Original Article

Serum Immunoglobulins, C-Reactive Protein, and Trace Element Level in Preeclamptic Nigerian Subjects

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ABSTRACT

Background: The mechanism involved in the pathogenesis of preeclampsia (PE) remains uncertain, and the research into a better understanding, its possible prediction, and subsequent prevention continues. **Aim:** This study evaluated changes in serum immunoglobulins (IgG, IgA, and IgM), C-reactive protein, and trace elements (Zn, Cu, and Mn) in preeclamptic, normotensive pregnant, and non-pregnant females. **Subjects and Methods:** The study was conducted among 150 subjects consisting of 50 preeclamptic subjects, 50 healthy normotensive pregnant women in their third trimester, and 50 non-pregnant women, all within the same age bracket. The serum concentration of the immunoglobulins and C-reactive protein were measured using standard immunoturbidimetric methods, whereas the trace elements were assayed using the atomic absorption spectrophotometric method. **Results:** Serum IgG and IgM levels were observed to be significantly lower ($P < 0.05$) in preeclamptic subjects (101.22 ± 4.44 and 769.43 ± 1.43 mg/dl), respectively, when compared to the normotensive pregnant women (123.87 ± 1.81 and 881.71 ± 2.80 mg/dl), respectively. There was a non-significant difference in immunoglobulin A levels between the groups ($P > 0.05$). The C-reactive protein was significantly higher, whereas the trace elements were significantly lower ($P < 0.05$) in preeclamptic subjects compared to the normotensives. There was a positive correlation between the immunoglobulin G and Zn levels (r = 0.334; $P = 0.046$) and also between immunoglobulin G and C-reactive protein levels (r = 0.340; $P = 0.043$) and a negative correlation between systolic blood pressure and manganese levels in preeclamptic subjects (r = −0.375; $P = 0.024$). **Conclusion:** This study therefore reveals significantly lower levels of immunoglobulins and trace elements among the preeclamptic subjects. These micronutrient deficiencies and low levels of immunoglobulins could be risk factors for the development of high blood pressure and PE.

Keywords: *Immunoglobulin, Nigeria, preeclampsia, trace element*

Introduction

Preeclampsia (PE) is a disorder of widespread vascular and endothelial malfunction and vasospasm that occurs mostly after 20 weeks of gestation and can present as late as 4–6 weeks postpartum.[1] Clinically, it is defined by high blood pressure (a diastolic pressure of ≥90 mmHg and a systolic pressure of ≥140 mmHg) and proteinuria. In severe cases, there may be red blood cell breakdown, low platelet count, impaired liver functions, and visual disturbances. It increases the risk of poor outcomes for both mother and baby. If left untreated, it progresses to eclampsia, at which point it is accompanied with seizures.[2]

It is a significant public health threat in both the developed and developing nations of the world, and

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despite progress in medical treatment, it remains one of the causes of maternal and perinatal morbidity. Worldwide, the incidence of PE ranges between 2 and 10% of pregnancies. It varies greatly among nations. The World Health Organization estimates the incidence of PE to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4% of live births).[3]

PE is one of the leading causes of complications during pregnancy which when undiagnosed culminates in eclampsia and has remained on the rise, posing a great danger to a lot of mothers and their fetuses. Unfortunately, to date, researchers have remained at a loss as to the definite cause of PE, and as a result, no preventive measures have been mapped out, leaving PE undetected or non-diagnosed until etiopathogenesis is fully completed, and then, symptoms manifested above 20 weeks.

Several pieces of evidence indicate that various elements might play important roles in PE.[4] Iron, copper, and zinc are redox transition metals and in excess may stimulate oxidative stress and endothelial cell injury. There are conflicting results on the link of these trace elements with pregnancy-related hypertensive disorders including PE, especially in case-control studies conducted late in pregnancy in non-diabetic women. Maternal copper, iron, manganese, selenium, and zinc were reduced in most reports where PE was present[5]; however, in some, copper, iron, and zinc were elevated in PE, and in others, there were no associations with PE.[6] Clearly, in these studies, any such associations could be a result, not a case of PE, or could be entirely unrelated. In a stated prospective study in non-diabetic women, maternal plasma copper was significantly raised in early pregnancy among those who afterward developed PE compared to the controls. In non-diabetic women, maternal zinc levels were increased in few studies of pregnancies complicated by PE.[7]

