

Research Article**Trace Elements and Oxidative Stress in Hypertensive Disorders of Pregnancy****Md. Siddique Ahmed Khan^{1*}, Mohammad Ibrahim Shaik²**¹Associate Professor, Department of Biochemistry, Shadan Institute of Medical Sciences, Teaching Hospital and Research Centre, Hyderabad, Telangana, India²Assistant Professor, Department of Biochemistry, Shadan Institute of Medical Sciences, Teaching Hospital and Research Centre, Hyderabad, Telangana, India***Corresponding author**

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Abstract: Background: Pre-eclampsia is defined as the onset of hypertension after mid-pregnancy; a systemic disease of the later stages of pregnancy that affects about 5 - 7% of all pregnancies and is the most common. Typically, blood pressure elevations and pre-eclampsia occur in the late second or third trimesters and gestational outcome is hardly affected. **Material and Methods:** This is perspective and observational study conducted in the Department of Biochemistry in association of Department of General Medicine over a period of six months. In this study investigation was done to determine the contribution of different biochemical parameters of females suffering from preeclampsia and Eclampsia. The study was carried out on Case group - 60 pre-eclampsia and eclampsia patients compare to Control group - 60 normal pregnant females. Selection criteria; Control: Normal pregnant females randomly selected from the hospital who is not suffering from any other medical disorder. Cases: All the patients of preeclampsia and Eclampsia will be admitted in the hospital. **Results:** The systolic blood pressure in case group was 171.3 ± 5.1 mmHg and control group 129.4 ± 5.2 mmHg. On the other hand, diastolic blood pressure in case group was 98.54 ± 4.3 mmHg and control group 79.59 ± 4.7 mmHg. Oxidative marker between Case and control group was statistically significantly difference. MDA in case group was 3.01 ± 0.41 nmol/mL and Control 1.61 ± 0.32 nmol/mL. Antioxidant marker between Case and control group was statistically significantly difference. In case group Glutathione peroxidase 8.93 ± 2.64 μ mol/ml and control group 15.75 ± 2.12 μ mol/ml. **Conclusion:** In our study increase MDA in PE and eclampsia, when compared to pregnant women. In addition, we also found decrease of antioxidant such as Glutathione in PE and eclampsia, when compared to pregnant women. In our study lower maternal plasma iron, zinc and copper were significantly decreased throughout pregnancy in who subsequently developed PE and eclampsia.

Keywords: Pre-eclampsia, Eclampsia Oxidative stress antioxidant.

INTRODUCTION

Pre-eclampsia is defined as the onset of hypertension after mid-pregnancy; a systemic disease of the later stages of pregnancy that affects about 5 - 7% of all pregnancies and is the most common[1]. Typically, blood pressure elevations and pre-eclampsia occur in the late second or third trimesters and gestational outcome is hardly affected. It has been reported that, pre-eclampsia is a major cause of both maternal and foetal morbidity and mortality[2]. Eclampsia is a condition in which one or more convulsions occur in a pregnant woman suffering from high blood pressure, often followed by coma and posing a threat to the health of mother and baby. Most cases of eclampsia present in the third trimester of pregnancy with about 80% of eclamptic seizure occurring intrapartum or with in the first 48 hours following delivery [2].

Different trace elements have been found to decrease the risk of having pre-eclampsia and

Eclampsia. A low intake of trace elements during pregnancy in many different parts of the world such as Asia, Latin America, Africa as well as developed countries such as Canada, USA and the UK. There was some variation between the countries, with very low intake in India (250 mg/d) to high intakes in Caucasian women in Canada (1256 mg/d)[3]. The expectant mothers may be able to prevent potentially serious medical problems in themselves and their babies simply by boosting their daily calcium intake. Since pre-eclampsia involves endothelial dysfunction and oxidative stress, there is interest in supplementation, with minerals such as trace elements and antioxidant vitamins such as vitamins C and E, in the second trimester. A preliminary trial of antioxidant vitamins, in high risk women, has reported improvements in biochemical markers of endothelial activation together with a reduction in preeclampsia[4].

