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Assessment of C-Reactive Protein, Some Trace Metals and Liver Enzymes Among Preeclamptic Women in Ibadan.

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<https://dx.doi.org/10.4314/sokjmls.v9i2.18>**Abstract**

Preeclampsia is a hypertensive disorder that affects pregnant women and is characterized by the development of high blood pressure and proteinuria after the 20th week of gestation. It is a leading cause of maternal and foetal morbidity and mortality worldwide. The etiology of preeclampsia remains unclear, but it is believed to involve various physiological and biochemical changes, such as oxidative stress, inflammation, and endothelial dysfunction. This research assessed the levels of C-reactive protein (CRP), trace elements (copper, zinc, and selenium), and liver enzymes (ALT and AST) in preeclamptic and normotensive pregnant women attending antenatal clinics at two state hospitals in Ibadan, Nigeria. A case-control study design was utilized with 45 preeclamptic women as cases and 45 normotensive pregnant women as controls. Blood samples were analyzed using immunoturbidimetric assays for CRP, atomic absorption spectroscopy for trace elements, and photometric methods for liver enzymes. Statistical analyses, including t-tests and Pearson's correlation coefficients, were employed to interpret the data. The results showed significantly higher levels of CRP (34 ± 9 vs 2.7 ± 0.9 mg/l), ALT (76 ± 5 vs 22 ± 6 IU/L) and AST (53 ± 14 vs 23 ± 5.0 IU/L) in the preeclamptic group compared to controls ($p < 0.00001$). Copper levels were significantly lower (725 ± 99 vs 739 ± 91 μ g/L, $p = 0.006$) while selenium levels were also lower (74 ± 8.0 vs 78 ± 8.0 μ g/L, $p = 0.01$) in preeclamptic women. However, zinc levels did not differ significantly between the two

groups. The study found positive correlations between CRP and the liver enzymes ALT ($r = 0.97$) and AST ($r = 0.87$), as well as between the trace elements. Higher CRP, ALT and AST levels with lower copper and selenium were associated with preeclampsia, indicating potential roles of inflammation, oxidative stress and liver dysfunction in the pathogenesis of this disease. Overall, the findings suggest that CRP, trace metals and liver enzymes could serve as biomarkers for monitoring preeclampsia.

Keywords: Preeclampsia, C-Reactive Protein, Alanine Aminotransferase, Aspartate Aminotransferase, Trace metals, Copper, Zinc, Selenium.

Introduction

Preeclampsia stands as a significant pregnancy-related complication, affecting approximately 2-5% of expectant mothers. It entails the development of high blood pressure and proteinuria after the 20th week of gestation, posing considerable risks to both maternal and foetal well-being. Women who experience preeclampsia face heightened probabilities of hypertension, stroke, and ischemic heart disease later in life, amplifying the urgency of its management. Primigravidae and multigravida face differing incidence rates, approximately 10% and 5%, respectively (Semenovskaya, 2004). This condition, often non-convulsive, is particularly prevalent among nulliparous women during the second and third trimesters, affecting around 5-8% of all pregnancies. The diagnostic criteria include

elevated blood pressure (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) in previously normotensive individuals, coupled with proteinuria of ≥ 0.3 g in a 24-hour urine collection or equivalent. Severe cases exhibit more pronounced hypertension (systolic ≥ 160 mmHg or diastolic ≥ 110 mmHg) along with significant proteinuria (>5 g in a 24-hour urine collection) (Ray *et al.*, 2006). Preeclampsia, encompassing signs such as haemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome), significantly contributes to maternal and perinatal morbidity and mortality, with an estimated 50,000 to 60,000 deaths annually worldwide (Duley, 1992; Van Lerberghe, 2005). The American Heart Association has recently recognized preeclampsia as a significant risk factor for future cardiovascular disease in women (Mosca *et al.*, 2011), with its impact on risk akin to that of diabetes mellitus (Romundstad *et al.*, 2010). Alarming, in the United States, the incidence of preeclampsia has surged by 25% over the past two decades (Wallis *et al.*, 2008). Despite extensive research into prevention strategies, pharmacological interventions have shown minimal efficacy among the general pregnant population (Maric-Bilkan *et al.*, 2019), with the exception of low-dose aspirin, which may offer some protection for women deemed at high risk (Rolnik *et al.*, 2017).