Deficiencies of trace elements such as zinc, copper, and magnesium have been implicated in various reproductive events such as infertility, pregnancy wastage, congenital anomalies, PE, placental abruption, premature rupture of membranes, stillbirths, and low birth weight. The exact etiology of PE is still not known. There are inconsistent reports on the role of immunoglobulins in the etiology of PE. Immunoglobulins IgG, IgA, and IgM are a heterogeneous group of antiphospholipid antibodies which have a great affinity for several combinations of phospholipids, phospholipid-binding proteins, or both.[8] They are mostly targeted by platelets and endothelial cells.[9] It can damage phospholipids that are present in all endothelial cell surfaces. Damaged endothelial cells do not function normally which can cause thrombotic complications. A relationship between antiphospholipid antibodies and PE was first suspected because of the high rate of PE among women with antiphospholipid syndrome.[10] Deregulated immunity at the feto-maternal interface at the beginning of pregnancy leads to the onset of clinical symptoms of PE. One study shows that the IgM antibody was associated with PE.[8] Works on PE in Nigeria by Akiibinu *et al*.[11] focused on oxidative stress alongside thyroid functions. The report of Arinola *et al*.[12] concluded that immunoglobulins are significantly decreased in PE. The report of Ashan *et al*.[13] on serum immunoglobulins in PE concluded that they are significantly elevated. PE treatment has not changed significantly in the last 50 years.[14] However, early treatment can have strong preventive effects, making early diagnosis a priority. No tests have accurately predicted the onset of PE because of the heterogeneity of its clinical presentation.[15] A potential biomarker should have the ability to detect PE with high accuracy at the earliest stage. Widespread implementation of such a biomarker may be able to show who is at low or high risk. Because no definitive cause of PE is known, it becomes relevant to seek new biomarkers that can help in the early diagnosis. This study evaluated the serum concentrations of immunoglobulins, C-reactive protein, and some mineral elements in subjects with PE.

Subjects and Methods

Study design

This is a comparative cross-sectional study designed to compare the serum levels of C-reactive protein, immunoglobulins G, A, and M, and selected trace elements Zn, Cu, and Mn in preeclamptic, non-preeclamptic, and non-pregnant women attending the antenatal clinic in Holy Rosary Hospital, Onitsha.

Study setting

The study was carried out in the Obstetrics and Gynecology Department of Holy Rosary Specialist Hospital and Maternity, Onitsha. Onitsha is the largest city in Anambra State, South-eastern Nigeria. It is a reputable mission hospital in the State with a high child delivery rate and has facilities for the management of cases of PE on a 24-hour coverage. The hospital enjoys high patronage of patients (including pregnant women) due to the perceived relatively lower cost of services and round-the-clock availability of health personnel.

Study population and duration

The study population was made up of eligible women who received their antenatal care in Holy Rosary Hospital, Onitsha. The subjects who met the inclusion criteria and consented to the study were recruited.

They were grouped thus: pregnant women with established PE (group 1), pregnant women who were not preeclamptic (controls, group 2), and non-pregnant women. The non-pregnant women were recruited from apparently healthy age-matched hospital staff. The study was conducted between August 2016 and April 2017. The inclusion criteria for the study include hypertensive pregnant patients with blood pressure ≥140/90 mmHg and urine proteins of +2 or more, between 20 and 40 gestational weeks, normotensive pregnant patients in their third trimester, and apparently healthy non-pregnant women. Patients with a history of hypertension before pregnancy and with any known chronic diseases such as diabetes and asthma were excluded. Also, patients were excluded from the study if they had preterm birth owing to underlying medical conditions, more than three previous miscarriages, or interventions that may affect pregnancy outcomes.

Method of data collection

The sample size was determined as described by Boko *et al*.[15] A total of 150 consenting apparently healthy pregnant and non-pregnant women took part in the study. Pregnant women were recruited for the study from their twentieth week of pregnancy. They were evaluated using the inclusion criteria. The women who met the inclusion criteria were further grouped into preeclamptic and non-preeclamptic and were selected randomly. All eligible subjects were adequately counseled, and their informed written consent was obtained before they were included in the study. At the time of booking, complete clinical and medical history was taken from each subject by a trained official using a structured questionnaire. Blood pressure was taken twice in the sitting position after resting for 5 minutes, and the average reading was recorded using a mercury sphygmomanometer with an appropriate cuff at the level of the heart. A dipstick urine measurement for protein was performed on a random urine specimen collected from the patient. Testing was performed using multistix reagent strips (Bayer), and results were reported as negative, 1+, 2+, and 3+. PE was diagnosed with a blood pressure of at least 140/90 mmHg with at least 2+ of protein in the sample. Ethics approval was obtained from the Faculty of Health Sciences and Technology, Nnamdi Azikiwe University, and also from the Holy Rosary Specialist Hospital and Maternity, Onitsha.