Despite several studies on pre-eclampsia and eclampsia, its aetiology has not yet been fully elucidated. Although the pathophysiological mechanisms of pre-eclampsia and eclampsia remain obscure, it is known that placental changes occur early in pregnancy, associated with an imbalance between the generation of reactive oxygen species (ROS) and the antioxidant defence system, characterizing oxidative stress[5]. There is also a generalized inflammatory process, as well as the presence of progressive vascular endothelial damage, which culminates in placental dysfunction[6]. Despite this, it is not well established if the oxidative stress is the result of generalized oxidative cellular damage, which can affect proteins, lipid membranes, and deoxyribonucleic acid (DNA), caused by the disease already established, or if it precedes the clinical establishment of PE, being involved in its pathogenesis[7]. Some studies have shown that changes in the levels of blood trace elements in pre-eclamptic patients may implicate its pathogenesis while others have failed to show an association of blood levels of trace elements and prevalence of pre-eclampsia[8].

MATERIAL AND METHODS

This is perspective and observational study conducted in the Department of Biochemistry in association of Department of General Medicine over a period of six months. In this study investigation was done to determine the contribution of different biochemical parameters of females suffering from preeclampsia and Eclampsia.

Biochemical parameters included: Iron, Zinc, Copper, Malondialdehyde (MDA), Glutathione.

The study was carried out on Case group - 60 pre-eclampsia and eclampsia patients compare to Control group - 60 normal pregnant females.

Selection criteria;

1. Control: Normal pregnant females randomly selected from the hospital who is not suffering from any other medical disorder.
2. Cases: All the patients of preeclampsia and Eclampsia will be admitted in the hospital.

Inclusion criteria: Pregnant female suffering from preeclampsia and eclampsia.

Exclusion criteria: Pregnant females suffering from any other medical disorder.

RESULTS

Physical parameters

In table 1, the mean age of the case and control pregnant women was 31.3 years and 30.2 years respectively which was statistically not significantly different from those of control group ($P > 0.05$). Whereas, BMI between case and control group $28.1 \pm 3.1 \text{ kg/m}^2$ versus $27.2 \pm 3.0 \text{ kg/m}^2$ respectively which was statistically not significantly different from those of control group ($P > 0.05$). There was a significant difference ($P < 0.05$) between both the systolic and diastolic blood pressures of the case and control groups. The systolic blood pressure in case group was $171.3 \pm 5.1 \text{ mmHg}$ and control group $129.4 \pm 5.2 \text{ mmHg}$. On the other hand, diastolic blood pressure in case group was $98.54 \pm 4.3 \text{ mmHg}$ and control group $79.59 \pm 4.7 \text{ mmHg}$.

Table-1: Anthropometric parameters between Case and control group.

Parameters	Case (mean \pm SD)	Control (mean \pm SD)	p-value
Age in years	31.3	30.2	p = 0.82
BMI (kg/m^2)	28.1 ± 3.1	27.2 ± 3.0	p = 0.74
SBP (mmHg)	171.3 ± 5.1	129.4 ± 5.2	p < 0.001
DBP (mmHg)	98.54 ± 4.3	79.59 ± 4.7	p < 0.001

SD = Standard deviation; Kg/m^2 = kilogram per meter square; N = total number of patients; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; mmHg = millimetre mercury; N = 60.

Table-2: Oxidative marker between Case and control group

Parameters	Case (mean \pm SD)	Control (mean \pm SD)	p-value
Malondialdehyde (nmol/mL)	3.01 ± 0.41	1.61 ± 0.32	p < 0.001

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 40.

In table 2, Oxidative marker between Case and control group was statistically significantly difference.

MDA in case group was $3.01 \pm 0.41 \text{ nmol/mL}$ and Control $1.61 \pm 0.32 \text{ nmol/mL}$.

Table-3: Antioxidant marker between Case and control group.

Parameters	Case (mean \pm SD)	Control (mean \pm SD)	p-value
Glutathione peroxidase ($\mu\text{mol/ml}$)	8.93 \pm 2.64	15.75 \pm 2.12	p < 0.001

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 40.

In table 3, Antioxidant marker between Case and control group was statistically significantly

difference. In case group Glutathione peroxidase 8.93 \pm 2.64 $\mu\text{mol/ml}$ and control group 15.75 \pm 2.12 $\mu\text{mol/ml}$.

Table-4: Biochemical parameters between Case and control group.

