



Assessment of Serum Zinc and Copper Levels among Sudanese Pregnant Women with and without Pre-eclampsia

Nibras Mahdi¹, Suhair A. Ahmed¹, GadAllah Modawe^{2*}

1. Alneelain University, Faculty of Medical Laboratory Sciences, Clinical Chemistry Department, Khartoum, Sudan.

2. Omdurman Islamic University, Faculty of Medicine and Health Sciences, Biochemistry Department, Omdurman, Sudan.

Corresponding author: gadobio77@hotmail.com.

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Abstract:

Background: Zinc (Zn) and copper (Cu) are very important micronutrients with an interrelation with pathogenesis of preeclampsia. Preeclampsia is a serious medical complication during pregnancy characterized by high blood pressure and proteinuria, and associated with morbidity and mortality rate.

Objectives: To assess the levels of serum zinc and copper among preeclampsia and compare to normotensive pregnant women.

Methodology: analytical cross sectional hospital based study. Hundred and twenty pregnant women were studied. They were divided into 30 preeclampsia women, 30 normotensive in the first trimester, other 30 normotensive in the second trimester, and also 30 normotensives in the third trimester. Age ranged from 20 and 41 years, with an average of 31 years. Normal pregnant women and preeclamptic were referred to Omdurman Maternal Hospital from September to November 2018. The women were studied in their 12 to 38 weeks of pregnancy. Sampling techniques was simple random based on inclusion and exclusion criteria. Blood samples were collected under aseptic conditions and the sera were collected and preserved. Serum zinc and copper were assayed using auto-analyzer (Cobas C311). The analysis of data was done using SPSS program version (21).

Results: The results showed that the age distribution as 73 (61%) from 20 to 30 years and 47 (39%) from 31 to 41 years. The serum zinc was a highly significantly decreased in preeclampsia compared to normal pregnant women ($p=0.000$) and the levels of serum copper was highly significantly increased in preeclampsia compared to normal pregnant women ($p=0.000$). There was a negative correlation between serum zinc and copper in preeclampsia ($r=-0.655$, $p=0.000$).

Conclusion: Preeclamptic pregnant women had significantly decreased serum zinc and increased levels of serum copper, also there was a negative correlation of serum zinc and copper in preeclampsia, so analysis of these trace elements is recommended.

Key words: trace elements, pregnancy complications, pregnancy trimesters.

المستخلص:

الخلفية: يعتبر الزنك والنحاس من العناصر الغذائية الصغيرة المهمة و لهما علاقة بتسمم الحمل، مقدمات الإرتجاج من المضاعفات الطبية الخطيرة التي تحدث أثناء الحمل والتي تتميز بإرتجاج ضغط الدم و وجود البروتين في البول، وترتبط بمعدل إصابة و وفاة عاليتين.

الأهداف: تقييم مستويات الزنك والنحاس في الدم ومقارنة النتائج بين النساء الحوامل اللواتي يعانين من زيادة ضغط الدم والنساء الحوامل ذوات ضغط دم طبيعي.

المنهجية: كانت الدراسة عبارة عن مراقبة النساء الحوامل في المستشفى مع تحليل النتائج، تمت دراسة 120 امرأة حامل تم تقسيمهم إلي أربعة مجموعات: المجموعة الأولى 30 امرأة في الثلث الأول من الحمل ذات ضغط دم طبيعي ، المجموعة الثانية 30 امرأة في الثلث الثاني من الحمل ذات ضغط دم طبيعي ، المجموعة الثالثة 30 امرأة في الثلث الأخير من الحمل ذات ضغط دم طبيعي و المجموعة الرابعة 30 امرأة مصابه بزيادة ضغط الدم. يتراوح العمر بين 20-41 سنة بمتوسط 31 سنة. تمت الدراسة في مستشفى أم درمان في الفترة من سبتمبر إلي نوفمبر 2018م. فترة الحمل من 12-38 أسبوعا. تم جمع العينات بصورة عشوائية تحت ظروف التعقيم مع حفظ السيرم. تم فحص الزنك والنحاس في السيرم، وتم تحليل النتائج بواسطة الحزم الإحصائية للعلوم الاجتماعية (SPSS) نسخة 21.

