

## Lipid Peroxidation and Antioxidant Status in Preeclampsia

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### Abstract

The current theory suggests that in preeclampsia there is an increase in the lipid peroxidation products and leads to decrease in the serum antioxidants except uric acid, contributing to the pathogenesis of preeclampsia. In this context, this study was undertaken to determine the changes in blood levels of lipid peroxide and antioxidant levels in women with preeclampsia. Method: Case control study consisting of 30 preeclamptic and 30 healthy pregnant women. Fasting venous blood samples were collected during antepartum period and serum levels of malondialdehyde, ascorbic acid (Vitamin C) and uric acid were measured. In the preeclamptic group malondialdehyde (MDA), a lipid peroxidation product was significantly increased, while serum antioxidant ascorbic acid was significantly decreased ( $P < 0.001$ ), where as uric acid level increased significantly ( $P < 0.001$ ). The findings of the present study are consistent with previous studies, suggesting that lipid peroxidation is an important factor in the pathogenesis of preeclampsia. In preeclampsia serum antioxidants are excessively utilized to counteract the cellular changes mediated by free radicals.

**Keywords.** : Preeclampsia, Lipid peroxidation, Antioxidants

### 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. Pre-eclampsia 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  $\geq 300$  mg/24 hours or greater or equal to 1+ by dipstick response[1]. Oxidative stress increases during pre-eclampsia and results in increased production of lipid peroxides, reactive oxygen species and superoxide anion radicals to cause endothelial injury and dysfunction, platelet and neutrophil activation[2-3]. These observations in pre-eclampsia have given rise to increased interest in antioxidants such as Ascorbic acid(Vitamin C), Vitamin E and Uric acid. In this context the present study has been undertaken to determine the changes in serum levels of peroxidation product ie Malondialdehyde (MDA) and antioxidant levels namely ascorbic acid and uric acid in women with pre-eclampsia.

### Materials and Methods

In the present study 30 cases of pre-eclampsia and 30 normal pregnant women from HSK (Hangal Shree Kumareswar) Hospital and Research Centre Bagalkot were selected. The controls were normotensives. Both the cases and controls were primi

between 18 and 30 years of age and having more than 29 weeks of gestation. The cases and controls having past history of diabetes mellitus, hypertension, renal diseases, liver disorder and with the history of multivitamin intake were excluded. History and examination findings of both cases and control were noted. Fasting Blood samples were collected, the serum was separated and analyzed for the following parameters. MDA was measured by Thiobarbituric acid reactive substances assay (TBRAS) method[4] and ascorbic acid by Dinitrophenyl Hydrazine (DNPH) method.[5] The uric acid was measured by uricase method using Human diagnostics kit[6-8]. The optical densities of MDA and ascorbic acid were measured at 532 nm and 520nm respectively using spectrophotometer.

### Results

Blood pressure and BMI (Body Mass Index) of cases and controls is shown in Table 1. The mean value of SBP (Systolic blood pressure) in cases is  $144.67 \pm 10.56$  and in control  $115.3 \pm 6.81$ , there is significant difference ( $P < 0.001$ ) between cases and controls. The DBP (Diastolic Blood Pressure) mean in cases and control is  $97.73 \pm 5.7$  and  $75.45 \pm 5.25$  respectively, there is significant difference ( $P < 0.001$ ) between cases and controls. The mean BMI (Body Mass Index) of controls is  $25.53 \pm 3.08$  and in study group  $26.83 \pm 3.28$ , P value is more than 0.05, which is insignificant.

Table-1: Blood Pressure and Body Mass Index of Cases and Controls

		Cases = 30	Controls n = 30	P Value
BP	SBP mm Hg	$144.67 \pm 10.56$	$115.3 \pm 6.81$	$P < 0.001$
	DBP mm Hg	$97.73 \pm 5.7$	$75.45 \pm 5.25$	$P < 0.001$
BMI (kg/M <sup>2</sup> )		$26.83 \pm 3.28$	$25.53 \pm 3.08$	$P > 0.05$

Values are mean  $\pm$ SD; BP :Blood Pressure, SBP, Systolic blood pressure; DBP, Diastolic blood pressure ;BMI, Body mass index

Biochemical parameters to assess lipid peroxidation and antioxidant status of cases and controls were illustrated in Table-2.

Table- 2:Biochemical parameters to assess lipid peroxidation and antioxidant status of cases and controls

Biochemical Parameter	Cases n = 30	Controls n = 30	P Value
MDA n mol/L	$346.13 \pm 110.54$	$205.07 \pm 26.06$	$P < 0.001$
S. Ascorbic acid mg/dl	$0.62 \pm 0.21$	$0.97 \pm 0.19$	$P < 0.001$
S. Uric acid mg/dl	$7.16 \pm 1.68$	$4.75 \pm 0.91$	$P < 0.001$

Values are mean  $\pm$ SD; MDA : Malondialdehyde.

The mean MDA in cases and controls is  $346.13 \pm 110.54$  nmol/L and  $205.07 \pm 26.06$  nmol/L respectively. MDA is significantly more in pre-eclampsia patients compared to controls ( $P < 0.001$ ). The mean ascorbic acid level in cases and control is  $0.62 \pm 0.21$  mg/dl and  $0.97 \pm 0.19$  mg/dl respectively. There is significant decrease in ascorbic acid levels ( $P < 0.001$ ) in cases as compared to controls. The mean uric acid level in cases and controls is  $7.16 \pm 1.68$  mg/dl and  $4.75 \pm 0.91$  mg/dl, respectively. There is significant elevation of uric acid ( $P < 0.001$ ) in study group in comparison to controls.