Sample collection and storage

Six milliliters of blood was aseptically drawn from the cubital vein using a sterile needle and syringe into a plain bottle. The samples in plain tubes were allowed to clot undisturbed, and serum was separated by centrifugation for 5 minutes at 400 rpm. The serum was stored in a plain bottle at −20°C.

Biochemical estimations

The serum immunoglobulins (IgA, IgM, and IgG) were estimated using kits procured from Linear Chemical, S.L.U Joaquim Costa, Spain, as described by Narayanan.[16] The serum C-reactive protein was estimated by the immunoturbidimetric quantitative assay method.[17] The serum minerals were estimated by the atomic absorption spectroscopic method as described by Kaneko.[18]

Statistical analysis

Data was statistically analyzed using Statistical Package for Social Sciences (SPSS) for window version 21.0 software. All data were expressed as mean ± standard deviation. One-way analysis of variance followed by post-hoc Tukey's test was utilized to test for the differences between groups. Correlations between parameters were estimated using Pearson's correlation coefficient. The acceptable level of significance was $P < 0.05$.

Results

Table 1 shows the age and pressure values in preeclamptic and control subjects. There was a non-significant difference ($P > 0.05$) in the mean values of age, S1,

Table 1: Age and blood pressure values in preeclamptic and control subjects (Mean±SD)

Groups	Age (years)	S1 (mmHg)	D1 (mmHg)	S2 (mmHg)	D2 (mmHg)
Normotensive pregnant subjects (a) *n*=50	31.96±4.05	113.26±4.16	80.00±7.39	113.26±7.48	81.30±9.68
Preeclamptic subjects (b) *n*=50	31.22±5.74	113.33±5.86	81.11±7.85	194.44±15.94	105.56±8.43
Non-pregnant subjects (c) *n*=50	30.05±5.08	110.24±8.14	80.00±7.75	113.57±6.74	80.00±8.37
F	0.770	1.932	0.207	453.986	79.391
P	0.467	0.152	0.814	0.000	0.000
A vs B	*P*=0.854	*P*=0.999	*P*=0.851	*P*=0.000	*P*=0.000
A vs C	*P*=0.439	*P*=0.239	*P*=1.000	*P*=0.996	*P*=0.876
B vs C	*P*=0.684	*P*=0.165	*P*=0.859	*P*=0.000	*P*=0.010

Key: S1: Systolic blood pressure at the first visit to the hospital. D1: Diastolic blood pressure at the first visit to the hospital. S2: Systolic blood pressure at 20 weeks of gestation. D2: Diastolic blood pressure at 20 weeks of gestation. *n*=number of samples. *P*<0.05=significant. Post-hoc: Tukey

Table 2: Levels of serum immunoglobulins (IgG, IgM, and IgA) and CRP in preeclamptic, normotensive pregnant, and non-pregnant subjects (Mean±SD)

Groups	IgG (mg/dl)	IgM (mg/dl)	IgA (mg/dl)	CRP (mg/L)
Normotensive pregnant subjects (a) *n*=50	821.56±96.47	123.87±18.15	101.93±13.05	4.11±1.35
Pe subjects (b) *n*=50	769.43±143.01	101.22±16.44	109.65±22.92	5.37±1.39
Non-pregnant subjects (c) *n*=50	881.71±97.80	111.56±18.71	103.83±9.11	1.09±0.54
F	5.855	11.749	1.549	83.082
P	0.004	0.000	0.219	0.000
A vs B	*P*=0.048	*P*=0.000	*P*=0.233	*P*=0.000
A vs C	*P*=0.228	*P*=0.048	*P*=0.932	*P*=0.001
B vs C	*P*=0.003	*P*=0.087	*P*=0.454	*P*=0.001

Key: IgG: Immunoglobulin G. IgM: Immunoglobulin M. IgA: Immunoglobulin A. CRP: C-reactive protein. *n*=number of samples. *P*<0.05=significant

Table 3: Serum levels of Mn, Zn, and Cu in normotensive pregnant, preeclamptic, and non-pregnant subjects in the study (Mean±SD)

