Available online at www.elixirpublishers.com (Elixir International Journal)

Human Physiology

Elixir Human Physio. 47 (2012) 8786-8789

ISSN: 2229-712X

# Role of Lipid peroxidation and enzymatic antioxidants status in Postpartum Pre-eclamptic women

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**ARTICLE INFO**

**Article history:**

Received: 2 April 2012;

Received in revised form:

18 May 2012;

Accepted: 7 June 2012;

**Keywords**

Lipid peroxidation,

Oxidative stress,

Malondialdehyde,

Preeclampsia.

**ABSTRACT**

**Aims & Objective:** Objective of this study was to investigate the lipid peroxidation and enzymatic antioxidants status in women with preeclampsia and compare with that of women with normal pregnancy and postpartum preeclamptic women.

**Materials and Methods:** The study comprised of 100 cases out of which 25 were normal healthy non pregnant controls, 25 were normal healthy pregnant women in third trimester, 25 were in third trimester with preeclampsia and 25 were postpartum preeclamptic women. Whole blood was used to detect Malondialdehyde (MDA) a product of lipid peroxide, Enzymatic antioxidants like Superoxide dismutase, Glutathione peroxidase, Glutathione reductase and Catalase.

**Results:** There was 0significant increase in lipid peroxidation (MDA) in all the groups as compared to nonpregnant controls ($P< 0.001$). Elevated levels of malondialdehyde in pre-eclamptic subjects declined significantly ($p<0.001$) after delivery. A significant decrease ($P<0.001$) in the levels of enzymatic antioxidants viz. Superoxide dismutase, Glutathione peroxidase, Glutathione reductase and Catalase was observed in all the groups as compared to nonpregnant controls. In the postpartum preeclamptic group Glutathione reductase and Catalase levels were increased whereas the increase in the levels of Glutathione peroxidase and Glutathione reductase was not significant.

**Conclusion:** Our study shows clear insight into disturbances associated with preeclampsia with enhanced lipid peroxidation and decreased antioxidants which are help full in understanding the pathogenesis of preeclampsia.



## Introduction

Pre-eclampsia is a pregnancy-specific condition potentially affecting both mother and fetus is one of the most leading cause for maternal and fetal mortality which has been found to occur 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 [1]. The age specific mortality ratios for pre-eclampsia reflect slightly risks for younger women (under the age of 20 years) and markedly increased for older women. Studies have shown that preeclamptic women are prone to development of cerebrovascular, cardiovascular as well as other fetal and maternal complications [2][3][4]. Preeclampsia is associated with increased blood pressure accompanied by proteinuria edema or both. Without intervention pre-eclampsia progress to eclampsia a malignant hypertensive condition. Some of the reported predisposing factors of preeclampsia are maternal age, race, diet, low socioeconomic level, smoking, and geographical conditions. Lipid peroxidation has been suggested as one of the causative factor and is found to be increased in pregnancy [5]. Under normal conditions, a variety of antioxidant mechanisms serve to control this peroxidative process. However, a diminution of normal antioxidant function will allow an increase of peroxidative activity to occur which in turn may impair normal endothelial function. Preeclampsia is found to be associated with endothelial dysfunction [6]. The metabolic effects of lipid peroxides may be linked with an imbalance between the production of prostacyclin and thromboxane $A_2$ that is well-documented in pre-eclampsia. [5]

In the present study we measured enzymatic antioxidant levels relative to lipid peroxide in women with preeclampsia and compared with that of women with normal pregnancy and preeclamptic postpartum subjects so as to investigate the possible role of lipid peroxidation and enzymatic antioxidants status in above said groups.

## Materials and methods:

The present study was carried out jointly by the Department of Biochemistry and Obstetrics and Gynaecology. The study protocol was approved by ethical committee. Informed consent was taken from individual subjects.

**Sample size:** The study comprised of 100 cases out of which 25 were normal healthy non pregnant controls, 25 were normal healthy pregnant women in the third trimester, 25 were in the third trimester with preeclampsia and 25 were postpartum preeclamptic women. The subjects selected for the present study were attending and admitted to District Civil Hospital, Belgaum, whose age ranged from 20-40 years and were of low socioeconomic status which was based on low income.

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**Inclusion criteria:** The study consisted of normal women, normal pregnant women and women with preeclampsia diagnosed based on definition of ACOG [7] :1) Systolic blood pressure greater than 140 mm Hg or a rise of at least 30 mm Hg or 2) Diastolic blood pressure greater than 90 mm Hg or rise of at least 15 mm Hg (manifested on two occasions at least 6 hours apart), and 3) Proteinuria of 300mg or greater in 24 hour urine collection or protein concentration of 1gm/Liter (on two occasions at least 6 hours apart). Subjects with normal pregnancy were normotensive and had no proteinuria.