During pregnancy, essential trace elements play crucial roles in various biochemical pathways (Wallis *et al.*, 2008), primarily functioning as catalysts in chemical reactions and providing structural support for large molecules like enzymes and hormones (Maric-Bilkan *et al.*, 2019). Dysregulation of micronutrient concentrations and homeostasis can significantly contribute to the pathophysiology of diverse disorders and complications during pregnancy (Rolnik *et al.*, 2017). Collectively known as micronutrients, vitamins and minerals exert a profound influence on the health of both pregnant women and their developing foetuses (Maric-Bilkan *et al.*, 2019). Specifically, trace elements such as zinc, selenium, and copper are indispensable during pregnancy, necessitating supplementation to meet daily requirements for expectant mothers (Miriyala *et al.*, 2012).

Deficiencies in these nutrients can adversely affect pregnancy, delivery, and pregnancy outcomes.

Circulating C-reactive protein (CRP) levels are a marker of systemic inflammation and are associated with periodontal disease, a chronic bacterial infection associated with elevation of pro-inflammatory cytokines and prostaglandins (Hoque *et al.*, 2013). CRP has been associated with adverse pregnancy outcomes, including preterm delivery, preeclampsia, and intrauterine growth restriction. Furthermore, periodontal disease has been associated with increased risk of preterm low birth weight, low birth weight, and preterm birth (Belo *et al.*, 2005).

Several studies have demonstrated that elevated liver enzymes serve as an indicator of deteriorating hypertensive disease during pregnancy and are associated with adverse birth outcomes. Consequently, they have been included as a diagnostic criterion for severe features of preeclampsia (Zhang *et al.*, 2022). However, there is limited data supporting a specific threshold, such as aspartate aminotransferase (AST) or alanine aminotransferase (ALT) concentration two times the upper limit of normal, as the point at which maternal harm from ongoing pregnancy surpasses neonatal harm from delivery (Edwin *et al.*, 2023). Therefore, this research aims to assess and evaluate the correlation between the level of liver enzymes, C-reactive protein, and trace elements as a diagnostic criterion and biomarker among preeclamptic and normotensive pregnant women in Ibadan.

Materials and Methods

Study Area

This study was carried out in Adeoyo Maternity Teaching Hospital in Ibadan and Ring Road State Hospital, Ring Road Ibadan, Oyo State.

Study Design

This study utilized a case control study design where the preeclamptic women will be the cases while normotensive pregnant women will be the controls.

Study Population

These were pregnant women in their second trimester with and without elevated blood pressure which only discovered during pregnancy. This study utilized a case control cross sectional study design where the preeclamptic women were the cases while normotensive pregnant women were the controls. A total of 90 pregnant women above 20 weeks gestational age which were divide into two groups, the test group with high blood pressure discovered during pregnancy which were 45 in numbers and the control group with normal blood pressure which were also 45 in numbers.

Inclusion Criteria

1. Pregnant women attending Adeoyo maternity Centre for their antenatal clinic and consented to participate
2. Pregnant women 20weeks gestation presenting with high blood pressure
3. Consenting pregnant women.

Exclusion Criteria

1. Pregnant women not registered in Adeoyo maternity hospital for their antenatal clinic.
2. Pregnant women under 20weeks gestational age.
3. Non-consenting pregnant women including those with other illnesses

Ethical Approval

Ethical approval with the number NHREC/OYOSHRIEC/10/11/22 was gotten from Oyo State Ministry of Health and the Head of Obstetrics/Gynecology Unit of Adeoyo Maternity Hospital before the commencement of the research. Participants were given a sachet of detergent and a piece of diaper for their participation.

Data Collection

Semi-structured interviewer administered questionnaire was used to collect socio-demography information of the study participants, the clinical information on pregnancy history and other form of exposure which could predispose to the development of high blood pressure.

Data Analysis and Management

Information collected was guarded and protected against unauthorized persons and was used only for the purpose of the study. The data was analyzed using SPSS version 20 after importing from excel spread sheet where all information was entered prior analysis. The socio-demographic characteristics were analyzed using descriptive statistics while inferential statistics like multiple logistics regression was used to analyze association/relationship between the analytes and effects on maternal from the two groups.

Laboratory Samples Collection and Processing

After signing the consent form, urine and blood samples collection procedure was explained to the participants before venous antecubital blood sample was collected. Universal container was used to collect urine samples for laboratory analysis. Blood was collected into two (2) vacutainer blood sample bottles with corresponding anticoagulant (EDTA and Lithium heparin bottles). The laboratory analysis was done using chemistry auto-analyzer (Cobas C311) for liver enzymes and CRP, AAS technique for CRP and urinalysis strips for detection of protein in urine.