Groups	Mn (µg/dl)	Zn (µg/dl)	Cu (µg/dl)
Normotensive pregnant subjects (a) *n*=50	0.51±0.11	83.57±11.35	53.35±5.02
Preeclamptic subjects (b) *n*=50	0.46±0.11	76.61±16.52	33.78±8.93
Non-pregnant subjects (c) *n*=50	0.68±0.12	106.62±23.11	92.48±9.90
F	25.153	20.395	332.044
P	0.000	0.000	0.000
A vs B	*P*=0.243	*P*=0.294	*P*=0.000
A vs C	*P*=0.000	*P*=0.000	*P*=0.000
B vs C	*P*=0.000	*P*=0.000	*P*=0.000

Key: Mn: Manganese. Zn: Zinc. Cu: Copper. *n*=number of samples. *P*<0.05=significant. Post-hoc: Tukey

Table 4: Correlation of immunoglobulins (IgG, IgM, and IgA), some trace elements, and CRP in subjects with PE

Categories	Mn	Zn	Cu	CRP
PE				
IgM				
r	0.152	0.036	−0.139	−0.136
P	0.375	0.837	0.420	0.430
PE				
IgG				
r	0.245	0.334	−0.221	0.340
P	0.150	0.046*	0.195	0.043*
PE				
IgA				
r	0.052	0.052	−0.036	−0.114
P	0.763	0.764	0.833	0.509

Key: *r*=Pearson correlation coefficient. *n*=number of samples (36)* = significant at *P*<0.05. IgG=Immunoglobulin G. IgA=Immunoglobulin A. IgM=Immunoglobulin M. CRP=C-reactive protein. Mn=manganese. Cu=Copper. Zn=Zinc

and D1 when compared among the preeclamptic, normotensive pregnant, and non-pregnant subjects. However, the S2 and D2 of normotensive pregnant women were significantly decreased ($P < 0.05$) when compared to preeclamptic and non-pregnant subjects in the study. The results of mean serum immunoglobulins and C-reactive protein (CRP) in preeclamptic, normotensive pregnant, and non-pregnant subjects are shown in Table 2. The post-hoc analysis showed that the mean values of IgG and IgM levels were significantly decreased in PE in comparison with the normotensive pregnant and non-pregnant subjects, whereas the mean CRP level was significantly increased in subjects with PE when compared with the normotensive pregnant and non-pregnant subjects in the study ($P < 0.05$). There was a non-significant difference in the mean immunoglobulin A levels when compared among the preeclamptic, normotensive, and non-pregnant subjects ($P > 0.05$). The results of the mean serum levels of the analyzed trace elements are in Table 3. The mean levels of Mn and Zn ions were significantly decreased in subjects with PE when compared with non-pregnant subjects and were also significantly decreased in normotensive pregnant subjects when compared to non-pregnant subjects ($P < 0.05$) but were not significantly different when compared between preeclamptic and normotensive pregnant subjects ($P > 0.05$).

The copper ion levels were significantly decreased in PE subjects when compared with the normotensive and non-pregnant subjects in the study ($P < 0.05$). The mean serum level of IgG showed a positive significant correlation with the mean serum levels of Zn ion (r = 0.334) and CRP (r = 0.340) but non-significantly correlated with the mean serum levels of Mn and Cu ions (r = 0.245 and 0.221), respectively, in subjects with PE, as shown in Table 4.

The mean serum levels of IgM and IgA showed a non-significant correlation with mean serum levels of Mn, Zn, and Cu ions and CRP ($P > 0.05$). In Table 4, a significant positive correlation exists between the mean serum levels of IgG and IgA (r = 0.746) and also between IgA and IgM (r = 0.507). There was a non-significant relationship between IgG and IgM (r = 0.490) in subjects

with PE. A significant inverse correlation exists between the mean values of systolic blood pressure and mean serum levels of manganese ion (r = −0.146). However, an inverse correlation also exists between the mean serum levels of immunoglobulins G, A, and M and the mean values of systolic and diastolic blood pressure, which were statistically non-significant ($P > 0.05$).

Discussion

The mechanisms involved in the pathogenesis of PE remain uncertain; therefore, the search for a better understanding of the disorder and its subsequent prevention continues. In this study, the mean level of immunoglobulin G was observed to be significantly lower in normotensive pregnant women when compared to non-pregnant subjects.