**Exclusion criteria:** Women with diabetes mellitus under medication and untreated diabetes, obese women, women with severe anemia (<6.0g% of Hb), alcoholic, and women suffering from any other disorder were excluded from the study.

None of the women had received antihypertensive medication until the study sample was taken. Blood pressure levels and proteinuria were determined at the time of sampling.

**Collection and storage of blood samples:** 5ml of blood sample was drawn by venipuncture and collected in a heparinized tube. Malondialdehyde, a product of lipid peroxides detectable in blood, was used as an indicator of lipid peroxidation. Malondialdehyde concentrations were determined by using Thiobarbituric acid [8]. Hemolysate was prepared to determine the enzymatic antioxidant acivities like Superoxide dismutase (SOD) [9], glutathione peroxidase (GSH-Px), glutathione reductase (GSH-Rx), catalase [10] and hemoglobin [11]. Statistical data were expressed as mean ± SD, and statistical significance was determined by ANOVA and multiple comparison tests.

**Results**

The characteristics of the four groups are summarized in Table no 1. There was a consistent significant increase in lipid peroxidation (MDA) in all the groups as compared to nonpregnant controls (P< 0.001) and MDA in 3rd trimester preeclamptic women was more (P< 0.001) when compared to normal pregnant 3rd trimester women. Increased levels of malondialdehyde in preeclamptic subjects declined significantly (p<0.001) after delivery. A significant decreased activity of all the enzymatic antioxidant (SOD, GSH-Px, GSH-Rx and Catalase) was observed in normal pregnant women as compared to non-pregnant controls. Further decreased activities of all the enzymatic antioxidants were observed in preeclemptic women when compared to normal pregnant. In preeclamptic subjects, decreased levels of superoxide dismutase and catalase were increased (p<0.001) after delivery but increase in glutathione reductase and glutathione peroxidase were not significant.

**Discussion**

The present study evaluated the oxidative stress by analyzing the pro oxidant and enzymatic antioxidants in non-pregnant, normal pregnant, 3rd trimester preeclamptic and postpartum preeclamptic women. Lipid peroxidation (MDA) was considered as a marker for pro oxidant whereas Superoxide dismutase, glutathione peroxidase,glutathione reductase and Catalase were considered as enzymatic antioxidants. Unstable and transient nature of free radicals makes it difficult to measure them directly but their tendency to cause lipid peroxidation has been used as an indirect measure.

Table no. 1 depicts the blood levels of malondialdehyde in different study groups. In the present study MDA was observed to be increased remarkably at 3rd trimesters of pregnancy as compared to non-pregnant women and the increase in 3rd trimester pre eclamptic was more remarkable than that at 3rd trimester of normal pregnancy. Increase in free radicals may increase the susceptibility of polyunsaturated fatty acid to peroxidative damage, leading to the formation of malondialdehyde (MDA) revealing an increase in lipid membrane damage in pre-eclamptic patients as compared with healthy pregnant women. Kharb S., et al [12] have shown with similar results that serum lipid peroxides are known to increase in pregnancy and this increase was still higher in pre-eclampsia. Increased lipid peroxides leads to an imbalance between the production of prostacyclin and thromboxane $A_2$ [13]. Lipid peroxidation products are candidate factors that may mediate disturbance of the maternal vascular endothelium [14]. In our study it was noticed that increased levels of malondialdehyde in pre-eclamptic subjects declined significantly (p<0.001) after delivery. The cells carry a protective antioxidant mechanism in order to counteract the toxic action of oxygen radicals. In this respect defence is provided by antioxidant enzyme activities like superoxide dismutase, glutathione peroxidase, Catalase.

Superoxide dismutase is the major intracellular antioxidant enzyme, which inactivates superoxide. Enzymatic antioxidant activity including superoxide dismutase was significantly elevated in the sera of women with normal pregnancy than those with pre-eclampsia. Ilhan N [15] showed that in pre-eclamptic subjects malondialdehyde levels were significantly increased, while superoxide dismutase levels were significantly decreased compared to non-pregnant controls and normal healthy pregnant women. Decreased Radical scavenging superoxide dismutase is thought to be consumed by the increased lipid peroxidation in pre-eclampsia which indicate an involvement of free radicals in the pathophysiology of pre-eclampsia. Reduced activity of antioxidants in pre-eclamptics promoted a greater potential for endothelial oxidative damage. The decreased activities of superoxide dismutase were significantly improved after delivery in women suffering from pre-eclampsia. Similar findings were noticed by Mutulu U.T. et al [16].