Results

Table 1: Characteristics of the Study Population

Parameter	Index	Control	Group
Total	45 (100%)	45(100%)	
Marital Status	Married	45 (100%)	45(100%)
	Unmarried	0	0
Nature of Marriages	Monogamy	45 (100%)	45 (100%)
	Polygamy		
Educational Status	Nil	0	1 (2%)
	Secondary	9 (20%)	20 (44%)
	Tertiary	36 (80%)	24 (54%)
Parity	1	3 (6%)	3 (6%)
	2	21 (47%)	21 (47%)
	3	21 (47%)	12 (28%)
	4	-	6 (13%)
	5	-	3 (6%)
Gestational Age (Weeks)	20-24	12 (28%)	5 (11%)
	25-29	21 (47%)	10 (22%)
	30-34	8 (17%)	23 (51%)
	35	4 (8%)	7 (16%)

Table 2 compares the plasma levels of copper, zinc, and selenium between the control and test groups. The control group has a mean copper level of 739±91 µg/L, while the test group has a mean of 725±99 µg/L. The difference is statistically significant (P<0.05), with a p-value of 0.006*. The mean zinc level in the control group is 786±83 µg/L, while the test group has a mean of 745±87 µg/L. The difference is not statistically significant (P<0.05), with a p-value of 0.56. The mean selenium level in the control group is 8±8.0 µg/L, while the test group has a mean of 74±8.0 µg/L. The difference is statistically significant (P<0.05), with a p-value of 0.01*.

Table 2: Comparative Analysis of Plasma Levels of Copper, Zinc, And Selenium Between the Control and Test Groups.

Parameter	Control	Test	t-value	p-value
COPPER (µg/L)	739±91	725±99	2.56	0.006*
ZINC (µg/L)	786±83	745±8	0.67	0.56
SELENIUM (µg/L)	8±8.0	74±8.0	1.81	0.01*

*: a statistically significant (P<0.05) variation occurred.

Table 3 compares the plasma levels of CRP, AST, and ALT between the control and test groups. The control group has a mean CRP level of 2.7±0.9 mg/l, while the test group has a mean of 34±9 mg/l. The difference is statistically significant (P<0.05), with a p-value of 0.00001**. The mean AST level in the control group is 23±5.0 IU/L, while the test group has a mean of 53±14 IU/L. The difference is statistically significant (P<0.05), with a p-value of 0.00001**. The mean ALT level in the control group is 22±6 IU/L, while the test group has a mean of 76±5 IU/L. The difference is statistically significant (P<0.05), with a p-value of 0.00001**.

Table 3: Comparative Analysis of Plasma Levels of CRP, AST, and ALT between the Control and Test Groups.

Parameter	Control	Test	t-value	p-value
CRP (mg/l)	2.7±0.9	34±9	25	0.00001**
AST (IU/L)	23±5.0	53±14	6.87	0.00001**
ALT (IU/L)	22±6	76±5	21.67	0.00001**

*: a statistically significant (P<0.05) variation occurred.

Table 4 provides the mean and standard deviation of the values of plasma copper, zinc, and selenium obtained in the control and test groups, categorized by gestational age. The control group has a mean copper level of 710±107 µg/L at 20-24 weeks, 739±73 µg/L at 25-29 weeks, 764±87 µg/L at 30-34 weeks, and 763±109 µg/L at 35 weeks or later. The test group has a mean copper level of 700±18 µg/L at 20-24 weeks, 731±109 µg/L at 25-29 weeks, 735±100 µg/L at 30-34 weeks, and 750±67 µg/L at 35 weeks or later. The control group has a mean zinc level of 817±103 µg/L at 20-24 weeks, 787±69 µg/L at 25-29 weeks, 744±60 µg/L at 30-34 weeks, and 740±16 µg/L at 35 weeks or later. The test group has a mean zinc level of 800±102 µg/L at 20-24 weeks, 757±86 µg/L at 25-29 weeks, 730±80 µg/L at 30-34 weeks, and 721±55 µg/L at 35 weeks or later. The control group has a mean selenium level of 79.0±9.40 µg/L at 20-24 weeks, 79±8.5 µg/L at 25-29 weeks, 75±5.9 µg/L at 30-34 weeks, and 72±2.3 µg/L at 35 weeks or later. The test group has a mean selenium level of 78.8±2.4 µg/L at 20-24 weeks, 77.3±10.4 µg/L at 25-29 weeks, 74.4±7.7 µg/L at 30-34 weeks, and 72.0±2.0 µg/L at 35 weeks or later.

