

To Estimate Trace Elements, Oxidative Stress and Antioxidant during Preeclampsia and Eclampsia

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Abstract

Introduction: Pregnancy is characterized by significant metabolic and hemodynamic changes that begin early in the gestational period. Major hemodynamic changes include an increase in the cardiac output during the first trimester, sodium and water retention leading to plasma volume expansion with a peak around week 30, and reductions in the systemic vascular resistance and systemic blood pressure. **Material and Methods:** This is prospective and observational study conducted at Department of Biochemistry in association of Department of General Medicine. In this study investigation was done to determine the contribution of different biochemical parameters of females suffering from preeclampsia and Eclampsia. **Results:** Serum iron level in case group 18.43 ± 8.49 $\mu\text{mol/L}$ and control group 15.92 ± 8.23 . Moreover, Serum Zinc level 8.4 ± 1.9 $\mu\text{mol/L}$ and control group 9.3 ± 1.2 $\mu\text{mol/L}$. Furthermore, Serum Copper level 17.3 ± 5.3 $\mu\text{mol/L}$ and control group 9.6 ± 1.9 $\mu\text{mol/L}$. Oxidative marker between Case and control group was statistically significantly difference. MDA in case group was 3.18 ± 0.43 nM/mL and Control 1.63 ± 0.32 nM/mL. Antioxidant marker between Case and control group was statistically significantly difference. In case group Glutathione peroxidase 9.53 ± 2.46 $\mu\text{mol/ml}$ and control group 11.68 ± 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: Preeclampsia, Eclampsia, Oxidative stress, Antioxidant during.

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INTRODUCTION

Pregnancy is characterized by significant metabolic and hemodynamic changes that begin early in the gestational period. Major hemodynamic changes include an increase in the cardiac output during the first trimester, sodium and water retention leading to plasma volume expansion with a peak around week 30, and reductions in the systemic vascular resistance and systemic blood pressure [1]. The reduction of the systemic vascular resistance is around 25% and is due to the increase in vasodilating agents, like nitric oxide and prostacyclin production, and the decrease in the sensitivity to norepinephrine and angiotensin [2]. The diastolic blood pressure begins to decrease from the 7th week of gestation, with a 10-mmHg decline between the 24th–26th gestation weeks, returning to normal values during the third trimester [3].

These are some of the changes that can occur during pregnancy. Hypertension is the most prevalent maternal complication worldwide (several studies estimate that it affects 7–10% of all pregnancies), and it is associated with a significant morbidity and mortality of the mother and fetus [4]. In fact, hypertension is the second largest cause of direct maternal death worldwide (14% of the total), and it is estimated that 192 people die every day because of hypertensive disorders in pregnancy [5].

Pre-eclampsia and eclampsia are two hypertensive disorders of pregnancy, considered as major causes of maternal and perinatal morbidity and mortality [6]. These diseases affect between 3% and 5% of all pregnancies and account for more than 60,000 maternal and 500,000 fetal deaths per year worldwide [7]. It is known that pre-eclampsia and eclampsia are

the hypertensive disorders that involve the most significant health risks for the pregnant woman and the fetus. In this context, it is imperative to evaluate whether all possible and necessary measures are being taken correctly in terms of prevention, maintenance, and treatment of the disease [8].

MATERIAL AND METHODS

In this study investigation was done to determine the contribution of different biochemical parameters of females suffering from preeclampsia and Eclampsia.

The present study was carried out in the Department of Biochemistry in association of Department of General Medicine.

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

The study was carried out on Case group - 100 pre-eclampsia and eclampsia patients compare to Control group - 100 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 29.3 years and 31.2 years respectively which was statistically not significantly different from those of control group ($P > 0.05$). Whereas, BMI between case and control group $26.4 \pm 3.8 \text{ kg/m}^2$ versus $25.7 \pm 3.0 \text{ kg/m}^2$ 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)	28.4	26.3 ± 2.9	167.24 ± 12.3	99.54 ± 7.2
Control (mean \pm SD)	30.2	25.8 ± 3.1	127.18 ± 10.6	79.32 ± 6.9
t-value	1.64	1.32	29.31	17.01
p-value	$p = 0.94$	$p = 0.81$	$p = 0.02$	$p < 0.001$

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 = 100.

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 167.24 ± 12.3 mmHg

and control group 127.18 ± 10.6 mmHg. On the other hand, diastolic blood pressure in case group was 99.54 ± 7.2 mmHg and control group 79.32 ± 6.9 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)	18.43 ± 8.49	8.4 ± 1.9	17.3 ± 5.3
Control (mean \pm SD)	15.92 ± 8.23	9.3 ± 1.2	9.6 ± 1.9
t-value	13.7	3.2	14.73
p-value	$p < 0.001$	$p = 0.06$	$p < 0.001$

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 100.

Biochemical Parameters

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 and Graph 2).

Serum iron level in case group $18.43 \pm 8.49 \mu\text{mol/L}$ and control group 15.92 ± 8.23 . Moreover, Serum Zinc level $8.4 \pm 1.9 \mu\text{mol/L}$ and control group $9.3 \pm 1.2 \mu\text{mol/L}$. Furthermore, Serum Copper level $17.3 \pm 5.3 \mu\text{mol/L}$ and control group $9.6 \pm 1.9 \mu\text{mol/L}$.

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

Parameters	Malondialdehyde (nM/mL)
Case (mean \pm SD)	3.18 ± 0.43
Control (mean \pm SD)	1.63 ± 0.32
t-value	14.29
p-value	$p < 0.001$

SD = Standard deviation; N = total number of patients; N = 100.

In Table-3 and Graph-3, Oxidative marker between Case and control group was statistically

significantly difference. MDA in case group was 3.18 ± 0.43 nM/mL and Control 1.63 ± 0.32 nM/mL.