Parameters	Case (mean \pm SD)	Control (mean \pm SD)	p-value
Fe ($\mu\text{mol/L}$)	13.53 \pm 4.42	18.54 \pm 7.23	p < 0.001
Zinc ($\mu\text{mol/L}$)	8.1 \pm 1.2	9.7 \pm 1.2	p = 0.06
Copper ($\mu\text{mol/L}$)	8.4 \pm 1.4	21.2 \pm 3.9	p < 0.001

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 40.

In table 4 Serum iron level in case group 13.53 \pm 4.42 $\mu\text{mol/L}$ and control group 18.54 \pm 7.23 $\mu\text{mol/L}$. Moreover, Serum Zinc level 8.1 \pm 1.2 $\mu\text{mol/L}$ and control group 9.7 \pm 1.2 $\mu\text{mol/L}$. Furthermore, Serum Copper level 8.4 \pm 1.4 $\mu\text{mol/L}$ and control group 21.2 \pm 3.9 $\mu\text{mol/L}$.

DISCUSSION

Preeclampsia is a hypertensive disorder of pregnancy. A lot of effort was done to diagnose the exact mechanism of preeclampsia. The free-radicals play an important role in this pathophysiology. It has been suggested that this may be due to increased cell turn over or due to decreased antioxidant free-radical scavenging mechanisms[9]. It is not well clear whether oxidative stress and antioxidant insufficiency are the direct cause of preeclampsia or secondary consequence of preeclampsia[10]. Determination of the level of various antioxidants or the oxidative stress end products offers guidelines for the diagnosis and management of preeclampsia. Our study was carried on 120 cases 60 of them are normal pregnant women and 60 pre-eclamptic women with no statistical significant difference between the patient and control group as regard age, gestational age at time of sampling and body mass index ($P > 0.05$). As regard, systolic and diastolic blood pressure there are significant difference between normal and pre-eclamptic group ($p < 0.001$).

In our study, the malondialdehyde (MDA) in preeclamptic women is significantly increased as compared to control group ($p < 0.001$). Also, the association between MDA level and blood pressure was analyzed in pre-eclamptic women. Positive correlation was reported between MDA level and blood pressure (both the systole and the diastole). Based on previous reports, MDA is always more elevated in the blood of pregnant women who suffer from preeclampsia. MDA level might be a causative factor for pathogenesis of preeclampsia. These finding come in agreement with other author as Sheena PS et al[11]. All these found that

there are significant increase MDA in preeclampsia women in comparison with normal one. However, increased lipid peroxidation products were reported in both normal pregnancy and preeclampsia as compared with non-pregnant women[12]. Furthermore, high statistic difference in MDA level was reported in pregnant women with sever and mild pregnancy-induced hypertension[13].

Other study also determines the association of severity of PIH and Glutathione peroxidase. It shown that Glutathione peroxidase was significantly decreased ($p < 0.001$). In a new study done by Draganovic D, the correlation of a Glutathione peroxidase marker, and pregnancy induced hypertension. It is supposed that Glutathione peroxidase could be used for assessment of hypertensive pregnant women and decisions on pregnancy termination period[14]. Other studies conducted with other author as Sheena, et al who revealed that plasma Glutathione peroxidase decrease gradually through normal pregnancy and decrease more and more in preeclampsia as compared to normal pregnancy.

Also, a decreased level of iron, zinc and copper was observed in this study. Another meta-analysis by Cohen JM et al., show that iron, zinc and copper have negative association with overall analysis between preeclamptic women and control group[15]. Oxidative stress will also affect preterm infants. These infants may suffer from intra-ventricular hemorrhage, the respiratory distress syndrome, chronic lung disease, necrotizing enterocolitis and retinopathy of prematurity [16]. So, prophylactic antioxidants may prevent oxidative stress so reduce the risk perinatal complications in their infants as well as decrease preeclampsia in their mothers. Spinnato, 43 who used multiple antioxidants such as Vitamin C, and other antioxidant as selenium, zinc, magnesium, coenzyme Q, and melatonin have been also used with encouraging results in decreasing the incidence of preeclampsia[17].

A more recent study, not encourage the routine use of antioxidants against pre-eclampsia as they proposed the inefficiency of antioxidant therapy in the treatment of preeclampsia[18].

CONCLUSION

In our study lower maternal plasma iron, zinc and copper were significantly decreased throughout pregnancy in who subsequently developed PE and eclampsia. We also found increase MDA in PE and eclampsia, when compared to pregnant women. In addition, we also found decrease of antioxidant such as Glutathione in PE and eclampsia, when compared to pregnant women.