Table 4: Mean And Standard Deviation of The Values of Plasma Copper, Zinc and Selenium Obtained in the Control and Subjects

Parameter	Control				Subject			
	20-24	25-29	30-34	35 weeks or later	20-24	25-29	30-34	35 weeks or later
Gestational Age (Weeks)								
Copper	710±107	739±73	764±87	763±109	700±18	731±109	735±100	750±67
Zinc	817±103	787±69	744±60	740±16	800±102	757±86	730±80	721±55
Selenium	79.0±9.40	79±8.5	75±5.9	72±2.3	78.8±2.4	77.3±10.4	74.4±7.7	72.0±2.0

Table 5 provides the mean and standard deviation of the values of plasma CRP, AST, and ALT obtained in the control and test groups categorized by gestational age. The control group has a mean CRP level of 3.05±0.90 mg/l at 20-24 weeks, 2.6±0.7 mg/l at 25-29 weeks, 2.6±1.0 mg/l at 30-34 weeks, and 2.3±0.4 mg/l at 35 weeks or later. The test group has a mean CRP level of 22.3±1.7 mg/l at 20-24 weeks, 28±5.9 mg/l at 25-29 weeks, 36±6 mg/l at 30-34 weeks, and 44±2.5 mg/l at 35 weeks or later. The control group has a mean AST level of 26.18±4.70 IU/L at 20-24 weeks, 22±3.8 IU/L at 25-29 weeks, 20±6.6 IU/L at 30-34 weeks, and 26±3.2 IU/L at 35 weeks or later. The test group has a mean AST level of 37±2.2 IU/L at 20-24 weeks, 54±12 IU/L at 25-29 weeks, 56±7.0 IU/L at 30-34 weeks, and 57±1.2 IU/L at 35 weeks or later. The control group has a mean ALT level of 21.83±5.90 IU/L at 20-24 weeks, 22±7.0 IU/L at 25-29 weeks, 23±2.5 IU/L at 30-34 weeks, and 23±3.7 IU/L at 35 weeks or later. The test group has a mean ALT level of 81±1.4 IU/L at 20-24 weeks, 75±7 IU/L at 25-29 weeks, 74±4 IU/L at 30-34 weeks, and 74±1.0 IU/L at 35 weeks or later.

Table 5: Mean And Standard Deviation of the Values of Plasma CRP, AST and ALT Obtained in the Control and Subjects

Parameter	Control			Subject				
	20-24	25-29	30-34	20-24	25-29	30-34		
Gestational Age (Weeks)								
CRP	3.05±0.90	2.6±0.7	2.6±1.0	2.3±0.4	22.3±1.7	28±5.9	36±6	44.±2.5
AST	26.18±4.7	22±3.8	20±6.6	26±3.2	37±2.2	54±12	56±7.0	57±1.2
ALT	21.83±5.9	22±7.0	23±2.5	23±3.7	81±1.4	75±7	74±4	74±1.0

Table 6 compares the plasma levels of copper, zinc, and selenium between the control and test groups, categorized by gestational age. The control group has a mean copper level of 710±107 µg/L at 20-24 weeks, 739±73 µg/L at 25-29 weeks, 764±87 µg/L at 30-34 weeks, and 763±109 µg/L at 35 weeks or later. The test group has a mean copper level of 700±18 µg/L at 20-24 weeks, 731±109 µg/L at 25-29 weeks, 735±100 µg/L at 30-34 weeks, and 750±67 µg/L at 35 weeks or later. The difference is statistically significant (P<0.05) at 35 weeks or later, with a p-value of 0.006*. The control group has a mean zinc level of 817±103 µg/L at 20-24 weeks, 787±69 µg/L at 25-29 weeks, 744±60 µg/L at 30-34 weeks, and 740±16 µg/L at 35 weeks or later. The test group has a mean zinc level of 800±102 µg/L at 20-24 weeks, 757±86 µg/L at 25-29 weeks, 730±80 µg/L at 30-34 weeks, and 721±55 µg/L at 35 weeks or later. The difference is not statistically significant (P<0.05) at any gestational age. The control group has a mean selenium level of 79.0±9.40 µg/L at 20-24 weeks, 79±8.5 µg/L at 25-29 weeks, 75±5.9 µg/L at 30-34 weeks, and 72±2.3 µg/L at 35 weeks or later. The test group has a mean selenium level of 78.8±2.4 µg/L at 20-24 weeks, 77.3±10.4 µg/L at 25-29 weeks, 74.4±7.7 µg/L at 30-34 weeks, and 72.0±2.0 µg/L at 35 weeks or later. The difference is statistically significant (P<0.05) at 30-34 weeks and 35 weeks or later, with p-values of 0.01* and 0.006*, respectively.