النتائج: أظهرت النتائج أن التوزيع العمري 73 (61%) من عمر 20-30 سنة و 47 (39%) من عمر 31 - 41 سنة. إنخفض معدل الزنك بشكل ملحوظ ($p= 0.000$) في النساء المصابات بالإرتجاج مقارنة مع النساء ذات الحمل الطبيعي. وزادت مستويات النحاس في الدم بشكل ملحوظ ($p= 0.000$) في النساء المصابات بالإرتجاج مقارنة مع النساء ذات الحمل الطبيعي. هناك علاقة سلبية بين معدلات الزنك والنحاس في النساء المصابات بالإرتجاج.

الخلاصة: إنخفض معدل الزنك بشكل ملحوظ وزاد معدل النحاس بشكل ملحوظ مع وجود علاقة سلبية بين العنصرين في النساء المصابات بالإرتجاج.

Introduction:

Preeclampsia (PE) is a potentially dangerous complication of pregnancy which develops during the second trimester after the fourth month of pregnancy. This is characterized by high blood pressure, up to 140/90 mm Hg or more and proteinuria with or without edema (Walker, 2000, Jain *et al.*, 2010). Overall, PE incidence varies from 2 to 8 per cent (Sibai *et al.*, 2005). Furthermore, PE risks are the third leading cause of pregnancy-related mortality, after hemorrhage and embolism (Wagner, 2004). PE is also associated with elevated risks of placental abruption, complications of the cardiovascular system, acute renal failure, spread of intravascular coagulation and maternal death (MacKay *et al.*, 2001)

Though extensively studied, its basic pathophysiology and etiology is hard to perceive (Newman and Fullerton 1990, Sibai, 1998). Nutritional insufficiency or excess of copper, zinc or other microelements may play an important role in the pathogenesis of PE, because these elements may regulate oxidative stress by raising or decreasing free radicals or antioxidants and by providing substrates for the formation of free radicals (Muna *et al.*, 2015). Pregnant women from third world countries typically eat low-nutritional minerals and vitamins (Akinloye *et al.*, 2010). Trace elements have a critical effect on pregnant women's health and developing embryos.

The serum zinc (Zn) and copper (Cu) levels were found to be inadequate or unchanged in women with PE (Ilhan *et al.*, 2012, Diaz *et al.*, 2012). Some studies have found that low copper and zinc levels are connected to preeclampsia's pathophysiological consequences. While others discovered no such association between preeclampsia and trace elements. Based on the above-mentioned and presumptive opinion of reduced trace elements in pregnancy and variable findings from various studies, the current study was designed to investigate changes in serum Zn and Cu levels and to determine the potential role of these micronutrients in PE pathogenesis. The purpose of the present study was to evaluate and compare the levels of serum zinc and copper between PE and normal pregnancy.

Materials and Methods:

Study population: This an analytical cross sectional hospital based study. It was done at maternal hospital in Omdurman. This study was performed from September through November 2018. Hundred and twenty pregnant women were examined, divided into 30 preeclampsia, 30 in the first trimester, another 30 in the second trimester, and 30 in the third trimester. Ages ranged from 20 to 41 years, the median age being 31 years.

Inclusion and exclusion criteria: The basic criteria for the diagnosis of PE were normal pregnant women in different trimesters and preeclampsia women, blood pressure (BP) above 140/90 and proteinuria > 300mg / dL in 24 h urine or 1 + in dipstick urine sample. Women with diabetes mellitus, other endocrine conditions, and kidney disease were removed from all cases and controls. After signing an informed consent, a detailed history was collected from all participants followed by physical and obstetrics review.

Blood pressure (BP) and proteinuria measurements: The sphygmomanometer

was used to measure BP of all subjects in two days, with a span of 6 hours. The protein content of 24 hour urine sample was regularly assessed for the diagnosis of proteinuria, or 2 midstream urine samples showing albumin reagent strips "+" in the morning and the evening.

