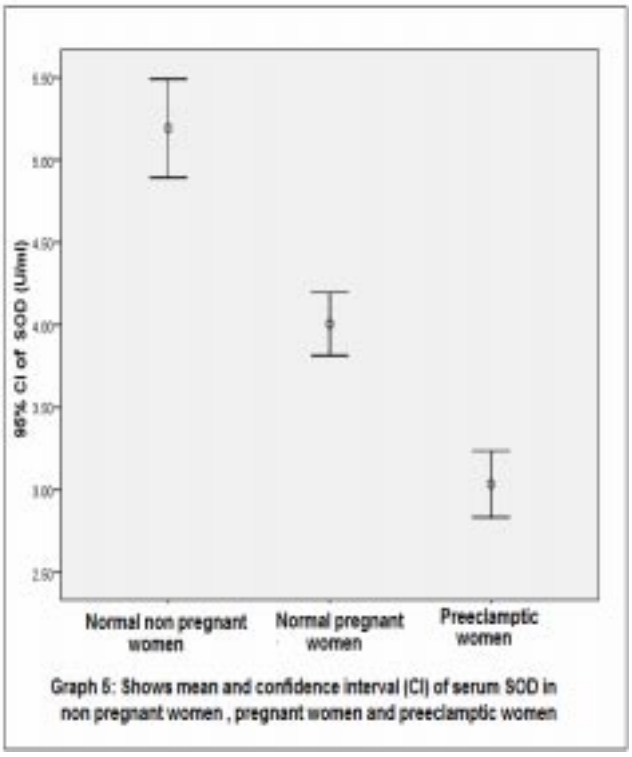
fatty acids involving direct reaction of oxygen and lipid to form lipid peroxides. Lipid peroxidation is particularly damaging because it proceeds as self perpetuating chain reaction [1].

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 and non pregnant women. These finding corroborate with other authors who have seen increase in MDA [8,9,10,11,12,13,14,15,16].

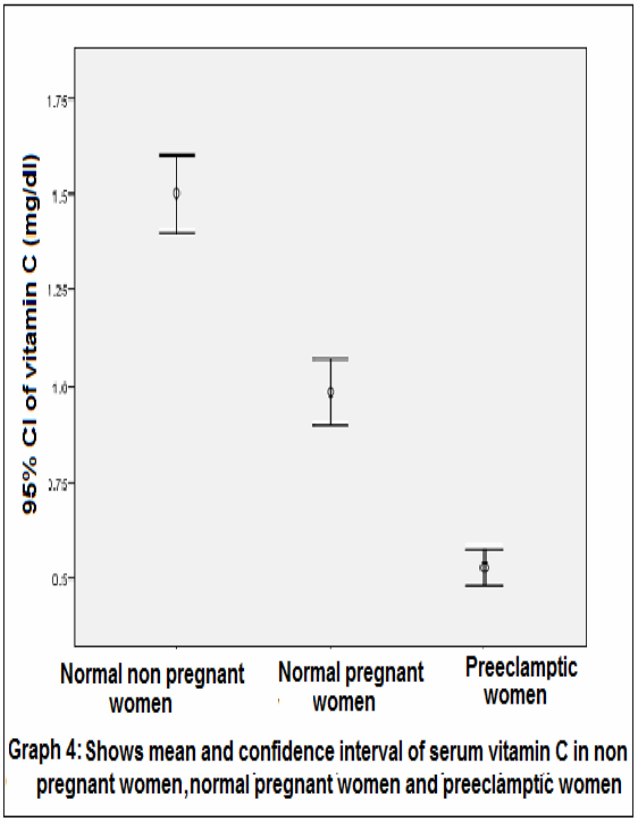
In view of its potentially destructive character, uncontrolled lipid peroxidation has been sug-



Graph3: Shows mean and confidence interval (CI) of vitamin E in non pregnant women, normal pregnant women and preeclamptic women



Graph 5: Shows mean and confidence interval (CI) of serum SOD in non pregnant women , pregnant women and preeclamptic women



Graph 4: Shows mean and confidence interval of serum vitamin C in non pregnant women, normal pregnant women and preeclamptic women

gested as an etiological factor in preeclampsia. 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 [1].

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 [17-24]. Serum uric acid is one of the parameters used in early diagnosis of preeclampsia.

An elevated level of uric acid reflects the degree of placental cell destruction as well as severity of preeclampsia [22]. Uric acid is a marker of oxidative stress, tissue injury and renal dysfunction. Abnormal trophoblast inva-

sion 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 [22]. 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 [23].

Thus hyperuricemia in preeclampsia is primarily due to decreased renal clearance and increased tubular reabsorption of uric acid, because of the reduction in glomerular filtration rate [25]. 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 [22].

There has been a significant decrease ($P< 0.01$) in vitamin E in cases as compared to non 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 preeclamptic women [14, 16, 22]. Antioxidant vitamins have been reported to have an important function in regulating blood pressure [26]. 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 [1]. Thus the antioxidant defense available within the cell and extracellularly should be adequate to protect against the oxidative damage [1].

Several studies have demonstrated decreased serum levels of vitamin C in preeclamptic patients ($P< 0.01$) [10]. Reduced ascorbate is quite effective in protecting plasma lipids and succesptible molecules from peroxidation. Plasma ascorbate level decreases gradually throughout normal pregnancy. Decrease in ascorbate concentration in preeclampsia relative to normal pregnany are seen and the present values also agree with the same [16].

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 [8, 27, 28]. 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 [29, 30].

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 [1].

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 preeclampsia. As oxidative stress can provoke endothelial dysfunction, pregnant and preeclamptic

subjects should be supplemented with antioxidants to prevent overwhelming effect of oxidative stress.

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