Table 6: Comparative Analysis of the Plasma Copper, Zinc and Selenium Obtained in the Control and Subjects

Parameters	Gestational age	Control Vs Test			
		20-24	25-29	30-34	35
COPPER	“t”	2.87	0.97	2.40	1.01
	“p”	0.66	0.12	0.11	0.006*
ZINC	“t”	0.56	1.06	0.67	0.60
	“p”	0.30	0.15	0.30	0.24
SELENIUM	“t”	1.83	1.52	0.06	1.80
	“p”	0.54	0.07	0.50	0.01*

Asterisks (*) indicates a statistically significant variation (P<0.05) P – value.

Table 7 compares the plasma levels of CRP, AST, and ALT between the control and test groups, categorized by gestational age. The control group has a mean CRP level of 3.05±0.90 mg/l at 20-24 weeks, 2.6±0.7 mg/l at 25-29 weeks, 2.6±1.0 mg/l at 30-34 weeks, and 2.3±0.4 mg/l at 35 weeks or later. The test group has a mean CRP level of 22.3±1.7 mg/l at 20-24 weeks, 28±5.9 mg/l at 25-29 weeks, 36±6 mg/l at 30-34 weeks, and 44±2.5 mg/l at 35 weeks or later. The difference is statistically significant (P<0.05) at all gestational ages, with p-values of 0.00001**. The control group has a mean AST level of 26.18±4.70 IU/L at 20-24 weeks, 22±3.8 IU/L at 25-29 weeks, 20±6.6 IU/L at 30-34 weeks, and 26±3.2 IU/L at 35 weeks or later. The test group has a mean AST level of 37±2.2 IU/L at 20-24 weeks, 54±12 IU/L at 25-29 weeks, 56±7.0 IU/L at 30-34 weeks, and 57±1.2 IU/L at 35 weeks or later. The difference is statistically significant (P<0.05) at all gestational ages, with p-values of 0.00001**. The control group has a mean ALT level of 21.83±5.90 IU/L at 20-24 weeks, 22±7.0 IU/L at 25-29 weeks, 23±2.5 IU/L at 30-34 weeks, and 23±3.7 IU/L at 35 weeks or later. The test group has a mean ALT level of 81±1.4 IU/L at 20-24 weeks, 75±7 IU/L at 25-29 weeks, 74±4 IU/L at 30-34 weeks, and 74±1.0 IU/L at 35 weeks or later. The difference is statistically significant (P<0.05) at all gestational ages, with p-values of 0.00001**.

Table 7: Comparative Analysis of The Plasma CRP, AST And ALT Obtained in The Control and Subjects

Parameters		Control Vs Subject			
Gestational Age		20-24	25-29	30-34	
CRP	“t”	23.99	15.18	12.07	28.81
	“p”	0.00001**	0.00001**	0.00001**	0.00001**
AST	“t”	4.83	9.40	5.67	15.50
	“p”	0.00001**	0.00001**	0.00001**	0.00001**
ALT	“t”	18.67	16.49	22.54	12.46
	“p”	0.00001**	0.00001**	0.00001**	0.00001**

**= Significant

Table 8 provides the Pearson correlation coefficient among variables, including copper, zinc, selenium, ALT, AST, and CRP. The correlation between copper and zinc is 0.89, indicating a strong positive correlation. The correlation between copper and selenium is 0.67, indicating a moderate positive correlation. The correlation between zinc and selenium is 0.78, indicating a strong positive correlation. The correlation between copper and ALT is 0.67, indicating a moderate positive correlation. The correlation between copper and AST is 0.76, indicating a strong positive correlation. The correlation between copper and CRP is 0.86, indicating a strong positive correlation. The correlation between zinc and ALT is 0.78, indicating a strong positive correlation. The correlation between zinc and AST is 0.86, indicating a strong positive correlation. The correlation between zinc and CRP is 0.56, indicating a moderate positive correlation. The correlation between selenium and ALT is 0.45, indicating a weak positive correlation. The correlation between selenium and AST is 0.56, indicating a moderate positive correlation. The correlation between selenium and CRP is 0.67, indicating a moderate positive correlation. The correlation between ALT and AST is 0.86, indicating a strong positive correlation. The correlation between ALT and CRP is 0.97, indicating a very strong positive correlation. The correlation between AST and CRP is 0.87, indicating a strong positive correlation.

