



Exploring the Role of Trace Elements, Antioxidant, and Oxidative Stress among Preeclampsia and Eclampsia.

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Abstract

Background: Deficiencies of trace elements such as zinc, copper, selenium and magnesium have been implicated in various reproductive events like infertility, pregnancy wastage, congenital anomalies, pre-eclampsia, placental abruption, premature rupture of membranes, still births and low birth weight. Different trace elements have been found to decrease the risk of having pre-eclampsia. It is hoped that this study will contribute to the knowledge of the role of trace elements in women presented with pre-eclampsia. The aim of this study is to determine the plasma level of selected trace elements on pregnant women presented with preeclampsia. We hypothesise that changes in the status of trace element of pregnant women may contribute to the pathogenesis of pre-eclampsia. **Materials & Methods:** This is a prospective study was conducted in the Department of Biochemistry, Tertiary Care Teaching Hospital over a period of 1 year. Primigravidae with singleton pregnancy between 20-32 weeks of gestation with Blood Pressure < 140/90 mmHg without proteinuria and edema were included. 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:** Serum iron level in case group $18.45 \pm 8.48 \mu\text{mol/L}$ and control group 15.94 ± 8.24 . Moreover, Serum Zinc level $8.6 \pm 1.9 \mu\text{mol/L}$ and control group $9.5 \pm 1.4 \mu\text{mol/L}$. Furthermore, Serum Copper level $17.5 \pm 5.5 \mu\text{mol/L}$ and control group $9.8 \pm 1.8 \mu\text{mol/L}$. Oxidative marker between Case and control group was statistically significantly difference. MDA in case group was $3.17 \pm 0.44 \text{ nM/mL}$ and Control $1.62 \pm 0.33 \text{ nM/mL}$. Antioxidant marker between Case and control group was statistically significantly difference. In case group Glutathione peroxidase $9.53 \pm 2.46 \mu\text{mol/ml}$ and control group $11.68 \pm 3.63 \mu\text{mol/ml}$. **Conclusion:** The results obtained support our initial hypothesis that common differences between all pregnant women and controls could be revealed, while preeclampsia and the other pregnancies would further differ indicating specific misbalance of the oxidative stress in preeclampsia.

Keywords: Oxidative stress, Antioxidants, Preeclampsia.



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INTRODUCTION

Pre-eclampsia is defined as the onset of proteinuric 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, yet least understood disorder of pregnancy.[1] It is a rapidly progressive condition characterized by high blood pressure, platelet aggregation, swelling of the lower extremities and protein in urine. [2] Sudden weight gain, headaches and changes in vision are important symptoms. Typically, blood pressure elevations and pre-eclampsia occur in the late second or third trimesters and gestational outcome is hardly affected. [3] It has been reported that, pre-eclampsia is a major cause of both maternal and foetal morbidity and mortality. [4]

Despite its prevalence and severity, the patho-physiology of this multi-system disorder is still poorly understood. [5] Placental oxidative stress has been shown to be a key feature in the pathogenesis of eclampsia. [6] Despite several studies on pre-eclampsia, its aetiology has not yet been fully elucidated. 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. [7] Nutritional deficiencies are common during pregnancy and pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins. [8]

An inadequate dietary intake before and during pregnancy might be a high risk not only for the mother but also for the foetus. Deficiencies of trace elements such as zinc, copper, selenium and magnesium have been implicated in various

reproductive events like infertility, pregnancy wastage, congenital anomalies, pre-eclampsia, placental abruption, premature rupture of membranes, still births and low birth weight. [9] Different trace elements have been found to decrease the risk of having pre-eclampsia. [10]

This was as a result of their findings that pregnant women from communities with low dietary calcium who received at least 1.5 g/day of calcium orally during the second half of pregnancy had a lower risk of hypertension and preeclampsia than women who received placebo treatment. [11] Since pre-eclampsia involves endothelial dysfunction and oxidative stress, there is interest in supplementation, with minerals such as calcium 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. [12] Adam et al. (2001) reported an increased incidence of pre-eclampsia in zinc-deficient regions and it was later found that zinc supplementation reduced the high incidence of the disease. [13]

Furthermore, decreased levels of selenium and copper have been observed in patients with pre-eclampsia. [14] In recent times, there has been an increasing prevalence in the incidence of pre-eclampsia globally but there are conflicting reports on the relationship between trace elements and pre-eclampsia. It is hoped that this study will contribute to the knowledge of the role of trace elements in women presented with pre-eclampsia. The aim of this study is to determine the plasma level of selected trace elements on pregnant women presented with preeclampsia. We hypothesise that changes in the status of trace element of pregnant women may contribute to the pathogenesis of pre-eclampsia.

MATERIALS AND METHODS

This is a prospective study was conducted in the Department of Biochemistry, Tertiary Care Teaching Hospital over a period of 1 year.