The enzyme glutathione reductase plays a pivotal role in replenishing and maintaining optimum concentration of reduced glutathione (GSH) in biological systems whereas catalase is a hemoprotein catalyzing the decomposition of hydrogen peroxide to water and oxygen. In the present study it is illustrated that both enzymes catalase and glutathione reductase were found to decrease in the 3rd trimester pre-eclamptic as compared to normal pregnant and non-pregnant women. Our findings are in consistent with Kumar CA and Das UN [17] with regard to decreasing levels of catalase. Decreased levels of glutathione reductase was increased in pre-eclamptic subjects after delivery but it was not significant whereas increase in levels of catalase was significant (p<0.001). Some studies have shown that delivery does not eliminate the risk for preeclampsia and its complications [18].

Glutathione peroxidase being a seleno enzyme catalyzes the degradation of hydrogen peroxide and hydroperoxides. Glutathione peroxidase acts on free lipid peroxides in the cytoplasm of the cell. Alex J.D., Jerca I [19] showed that significantly decreased levels of Glutathione peroxidase and marked elevation of malondialdehyde levels in women with pre-eclampsia when compared with normal pregnant women. Abnormally increased levels of lipid peroxides are toxic compounds that damage endothelial cells, increase thromboxane synthesis, decrease prostacyclin synthesis and increase peripheral vasoconstriction. The vasoconstriction thus produced can worsen hypertension causing ischemic injury to the cells and

subsequent peroxidation. By the above findings we may emphasize that, imbalance between lipid peroxides and reduced antioxidants may clearly demonstrates the presence of oxidative stress in preclampsia. Our findings clearly indicate and support some studies [20] that peroxidation may be important factor in the pathogenesis of preeclampsia.

**Conclusion**

The present study shows a clear insight into the disturbances associated with normal pregnancy, which are exaggerated in abnormal pregnancy like preeclampsia with an imbalance between lipid peroxides and reduced enzymatic antioxidants. However a large sample size is justifies for proper conclusion. Early attention, intensive management and treatment may be essential to improve maternal and fetal outcome.

**Reference**

[1] Villar K, Say L, Gülmezoglu AM, Merialdi M, Lindheimer MD, Betran AP, et al. Eclampsia and pre-eclampsia: a health problem for 2000 years. In: Critchley H, MacLean AB, Poston L, Walker JJ, eds. Pre-eclampsia. London: RCOG Press 2003; 189–207.

[2]F. W. Drislane and A M Wang. Multifocal cerebral hemorrhage in eclampsia and severe pre-eclampsia. J Neurol 1997; 244(3): 194-8.

[3] Gordon CS, Jill P, David W. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study. Lancet 2001; 357: 2002-6.

[4] Xiao R, Sorensen TK, Williams MA, Luthy DA. Influence of pre-eclampsia on fetal growth. J Matern Fetal Neonatal Med 2003;13(3):157-62.

[5] Hubel CA, James M,Robert MD, Robert N, Taylor MD, Thomas J, et al. Lipid peroxidation in pregnancy: New perspectives on pre-eclampsia. Am J Obstet Gynecol 1989; 161: 1025-34.

*[6] Robert JM*, Taylor RN, Musci TJ, Rogers GM, Hubel CA, Mclaughlin MK. Pre-eclampsia: An endothelial cell disorder. Am *J* Obstet Gynecol 1989; 161: 1200–4.

[7] ACOG technical bulletin. Management of preeclampsia. No. 91—February 1986. Committee on Technical Bulletins of the American College of Obstetricians and Gynecologists. Washington, D.C., 1986.

[8] Yagi K "Assay for Lipid peroxide level and its clinical significance" In Yagi K (ed) Lipid Peroxide Level in Biology Medicine. New York: Academic press; 1982.p. 223-42.

[9] Mishra HP and Fridovich I. The role of superoxide anion in the antioxidation of epinephrine and a simple assay for superoxide dismutase. J Biol Chem. 1972:247:3170-75.

[10] Beutler E, BlumeKG, Kaplan JC etal International committee for standardization in hematology, recommended methods for red cell enzyme analysis. Brit J Haemat. 1977:35:331-40

[11] Drabkin DL and Austin JH. Spectrometric constants for the common hemoglobin derivatives in human drug and rabbit blood. J Biol Chem. 1932:98:719-33.