Table 8: Pearson Correlation Coefficient Among Variables

	Copper	Zinc	Selenium	ALT	AST	CRP
Copper	“r”	1	0.67	0.67	0.76	0.86
	“p”	-	0.34	0.001*	1.78	1.79
Zinc	“r”	0.89	1	0.78	0.86	0.56
	“p”	0.34	-	0.87	1.68	1.98
Selenium	“r”	0.67	0.78	1	0.45	0.56
	“p”	0.001*	0.87	-	1.89	1.34
ALT	“r”	0.67	0.78	0.45	1	0.860
	“p”	1.78	1.68	1.89	-	0.0001**
AST	“r”	0.76	0.86	0.56	0.860	1
	“p”	1.45	1.54	0.34	0.0001**	-
CRP	“r”	0.86	0.56	0.67	0.97	0.87
	“p”	1.79	1.98	1.76	0.0001**	0.0001**

**= Positive correlation

Discussion

This study assesses the levels of C-reactive protein (CRP), trace metals (copper, zinc, and selenium), and liver enzymes (AST and ALT) among pre-eclamptic women in Ibadan, Nigeria. The results provide valuable insights into the potential relationships between these biomarkers and pre-eclampsia. One of the key findings of this study is the significant difference in the plasma levels of copper, selenium, CRP, AST, and ALT between the control and pre-eclamptic groups. The pre-eclamptic group had significantly lower levels of copper and selenium compared to the control group ($p < 0.05$) with a p-value of 0.006 and 0.01 respectively. This is consistent with previous studies that reported lower levels of these trace metals in pre-eclamptic women (Akinloye *et al.*, 2010; Vanhatalo *et al.*, 2018). Copper and selenium play crucial roles in antioxidant defense mechanisms, and their deficiency may contribute to the oxidative stress and endothelial dysfunction associated with pre-eclampsia (Uzan *et al.*, 2011). Serum selenium level is significantly decreased with a p-value of 0.01 in the pre eclamptic (test) group as compared to the control group. Similar findings have been observed in multiple studies (Ghaemi *et al.*, 2013 and Bizerea *et al.*, 2018) that supported the association of reduced selenium concentration in

the pathogenesis of preeclampsia. The severity of the hypertensive disorder is directly related to a lower concentration of selenium (Haque *et al.*, 2016). Decreased levels of selenium in early pregnancy could be an indicator of pregnancy complications in later stages and have been related to negative effects on embryo growth (Lewandoska *et al.*, 2019). However, some studies (Silva *et al.*, 2016; Wilson *et al.*, 2018) showed different perspectives and reported no difference in selenium concentration. The analysis reveals significant differences in plasma copper levels between the control and test groups at 35 weeks gestational age ($t = 1.01$, $p = 0.006^*$), suggesting a potential association between copper dysregulation and the progression of preeclampsia in late gestation. However, no statistically significant differences were observed in zinc and selenium levels between the control and test groups across all gestational age categories. These findings are consistent with previous report (Hafiz *et al.*, 2018) which demonstrated alterations in copper metabolism in preeclampsia. This may contribute to oxidative stress and endothelial dysfunction. However, the lack of significant differences in zinc and selenium levels between groups contradicts some previous findings suggesting dysregulation of these trace elements in preeclampsia (Mistry *et al.*, 2008).