Inclusion criteria: Primigravidae with singleton pregnancy between 20-32 weeks of gestation with Blood Pressure < 140/90 mmHg without proteinuria and edema were included.

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

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.
Pregnant female suffering from preeclampsia and eclampsia

Socio-demographic characteristics and delivery of information were obtained from the medical records system. The information on prepregnancy height and weight, smoking and drinking history, education level, past medical history, last menstrual period, parity history, and method of conception was gathered and recorded in our electronic medical record system, by the physicians at the first visit for pregnancy registered, which self-reported by pregnant women. The first visit for pregnancy registered usually opens at 8–12 weeks of gestation in this city. The typical schedule of routine antenatal visits is at weeks 8–12, week 16, week 20, week 24, week 28, and thereafter every 2 weeks until birth.

Trace elements were directly taken from the laboratory data system of our hospital. In our study, trace elements of all participants were measured in maternal whole blood in 12–27 (+6) weeks of pregnancy, before the date of diagnosis preeclampsia. Blood samples were collected from the antecubital vein of pregnant women declaring themselves to be fasting, using heparin anti-coagulation vacuum blood vessel collection. In our hospital laboratory, the whole blood trace elements were measured by flame atomic absorption spectrometer method.

Biochemical parameters included: Iron, Zinc, Copper, Malondialdehyde (MDA), Glutathione, Vitamin C, Vitamin E, Uric acid. The study was carried out on Case group - 100 pre-eclampsia and eclampsia patients compare to Control group - 100 normal pregnant females.

Statistical analysis

Statistical analysis was done by using descriptive and inferential statistics using chi-square test. The software used in the analysis were SPSS (Statistical Package for Social Sciences) version 27. All the results were tested at 5% level of significance.

RESULTS

In Table-1, the mean age of the case and control pregnant women was 28.5 years and 30.1 years respectively which was statistically not significantly different from those of control group ($P > 0.05$). Whereas, BMI between case and control group $27.2 \pm 2.8 \text{ kg/m}^2$ versus $25.7 \pm 3.2 \text{ kg/m}^2$ respectively which was statistically not significantly different from those of control group ($P > 0.05$).

Table-1: Distribution of Anthropometric parameters between Case and control group

Parameters	Age in years	BMI (kg/m ²)	SBP (mmHg)	DBP (mmHg)
Case (mean $\pm$ SD)	28.5	27.2 ± 2.8	167.25 ± 12.4	99.55 ± 7.3
Control (mean $\pm$ SD)	30.1	25.7 ± 3.2	127.19 ± 10.7	79.33 ± 6.9
t-value	1.63	1.33	29.32	17.02
p-value	$p = 0.95$	$p = 0.82$	$p = 0.02$	$p < 0.001$

SD = Standard deviation; Kg/m² = 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 = 120. In Table-1, 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 $167.25 \pm 12.4 \text{ mmHg}$ and control group $127.19 \pm 10.7 \text{ mmHg}$. On the other hand, diastolic blood pressure in case group was $99.55 \pm 7.3 \text{ mmHg}$ and control group $79.33 \pm 6.9 \text{ mmHg}$.

Table-2: Distribution of Biochemical parameters between Case and control group

Parameters	Fe ($\mu\text{mol/L}$)	Zinc ($\mu\text{mol/L}$)	Copper ($\mu\text{mol/L}$)
Case (mean $\pm$ SD)	18.45 ± 8.48	8.6 ± 1.9	17.5 ± 5.5
Control (mean $\pm$ SD)	15.94 ± 8.24	9.5 ± 1.4	9.8 ± 1.8
t-value	13.9	3.4	14.75
p-value	$p < 0.001$	$p = 0.06$	$p < 0.001$

The mean serum concentrations of zinc, copper, and iron statistically significantly difference ($P < 0.05$) in pre-eclampsia and eclampsia patients in comparison to the control group. Table 2 Serum iron level in case group $18.45 \pm 8.48 \mu\text{mol/L}$ and control group 15.94 ± 8.24 . Moreover, Serum Zinc level $8.6 \pm 1.9 \mu\text{mol/L}$ and control group $9.5 \pm 1.4 \mu\text{mol/L}$. Furthermore, Serum Copper level $17.5 \pm 5.5 \mu\text{mol/L}$ and control group $9.8 \pm 1.8 \mu\text{mol/L}$.

Table-3: Distribution of Oxidative marker between Case and control group

Parameters	Malondialdehyde (nM/mL)
Case (mean $\pm$ SD)	3.17 ± 0.44
Control (mean $\pm$ SD)	1.62 ± 0.33
t-value	14.30
p-value	$p < 0.001$

SD = Standard deviation; N = total number of patients; N = 120

Table-4: Antioxidant marker between Case and control group

Parameters	Glutathione peroxidase ($\mu\text{mol/ml}$)
Case (mean $\pm$ SD)	9.49 ± 1.58
Control (mean $\pm$ SD)	12.96 ± 3.74
t-value	16.39
p-value	$p < 0.001$

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 120.