This is in line with a previous study[19] which reported that the mean levels of immunoglobulins, IgG and IgM, were reduced in the normal pregnant subjects compared to the non-pregnant subjects but varied from the report by Al-Hayani,[20] who observed that the mean levels of IgG and IgM were significantly higher in subjects with normal pregnancy when compared with non-pregnant controls. However, no statistical difference was observed for IgA between the two groups in the study. This is in concordance with a previous report.[12]

The study compared the immunoglobulins between normal and PE-complicated pregnancies and found the mean serum levels of immunoglobulins G and M to be significantly decreased and non-significant difference in IgA in preeclamptic women when compared with normotensive pregnant and non-pregnant subjects. This agrees with the findings by Amah-Tariah *et al*.[21] However, it disagrees with that of Arinola *et al*.[12] who reported a significant decrease in IgA and a non-significant difference in IgM in PE compared to normotensive subjects and Ashan *et al*.[13] who reported a significant increase in the immunoglobulins in PE when compared to normotensives. Several health conditions including pregnancy and the presence of disease (s) affect the immune system of an individual.

The reductions in the immunoglobulins as seen in this study could be an indication of the positive outcome of a normal pregnancy. There may be mild suppression of the maternal immune system response to allow for protection for the growing placenta and fetus. It could be suggested that for a successful outcome of pregnancy, the sensitivity of maternal immunity is reduced to tolerate the developing allograft. However, the event of markedly increased or decreased immune responses in pregnancy may result in some forms of complexities.

Reports have shown that not only is the immune function affected in disease conditions in non-pregnant states but much more severe during pregnancy. However, the roles of immunoglobulins in PE remain unclear; in some cases, they develop protective mechanisms which, when overwhelmed or inadequate, allow PE to occur. In other cases, they can form part of the cascade of aggressions, leading to the abnormalities encountered in PE. This would also mean alterations in the immune-related complications in pregnancy. The decrease in IgG and IgM in PE could be a result of associated immunosuppression or could be due to increased urinary losses of the immunoglobulins, especially the intermediate group of macroglobulins, or due to depression in their synthesis.[22]

This study observed the mean CRP to be significantly elevated in pregnant women when compared to non-pregnant subjects and also in PE when compared to normotensive subjects. This corroborated another previous study.[23] CRP is a hepatically derived classical acute phase reactant, although not specific as a sensitive indicator of an overall inflammatory process within the body. It increases in infections and malignancy and binds to chromatin and small nuclear ribonucleoprotein particles. Interestingly, there is evidence that normal pregnancy itself stimulates the maternal inflammatory response, and CRP levels are elevated in healthy pregnant women compared with non-pregnant women, although to a lesser extent than seen in PE.[24] In PE, increased CRP reflects the presence of an underlying systematic inflammatory disorder, an acute phase response induced by pro-inflammatory cytokines (interleukin 1 and 6) secreted from the inflamed tissue by parenchymal or inflammatory tissues, resulting in the synthesis of the acute phase proteins, and this goes to suggest that inflammation could play an important role in the pathogenesis of PE.[23] Again, there is increasing evidence that endothelial cell damage associated with placental dysfunction may be central to its pathogenesis and this damage is accompanied by elevated inflammatory markers. Furthermore, there is human evidence showing the CRP transcript in syncytiotrophoblast cells of normal placentas, but it further increased in the placentas with PE, indicating that syncytiotrophoblast cells in the placenta are a previously unrecognized additional source for increased circulating CRP seen in patients with PE. This pathogenicity of CRP in pregnant mice was sufficient to regenerate the key features of PE, including hypertension, proteinuria, kidney damage, and impaired placentas.[25] In this study, significantly lower levels of all the trace elements were observed in the pregnant women compared to the non-pregnant controls. These observed lower levels may be a result of the increase in

body requirements during pregnancy to meet the mother and baby's needs. However, a further decrease was observed in preeclamptic women when compared to the normotensive pregnant women, suggesting their possible involvement in the development and pathogenesis of PE.

Trace elements are crucial for maintaining human health, as well as for preventing several health problems. Alteration of normal homeostasis of trace elements may adversely affect biological processes, leading to many disease processes.[25] Trace elements are present as metalloproteins (zinc), ceruloplasmin (copper), superoxide dismutase (Cu, Zn, and Mn), and hemoglobin (iron), indicating that deficiency or decreased concentration may be a predisposing factor in the development of PE. Decreased zinc levels in our study agreed with the reports from other studies where preeclamptic women had 43% lower zinc levels than normotensives.[26] Akhtar *et al*.[27] and Al-Jameil *et al*.[2] also noted reduced levels of zinc in women with PE. The finding was, however, different from some other findings[28,29] that reported non-insignificant differences between the serum zinc levels in preeclamptics and non-preeclamptics.