[12] Kharb S. Evaluation of oxidative stress in pre-eclampsia. J Obstet Gynecol India 2000; 50 (3): 56-8.

[13]Walsh SW, Wang Y, Robert J. Peroxide induces vasoconstriction in the human placenta by Stimulating thromboxane. Am J Obstet Gynecol 1993; 169: 1007-12.

[14]Hubel CA. Dyslipidemia, iron, and oxidative stress in preeclampsia:Assessment of maternal and feto-placental interactions. Sem Reprod Endocrinol **16:**75–92, 1998.

[15] Ilhan N., Ilhan N. and Simsek M., 2002 "The changes of trace elements, malondialdehyde levels and superoxide dismutase activities in pregnancy with or without pre-eclampsia." Clin. Biochem., 35(5): 393-7.

[16]Mutulu U., Turkoglu, E. Ademoglu, L.Ibrahimoglu, et al. 1998 "Imbalance between lipid peroxidation and antioxidant status in pre-eclampsia". Gynecol. Obstet. Invest., 46 : 37-40.

[17]Kumar C.A., Das U.N., 2002 "Oxidant stress in pre-eclampsia and essential hypertension." J. Assoc. Physicians. India, 50: 1372-1375.

[18] Matthys LA, Coppage KH, Lambers DS. Delayed postpartum preeclampsia: an experience of 151 cases. Am J Obstet Gynecol 2004 ; 190(5) :1464-6

[19]Alex J.D., Jerca I., 1996 "The role of oxidative stress in the etiology of pre-eclampsia: changes at the GSH and GSH-Px levels in normal pregnancy and pre-eclampsia". Rev. Med. Chir. Soc. Med. Nat. Iasi., 100(1-2): 131-5.[Article in Romanian]

[20] Kumar CA, Das UN. Oxidant stress in pre-eclampsia and essential hypertension. J Assoc Physicians India 2002; 50: 1372-75.

**Table No 1. Malondialdehyde (MDA) and enzymatic antioxidants levels in the normal non pregnant controls, 3rd trimester pregnant, 3rd trimester preeclamptic and postpartum preeclamptic women**

| GROUP | A | B | C | D | |
|---|---|---|---|---|---|
| | Non – Pregnant Controls (n= 25) | 3rd Trimester Pregnant Women (n=25) | 3rd Trimester Pre-elamptic Women (n=25) | Postpartum Pre-elamptic Women (n=25) | F value |
| MDA n mol/ml | 1.19 ± 0.09 | 1.79 ± 0.14 | 2.93 ± 0.54 | 2.07 ± 0.51 | F3,96 = 86.900 |
| Range | (1.04-1.38) | (1.41-1.92) | (1.83-4.01) | (1.44-3.75) | |
| p values | | <0.001* | <0.001*♦ | <0.001• | |
| SOD IU/G Hb | 683.9 ±155.25 | 542.64 ±139.98 | 452.07 ±103.91 | 595.96± 108.21 | F 3,96= 13.794 |
| Range | (476.19-1041.66 ) | (334.45-88.89) | (357.14-33.33) | (261.44-657.89) | |
| p values | | <0.001* | <0.001*<br><0.02♦ | <0.001• | |
| GSH-Px IU/G Hb | 31.08 ± 4.45 | 23.45 ± 4.79 | 18.58±4.46 | 18.30± 4.39 | F3,96 = 41.736 |
| Range | (23.92-40.19) | (11.69-35.37 ) | (11.69-35.37 ) | (12.86-29.23) | |
| p values | | <0.001* | <0.001*♦ | N.S• | |
| GSH-Rx IU/G Hb | 10.52 ± 4.67 | 7.78 ±3.40 | 6.86 ± 2.33 | 7.05 ± 2.22 | F 3,96 = 6.406 |
| Range | (5.71-18.33) | (4.82-16.08) | (3.71-12.06) | (4.29-13.15) | |
| p values | | NS* | <0.01*<br><0.05♦ | N.S• | |
| Catalase IU/G Hb | 8.13 ± 2.21 | 6.2 ± 1.69 | 5.07 ± 1.31 | 6.59 ± 1.8 | F3,96 = 12.136 |
| Range | (3.84-12.52) | (3.79-9.86 ) | (2.56-7.82 ) | (3.02-9.75) | |
| p values | | <0.001* | <0.001* | <0.001• | |