Table-5: Antioxidant marker between Case and control group

Parameters	Vitamin C (mg/dl)	Vitamin E (mg/L)	Uric acid (mg/dl)
Case (mean $\pm$ SD)	0.64 ± 0.11	7.64 ± 1.47	7.55 ± 1.63
Control (mean $\pm$ SD)	1.38 ± 0.14	12.48 ± 2.54	4.44 ± 0.40
t-value	7.54	12.55	15.58
p-value	$p < 0.001$	$p < 0.001$	$p < 0.001$

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 120.

In Table-5, Antioxidant marker between Case and control group was statistically significantly difference. In case group Vitamin C was 0.64 ± 0.11 mg/dl and control group 1.38 ± 0.14 mg/dl/ml. In case group Vitamin E was 7.64 ± 1.47 mg/L and control group 12.48 ± 2.54 mg/dl/L. In case group of Uric acid was 7.54 ± 1.63 mg/dl and control group 4.44 ± 0.40 mg/dl/ml.

DISCUSSION

An excessive increase in biomarkers of oxidative stress and lipid peroxidation has been reported in women with preeclampsia. Increased lipid peroxidation is considered to be a causative pathogenesis factor for preeclampsia.[15] To support this concept, increased plasma lipid peroxidation products known as malondialdehyde (MDA) have been reported in preeclamptic women compared with healthy pregnant women. [16] In fact the increased production of lipid peroxides in preeclamptic women may cause vascular endothelial cell dysfunction. However, despite these reports, a few studies failed to approve the association between lipid peroxidation level and endothelial dysfunction in early or late preeclampsia. [17]

The association of maternal oxidative stress with subsequent development of pregnancy complications has been investigated in some studies. Although scientific evidence indicated that free radicals and oxidative stress might play a significant role in pre-eclampsia, not all studies have produced consistent results about antioxidant balance in preeclampsia. While some studies reported a decreased level of enzymatic and non-enzymatic antioxidant in placenta, erythrocytes or plasma. [18]

The present study was conducted to assess oxidative stress in pregnant women. We found that BMI between case and control group 27.2 ± 2.8 kg/m² versus 25.7 ± 3.2 kg/m² respectively which was statistically not significantly different from those of control group ($P > 0.05$). the mean age of the case and control pregnant women was 28.5 years and 30.1 years respectively which was statistically not significantly different from those of control group ($P > 0.05$). Taravati et al [11] included 2953 cases and 3621 controls, a statistically significant reduction in total antioxidant capacity, nitric oxide, superoxide dismutase, glutathione, vitamin E and C was observed in preeclampsia women.

On the other hand, a statistically significant increase in malondialdehyde, protein carbonyl, total peroxide, glutathione peroxidase, catalase and uric acid were observed in preeclampsia women. [19] The increased products of oxidative stress, which were found in the present meta-analysis might be an underlying mechanism for endothelial dysfunction in preeclampsia. This metaanalysis provides a scientific support that primary reduction of antioxidant capacity and increased levels of oxidative stress products may induce a condition in which the pathways responsible for blood pressure homeostasis are disrupted. [20]

In conclusion, it is hypothesized when oxidative stress is established, a protective response is induced by increasing some antioxidants. Further studies are warranted to investigate the role of dietary supplementation and genetic variation in women with different ethnicity. Cases have significantly higher mean MDA levels (3.17 ± 0.44 nM/mL) compared to controls (1.62 ± 0.33 nM/mL). This indicates elevated oxidative stress in the cases. A high t-value of 14.30 suggests a large difference between the two groups.

Karacey et al [21] assessed the plasma and serum maternal total antioxidant status, circulating levels of lipid peroxidation breakdown products (MDA), protein oxidation markers (AOPPs), myeloperoxidase (MPO) and lipid hydroperoxide (LHP) in preeclampsia, gestational diabetes mellitus (GDM) patients and compared them with noncomplicated normal pregnancies between 24 and 36 weeks of gestation. [22] GDM, preeclampsia and noncomplicated singleton pregnancies were included. TAS was decreased in GDM and preeclampsia when compared to normal pregnancies. MDA levels were higher only in GDM group than normal pregnancies. [23] AOPP levels were increased but MPO and LHP levels were not changed both in GDM and preeclampsia when compared to normal pregnancies.

CONCLUSION

In the light of the above interpretations it can be determined that pre-eclamptic pregnant women have higher levels of MDA while decreased level of reduced glutathione and the difference were very highly significant. Our finding on role of antioxidant in preeclampsia normal pregnant women the result showed beneficial affect with the significant differences. It may provide new insight into a potentially modifiable way to prevent preeclampsia when the vitamins are administrated in diets.

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