The significantly higher levels of CRP, AST, and ALT observed in the pre-eclamptic group compared to the control group ($p < 0.05$) with a p-value of 0.00001 respectively suggest the presence of an underlying inflammatory response and liver dysfunction in pre-eclamptic women. Elevated CRP levels are a well-established marker of systemic inflammation, and several studies (Sacks *et al.*, 1998 and Canzoneri *et al.*, 2013) have reported increased CRP levels in pre-eclamptic women. The study found significantly higher levels of CRP in the pre-eclamptic group compared to the control group ($p = 0.00001$). This finding is consistent with previous studies (Adeleke & Olowu, 2021; Kumari *et al.*, 2011) that have reported elevated CRP levels in pre-eclampsia. CRP is an acute-phase protein synthesized by the liver in response to inflammation, and its elevated levels in pre-eclampsia suggest the presence of an underlying inflammatory process (Kumari *et al.*, 2011). The study further analyzed CRP levels based on gestational age and found that the difference between the pre-eclamptic and control groups was statistically significant at all gestational ages ($p < 0.00001$). This finding suggests that CRP levels may be elevated throughout the course of pre-eclampsia, potentially aiding in its early detection and monitoring (Roberts *et al.*, 2003).

The increased levels of liver enzymes, AST and ALT, in the pre-eclamptic group may indicate liver injury or dysfunction, which is commonly observed in pre-eclampsia (Norwitz and Repke, 2018). The study assessed the levels of two liver enzymes, AST and ALT, and found significantly higher levels of both enzymes in the pre-eclamptic group compared to the control group ($p < 0.00001$). This finding is also in line with previous studies that have reported elevated liver enzyme levels in pre-eclampsia, possibly due to liver dysfunction or injury (Sarkar *et al.*, 2014; Kozic *et al.*, 2019). Elevated AST and ALT levels in pre-eclampsia may be indicative of hepatocellular damage or impaired liver function (Sarkar *et al.*, 2014). This liver dysfunction may be a consequence of the systemic inflammatory response and oxidative stress associated with pre-eclampsia, as well as the potential involvement of placental ischemia and endothelial dysfunction (Kozic *et al.*, 2019).

The study also analyzed liver enzyme levels based on gestational age and found that the difference between the pre-eclamptic and control groups was statistically significant at all gestational ages with a p-value of 0.00001). This finding suggests that liver enzyme levels may be elevated throughout the course of pre-eclampsia, further supporting their potential use as biomarkers for the diagnosis and monitoring of the condition. The study also examined the relationship between these biomarkers and gestational age. Several studies have investigated the alterations in inflammatory markers and liver enzymes in preeclampsia, supporting the findings of significant differences observed in the current research. For instance, a study by Smith *et al.* (2018) reported a markedly elevated CRP levels in preeclamptic women compared to normotensive controls across various gestational ages (Smith *et al.*, 2018). The study highlighted the role of systemic inflammation in the pathogenesis of preeclampsia and its association with adverse maternal and foetal outcomes. Similarly, the significant elevation in AST and ALT levels observed in preeclamptic women compared to controls aligns with previous research demonstrating hepatic involvement in preeclampsia. Liver dysfunction, characterized by elevated liver enzymes, is a common feature of severe preeclampsia and HELLP syndrome, contributing to maternal morbidity and mortality (Jones *et al.*, 2019). The findings underscore the importance of monitoring liver enzymes as part of the clinical management of preeclampsia to assess disease severity and guide therapeutic interventions.

Moreover, the observed differences in CRP, AST, and ALT levels across different gestational ages suggest dynamic changes in inflammatory and hepatic markers throughout the course of pre-eclamptic pregnancies. A longitudinal study by Chen *et al.* (2020) demonstrated progressive increases in CRP, AST, and ALT levels with advancing gestational age in preeclamptic women, highlighting the need for serial monitoring to identify patients at higher risk of complications (Chen *et al.*, 2020). The results showed that the differences in copper, selenium, CRP, AST, and ALT levels between the control and pre-eclamptic groups were statistically significant at various gestational age categories. This suggests that these biomarkers may have potential as

diagnostic or prognostic tools in the management of pre-eclampsia, as their levels may vary depending on the stage of the condition.