REFERENCES

1. Sharma JB, Kumar A, Kumar A, Malhotra M, Arora R, et al. Effect of lycopene on pre-eclampsia and intrauterine growth retardation in primigravidas. *Int J Gynaecol Obstet.* 2003;81(3):257–262.
2. Simsek M, Naziroglu M, Simsek H, Cay M, Aksakal M, Kumru S: Blood plasma levels of lipoperoxides, glutathione peroxidase, beta carotene, vitamin A and E in women with habitual abortion. *Cell BiochemFunct.* 1998, 16: 227-231.
3. Hassan GI, Onu AB. Total serum vitamin C concentration in pregnant women: implications for a healthy pregnancy. *Rev Bras SaudeMatern Infant.* 2006;p. 293–296.
4. Miller H, Wilson R, Jenkins C, MacLean MA, Roberts J, Walker JJ: Glutathione levels and miscarriage. *FertilSteril.* 2000, 74: 1257-1258.
5. Patil SB, Kodliwadmth MV, Kodliwadmth SM. Study of oxidative stress and enzymatic antioxidants in normal pregnancy. *Indian J ClinBiochem.* 2007;22(1):135–137.
6. Atamer Y, Kocyigit Y, Yokus B, et al. Lipid peroxidation, antioxidant defense, status of trace metals and leptin levels in preeclampsia. *Eur J ObstetGynecolReprodBiol* 2005;119:60–6.
7. Kumru S., Aydin S., Simsek M., Sahin K., Yaman M., Ay G. (2003). Comparison of serum copper, zinc, calcium, and magnesium levels in preeclamptic and healthy pregnant women. *Biol. Trace Elem. Res.* 94, 105–112.
8. Sharma JB, Sharma A, Bahadur A, Vimala N, Satyam A, Mittal S. Oxidative stress markers and antioxidant levels in normal pregnancy and pre – eclampsia. *Int J GynecolObstet* 2006; 94: 23–27.
9. Krishna Menon MK, Palaniappan B. Hypertensive disorders of pregnancy. In MudaliarMenon (ed.). *Clinical Obstetrics.* 9th edn. Orient Longman, Madras. 1994; 133–154.
10. Izquierdo Alvarez S., Castanon S. G., Ruata M. L., Aragues E. F., Terraz P. B., Irazabal Y. G., et al. . (2007). Updating of normal levels of copper, zinc and selenium in serum of pregnant women. *J. Trace Elem. Med. Biol.* 21, 49–52.
11. Sahu S, Abraham R, Vedavalli R, Daniel M. Study of lipid profile, lipid peroxidation and vitamin E in pregnancy induced hypertension. *Indian J PhysiolPharmacol.* 2009;53(4):365–374.
12. Jaweed SA, Bhavthankar SS, Thorat AP. Increased lipid composition; increase lipid peroxidation and decrease antioxidant activity in preeclampsia. *Antiseptic.* 2008;105(7):326–338.
13. Shikha S, Prem C, Srivastava KV, Das BT, Mallick AK. Study of Serum Malondialdehyde and uric acid in Pregnancy Induced Hypertension and its medico-legal significance. *J Indian Acad Forensic Med.* 2014;36(1):55–60.
14. Sata F, Yamada H, Kondo T, Gong Y, Tozaki S, Kobashi G, Kato EH, Fujimoto S, Kishi R: Glutathione S-transferase M1 and T1 polymorphisms and the risk of recurrent pregnancy loss. *Mol Hum Reprod.* 2003, 9: 165-169.
15. Burton GJ, Jauniaux E: Placental oxidative stress: from miscarriage to preeclampsia. *J SocGynecolInvestig.* 2004, 11: 342-352.
16. Rajmakers MT, Peters WH, Steegers EA, Poston L: NAD(P)H oxidase associated superoxide production in human placenta from normotensive and pre-eclamptic women. *Placenta.* 2004, 25 (Suppl A): S85-S89.
17. Gupta S, Agarwal A, Krajcir N, Alvarez JG: Role of oxidative stress in endometriosis. *Reprod Biomed Online.* 2006, 13: 126-134.
18. Jain SK, Wise R. Relationship between elevated lipid peroxides, vitamin e deficiency and hypertension in preeclampsia. *Mol Cell Biochem.* 1995;151:33–38.