Table-4: Antioxidant marker between Case and control group

Parameters	Glutathione peroxidase ($\mu\text{mol/ml}$)
Case (mean \pm SD)	9.48 ± 1.59
Control (mean \pm SD)	12.95 ± 3.75
t-value	16.38
p-value	$p < 0.001$

SD = Standard deviation; $\mu\text{mol/}$ = millimole per litre; N = total number of patients; N = 100.

In Table-4, Antioxidant marker between Case and control group was statistically significantly

difference. In case group Glutathione peroxidase 9.53 ± 2.46 $\mu\text{mol/ml}$ and control group 11.68 ± 3.63 $\mu\text{mol/ml}$.

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)	0.63 ± 0.12	7.63 ± 1.48	7.54 ± 1.64
Control (mean \pm SD)	1.37 ± 0.15	12.49 ± 2.53	4.43 ± 0.41
t-value	7.53	12.54	15.59
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 = 100.

In Table-5, Antioxidant marker between Case and control group was statistically significantly difference. In case group Vitamin C was 0.63 ± 0.12 mg/dl and control group 1.37 ± 0.15 mg/dl/ml. In case group Vitamin E was 7.63 ± 1.48 mg/L and control group 12.49 ± 2.53 mg/dl/L. In case group of Uric acid was 7.54 ± 1.64 mg/dl and control group 4.43 ± 0.41 mg/dl/ml.

DISCUSSION

Preeclampsia, which affects 2–7% of all pregnancies, is a syndrome that is associated with multiorgan dysfunction and is characterized by new-onset hypertension (blood pressure $>140/90$ mm Hg) and proteinuria (>300 mg/24 h) after 20 wk of gestation [9]. The precise mechanisms that lead to preeclampsia, which often occurs without warning and may follow a precipitous course, are not known; however, failure of the normal processes of placentation followed by inadequate placental perfusion would seem to be a necessary prelude to the cascade of molecular events that culminate in the maternal syndrome [10]. Numerous studies have described elevated markers of oxidative stress in placental tissue from women with preeclampsia [11].

Pregnancy increases oxidative stress, a condition that can be aggravated with preeclampsia, because free radicals are detrimental to the integrity of the endothelium, causing maternal vascular dysfunction [12]. According to this knowledge, preeclampsia is a condition where there is an imbalance between the endogenous antioxidant system and free radicals, mostly ROS. These species are caused by:

mitochondrial aerobic metabolism, activation of NADPH oxidase, xanthine oxidase (XO), cytochrome P450 and lipid peroxidation process (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR)) and nonenzymatic (vitamin E, C, carotene, glutathione) [13]. Under physiological conditions, these defense mechanisms maintain a low concentration of ROS in the cell and its activity is regulated, hence the balance between ROS production and antioxidant defenses determines the degree of oxidative stress [14].

MDA is constantly being generated in body fluids though various mechanisms and is continually removed by the endogenous antioxidant defense system. In addition to the technical points, MDA levels change with the circadian rhythm, which is another shortcoming in its role as an acceptable biomarker [15]. To further support our hypothesis, we compared the MDA levels of healthy non-pregnant group from some available studies from a given university, i.e., Kahramanmaraş Sutcu Imam University. Serum MDA levels of 8.7 nmol/mL, 2.20 ± 0.28 nmol/mL, 4.4 ± 0.5 nmol/mL were found from various study [16-18]. It should be noted that the two latter works employed slightly different analytical conditions. Interestingly, the results reported in reference are a thousand times higher than the values in other reports [19].

Several antioxidant markers have been shown to be significantly decreased in preeclamptic women [20]. In the maternal circulation, the levels of enzymatic as well as nonenzymatic antioxidant markers, such as vitamins C, E, glutathione, iron, zinc, and copper may

be altered [21]. Studies have also shown that women with preeclampsia have significantly reduced serum coenzyme Q10 [22] as well as serum and/or placental -carotene, lycopene, and canthaxanthin [23]. One study focused on the evaluation of the total antioxidant response (TAR) determined by the redox status of the plasma, as well as the oxidative stress index (OSI), calculated from the percent ratio of the total plasma peroxide levels in preeclamptic women [24]. Both parameters were found to be significantly higher in patients with preeclampsia. A twofold increase in the ratio between LPO and antioxidant capacity was observed in the antepartum period in women with preeclampsia [25]. At the same time, Hilari et al. found that women whose pregnancies were complicated by mild preeclampsia had increased levels of total oxidant status (TOS) and a decreased total antioxidant status (TAS) level compared to women with normal pregnancies [26].

Glutathione is another antioxidant to be found modified in a preeclamptic placenta [27]. Furthermore, Rosta et al. [28] suggested the role of SOD3 single nucleotide gene polymorphisms in the increased oxidative stress in preeclampsia. Significantly lower levels of ascorbic acid were reported in the plasma of women with mild to severe preeclampsia [29]. Similarly, serum alpha-tocopherol levels were significantly reduced in pregnancies complicated by severe preeclampsia. As LPO is commonly observed in preeclamptic patients, the balance between lipid peroxides and antioxidant vitamin E will be tipped in favor of lipid peroxides in patients with mild and severe preeclampsia. In a controlled clinical trial, significantly lower levels of vitamin C, E, and total thiols were seen in women with preeclampsia [30]. Furthermore, significantly reduced whole blood glutathione levels have been reported in women with preeclampsia and HELPP syndrome [31].

CONCLUSION

Our study has noticed that the role of oxidative stress and antioxidant capacity in preeclampsia and Eclampsia. By assessing markers of lipid peroxidation and antioxidant capacity, we achieved unequivocal evidence for oxidative stress in this disorder. 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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