### Discussion

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 pre-eclampsia[9]. Foetoplacental unit may be the origin of oxygen free radicals and lipid peroxides[10-11]. Recent investigation suggested that endothelial cell injury may be the initiator of the pathophysiological events of pre-eclampsia[12]. Either placental hypercorrection of lipid peroxides or decreased placental antioxidant enzyme activity can lead to endothelial dysfunction. Insufficient antioxidant capacity leads to oxidative stress and subsequently oxidative injury may occur in both the maternal and placental compartments<sup>9</sup>. A number of reports indicate that blood levels of lipid peroxidation products are elevated in women with pre-eclampsia relative to normal pregnancy [3,9,13-15]. Furthermore placental production of lipid peroxides have been demonstrated to be abnormally increased in pre-eclampsia<sup>10</sup>, consistent with previous reports, in the present study also there is increase in serum levels ( $P < 0.001$ ) of MDA in the pre-eclamptic patients. Pre-eclampsia is associated with increased utilization of antioxidants. Several studies have demonstrated decreased serum levels of ascorbic acid compared to normal pregnant women, [3,11,16] similarly in the present study we have observed a significant decrease in serum levels of ascorbic acid in the pre-eclamptic patients ( $P < 0.001$ ). Uric acid is water soluble and a weak serum antioxidant. Nevertheless, the patients with pre-eclampsia show hyperuricemia, which mean that the serum levels doesn't protect the pre-eclamptic patients against free radical activity [9,16-17]. The present study has also shown a significant rise in serum uric acid ( $P < 0.001$ ). The rise in uric acid in pre-eclampsia is not merely a non-specific reflection of kidney damage, but a sign of antioxidative response, possibly related to the pathogenesis of pre-eclampsia[13]. In conclusion the present study is consistent with previous studies suggests that lipid peroxidation appears to be of immense value in understanding the pathogenesis of preeclampsia. In preeclamptic patients antioxidants may be utilized to a greater extent to counteract free radical mediated cellular changes, resulting in the reduction of plasma antioxidant levels.

### References

1. Cummingham FG, Grant NF, Leveno KJ, Gilstrap LCIII, Hanth JC, Wenston KC in "Hypertensive disorders in pregnancy", Williams Obstetrics, 21<sup>st</sup> Edition, McGraw Hill pp 568-569,572.
2. Dutta DC, Konar HL, Test Book of Obstetrics, 6<sup>th</sup> edn. New Central Book Agency (P) Ltd. 2004 ,pp222-223.

3. Riza Madazli, Ali Benian, Koray Gumata et al. Lipid peroxidation and antioxidants in pre Eclampsia. *Eur J Obstet Gynecol & Reprod Biol* 1999; 85 (2): 205-208.
4. Draper HH, Hadley M. Methods of Enzymol. 1990-, pp 421-431.
5. Weinstein L. Syndrome of haemolysis, elevated liver enzymes and the platelet count. A severe consequence of hypertension in pregnancy. *Am J Obstet Gynecol* 1982; 142 : 159-167.
6. Barham D, Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system. *Analyst* 1972; 97 : 142-145
7. Fossati LP, Berti G. Use of 3,5-dichloro-2-hydroxybenzenesulfonic acid/4-aminophenazone chromogenic system in direct enzymic assay of uric acid in serum and urine. *Clin Chem* 1980;26(2):227-231.
8. Thefeld L. Dtsch. Untersuchungen zur Frage der Hämodialyse bei der Knollenblätterpilzvergiftung. *Med. Wschr* 1973; 98: 300.
9. Mehmet Harma, Muge Harma and Ozcan Erel : Measurement of total antioxidant response in pre-eclampsia with a novel automated method. *Eur J Obstet Gynecol & Reprod Biol* 2005;118 (1) : 47-51.
10. Poranen AK, Ekblad U, Uotila P, Ahotupa M. Lipid peroxidation and antioxidants in normal and pre-eclamptic pregnancies. *Placentas* 1996; 17: 401-405.
11. Wang Yand ,Walsh SW. Antioxidant activities and mRNA expression of superoxide dismutase, catalase and glutathione peroxidase in normal and pre-eclamptic placenta. *J Soc Gynecol Investig* 1996; 3 : 179-184
12. Simmi Kharb, Sharina BD. Vitamin E and C in preeclampsia. *Euro J Obstet. & Gynecol. Reprod Biol* 2000; 93 (1) : 37-39.
13. Utoila JT, Tuimala RJ, Aarnio TM, Pyykko KA, Ahotupa MO, Findings on lipid peroxidation and antioxidant function in hypertensive complications of pregnancy. *Br J Obstet Gynecol* 1993;100: 270-276.
14. Jain SK , Wise R, Relationship between elevated lipid peroxides, vitamin E deficiency and hypertension in pre-eclampsia. *Mol Cell Biochem* 1995 : 151, 33-38.
15. Kaur Gurjit, Mishra S, Sehgal A, Prasad R. Alterations in lipid peroxidation and antioxidant status in pregnancy with preeclampsia. *Mol Cell Biochem* 2008, 313(1-2):37-44.
16. Chappell LC, Seed PT., Briley A, Kelly SRN, Frank J, Hunt BJ et al. A longitudinal study of biochemical variables in women at risk of preeclampsia. *Am J Obstet Gynecol* 2002, 187(1):127-136.
17. Magann, EF, Martin JN Jr. The Laboratory Evaluation of Hypertensive Gravidas. 1995, 50(2): 138-145

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