Zinc (Zn) is an important trace element in metabolism, growth, development, and reproduction. It is a structural component of several proteins such as growth factors, cytokines, receptors, enzymes, and transcription which play an important role in the cellular signaling pathways. Approximately 10% of all proteins in the human body bind with zinc, and the biological activity of these zinc-bound proteins depends on the concentration of zinc in the body.[30] Its deficiency has been associated with complications of pregnancy, part of which is PE. Zinc is passively transferred from the mother to the fetus across the placenta, and there is also decreased zinc binding capacity of maternal blood during pregnancy, which facilitates efficient transfer of zinc from the mother to the fetus. During pregnancy, there is a decline in circulating zinc, and this increases as the pregnancy progresses, possibly due to the decrease in the zinc binding capacity of maternal blood and increased transfer of zinc from the mother to the fetus. Zinc is essential for proper growth of the fetus, and a fall in zinc during pregnancy could also be a physiological response to expanded maternal blood volume. In addition, zinc deficiency has a negative effect on the Cu–Zn superoxide dismutase enzyme system.[31,32] Subsequently, impaired Cu–Zn superoxide dismutase activity contributes to oxidative damage in the body, which may worsen several disease states.[33] Besides, it has been reported that zinc deficiency can increase the susceptibility of neurons to oxidative stress[34] and also a defect in the transport of many vital elements such as Mn and iron because of a decrease in zinc–iron–protein (ZIP) transporters. It was reported that an increased incidence of PE in zinc-deficient regions was corrected by zinc supplementation in those regions.[35]

This study also observed significantly lower levels of serum copper between the preeclamptic and normotensive women. This finding corroborated the findings of Ugwuja *et al*.[28] and Ikaraoha *et al*.,[26] respectively, but disagreed with those of Diaz *et al*.[36] and Ilhan and Simsek,[37] who reported an increase in copper levels in PE. Copper has been shown to be involved in the function of several cupro-enzymes that are pertinent for life. Copper is a component of ceruloplasmin and superoxide dismutase, which are notable antioxidants. This has led to the conclusion by some researchers that copper deficiency may increase the risk of vascular diseases.[38]

Manganese levels were also found to be significantly lower in preeclamptics when compared to the normotensives. This agreed with a previous report.[28] Manganese acts as a cofactor for a large number of enzymatic systems including transferases, oxidoreductases, hydrolases, lyases, isomerases, ligases, and lectins. Recent evidence suggests that manganese concentrations may be affected by the deficiency of zinc because some ZIP transporters including ZIP8 and ZIP14 also mobilize manganese across biological membranes, and thus, manganese homeostasis is regulated by these zinc transporters.[39]

Manganese is a component of the Mn-superoxide dismutase (MnSOD) enzyme system that deals with the toxic effect of superoxide, formed from the electron reduction of dioxygen.[40] It has been reported that MnSOD deficiency enhanced 12-0-tetradecanoylphorbol-13-acetate (TPA)-induced oxidative stress, and uncontained reactive oxygen species (ROS) cause tissue damage and dysfunction by directly attacking and denaturing functional and structural molecules and by activating redox-sensitive transcription factors and signal transduction pathways, thus playing a critical part in the pathogenesis of many acute and chronic illnesses, including hypertension.[41,42]

Copper, zinc, and manganese are essential components of the antioxidant enzyme superoxide dismutase, which is involved in the destruction of free radicals/ROS, and consequently protect cells from damage. Their deficiency might cause insufficiency of the superoxide dismutase enzyme system, thereby exposing women to free radical/ROS accumulation and oxidative stress and cell damage, which results in oxidative stress, playing a critical role as a possible mediator of endothelial cell dysfunction,[43]

hypertension, and thus clinical manifestations of PE.[44] Therefore, it seems that as there is an increase in oxidative stress, copper, zinc, selenium, and manganese get involved in the antioxidant mechanism, and it is reduced in the process,[26] thus possibly explaining their decrease in women with PE compared to the normal pregnant women as observed in the present study. The relatively lower level of these trace elements in preeclamptic pregnant women compared with healthy pregnant women may also result from hemodilution due to fluid retention in these patients, transfer of these minerals from the mother to the growing fetus, and increased excretion of these minerals in urine.

This study therefore reveals significantly lower levels of immunoglobulins and trace elements among the preeclamptic subjects. These micronutrient deficiencies and low levels of immunoglobulins could be risk factors for the development of high blood pressure and PE.

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Conflicts of interest

There are no conflicts of interest.

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