The Pearson correlation analysis revealed several noteworthy associations among the variables. The strong positive correlations observed between copper and zinc ($r=0.89$, $p<0.05$), copper and selenium ($r=0.67$, $p<0.05$) with a p-value of 0.001 and zinc and selenium ($r=0.78$, $p<0.05$) with a p-value of 0.87 suggest a close interplay among these trace minerals. This is consistent with the known interdependence of these nutrients in various physiological processes (Wessells and Brown, 2012). The moderate to strong positive correlations between the trace metals and the liver enzymes (ALT and AST) further highlight the potential role of these minerals in liver function and the pathogenesis of pre-eclampsia. The strong positive correlations between CRP and the trace metals, as well as the liver enzymes, suggest a complex interplay between inflammation, oxidative stress, and liver dysfunction in pre-eclampsia. These findings align with the current understanding of pre-eclampsia as a multifactorial condition involving endothelial dysfunction, oxidative stress, and systemic inflammation according to previous reports (Redman and Sargent, 2005; Karumanchi and Stillman, 2006). A study by Mistry *et al.* (2019) investigated the alterations in trace metal levels in preeclampsia and reported similar findings of positive correlations between copper, zinc, and selenium levels in preeclamptic women compared to normotensive controls. These correlations were attributed to compensatory responses to oxidative stress and inflammation characteristic of preeclampsia (Mistry *et al.*, 2019). A study by Rani *et al.* (2020) also explored the associations between liver enzymes and inflammatory markers in preeclampsia and corroborated the findings of significant correlations between ALT, AST, and CRP levels. The study highlighted the clinical relevance of monitoring liver enzymes and inflammatory markers in predicting adverse outcomes and guiding management strategies in pre-eclamptic pregnancies (Rani *et al.*, 2020).

The present study has several implications for the management of pre-eclampsia. The observed

alterations in the levels of trace metals, liver enzymes, and CRP in pre-eclamptic women highlight the importance of monitoring these biomarkers in the antenatal care of pregnant women. Early detection of these changes may facilitate early intervention and better management of pre-eclampsia, potentially improving maternal and foetal outcomes.

The correlations between the biomarkers suggest that a combination of these markers may provide a more comprehensive assessment of the underlying pathophysiological mechanisms in pre-eclampsia. This information could aid in the development of targeted nutritional or therapeutic interventions to address the imbalances in trace mineral status, liver function, and inflammatory responses.

Conclusion

The findings revealed significant differences in the levels of these biomarkers between pre-eclamptic and normotensive pregnant women, highlighting their potential roles in the pathogenesis of pre-eclampsia. The findings of this study contribute to the growing body of evidence on the role of trace metals, liver enzymes, and inflammatory markers in the pathogenesis of pre-eclampsia. The significant differences in the levels of these biomarkers between the control and pre-eclamptic groups, as well as their associations, underline the complex interplay of various factors in the development of this condition. These results underscore the importance of incorporating the assessment of these biomarkers into the routine antenatal care of pregnant women, which may enhance the early detection and management of pre-eclampsia.

Recommendations

1. Regular monitoring of trace mineral levels (copper, zinc, and selenium), CRP, and liver enzymes (AST and ALT) during antenatal care is recommended to facilitate early detection and intervention in cases of pre-eclampsia.
2. Nutritional interventions or supplementation strategies targeting the identified trace mineral deficiencies (copper and selenium) should be explored to potentially mitigate the risk or severity of pre-eclampsia.

3. Further research is warranted to elucidate the underlying mechanisms and interactions among the biomarkers, as well as their diagnostic and prognostic utility in the management of pre-eclampsia.
4. Comprehensive antenatal care protocols should be developed, incorporating the assessment of these biomarkers, to enhance the early identification and appropriate management of pre-eclampsia, ultimately improving maternal and fetal outcomes.
5. Public health initiatives and awareness campaigns should be implemented to educate pregnant women and healthcare providers about the importance of adequate trace mineral intake and the potential risks associated with deficiencies or imbalances during pregnancy.

Findings

1. Preeclamptic women exhibited significantly lower plasma levels of copper and selenium compared to normotensive controls, suggesting a potential deficiency of these trace minerals and their involvement in oxidative stress and endothelial dysfunction associated with pre-eclampsia.
2. Levels of CRP, AST, and ALT were significantly higher in the pre-eclamptic group, indicating the presence of an underlying inflammatory response and liver dysfunction in these women.
3. The differences in the levels of copper, selenium, CRP, AST, and ALT between pre-eclamptic and normotensive women were statistically significant at various gestational age categories, suggesting their potential as diagnostic or prognostic markers for pre-eclampsia.
4. Strong positive correlations were observed among the trace metals (copper, zinc, and selenium), suggesting their interdependence and potential interplay in physiological processes.
5. Moderate to strong positive correlations were found between the trace metals and liver enzymes (ALT and AST), highlighting the potential role of these minerals in liver function and the pathogenesis of pre-eclampsia.
6. CRP exhibited strong positive correlations with the trace metals and liver enzymes, implying a complex interplay between inflammation, oxidative stress, and liver dysfunction in pre-eclampsia.

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