Blood samples and data collections:

Samples were obtained using dry syringes made from plastic, tourniquet used to make veins more prominent. Three ml of blood samples from each volunteer under Aseptic condition were obtained in clear containers. Over 10 minutes, the blood was centrifuged at 5000 rpm, and the serum was collected and analyzed. Data from pregnant women at Omdurman Maternal Hospital were obtained using questionnaire format and blood sample Serum zinc and copper were analyzed using auto-analyzer (Cobas C311). Sing standard solutions for every ten-test sample ensured the quality control and assay accuracy.

Ethical considerations: The ethical approval received from the Ethical Committee, Alneelain University, Faculty of Medical Laboratory Sciences, and Department of Clinical Chemistry. An informed consent was obtained from each participant .

Data analysis: Data were analyzed using statistical package for social sciences (SPSS) computer program version 21.0.the results expressed in percentage,(Mean±SD). independent t-test was used for comparison between groups and Pearson, correlation test was done to determine the association between study variables,and ($p \leq 0.05$) value was considered significant.

Results:

Hundred and twenty pregnant women were examined. Thirty in the first trimesters, 30 in the second trimesters, 30 in the third trimesters and 30 preeclampsia.

The ages ranged from 20 and 41 years, with the mean age of 31 years. Of all subjects 47(39%) of pregnant women were 31 and 40 years and 73(61%) from 20 to 30 years, were presented in figure (1). Serum zinc and copper in pregnant women respectively were (90.81±12.12 mg/dl, 23.78±9.36 µmol/l). Serum zinc and copper in preeclampsia respectively were (79.3±11.5 mg/dl, 30.83±12.6 µmol/l), the serum zinc was a highly significantly decreased (p=0.000) compared to normal pregnant women, while serum copper a highly significantly increased (p= 0.000) compared with normal pregnant women was presented in table (1). In table (2) serum zinc was

significantly decreased (p=0.000) in preeclampsia compared to normal pregnant women in different trimester while serum copper was significantly increased (p=0.000) in preeclampsia compared to normal pregnant women with different trimester also the zinc copper ratio were significantly decreased (p=0.000) in preeclampsia compared to normal pregnant women in different trimesters, (table 3). Figure (2) shows. The negative correlation between serum zinc and copper in the study population (r= -0.655, p=0.000).

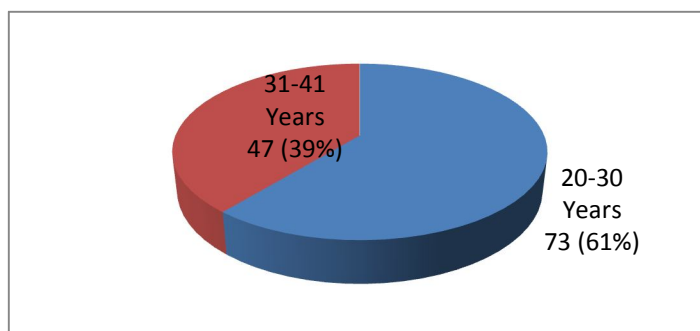


Figure 1: Distribution of the age in the study groups.

Table (1): (Mean±SD) of serum zinc and copper in the study population

Parameter	Pregnant normotensive women	Preeclampsia	P- value
Zinc (mg/dl)	90.81±12.12	79.3±11.5	0.000
Copper (µmol/l)	23.78±9.36	30.83±12.6	0.000

Table (2): (Mean±SD) of serum zinc and copper in the normal pregnant with different trimesters

Parameters	First Trimester	Second Trimester	Third Trimester	p-value
Zinc (mg/dl)	99.4±16.3	95.4±17.5	89.2±15.9	0.000
Copper (µmol/l)	19.13±4.25	19.80±5.80	25.33±7.5	0.000
Zn/Copper	5.51±1.58	5.33±1.99	3.89±1.5	0.000

Table (3): Serum level of zinc, copper and zinccopper ratio in the study populations

Parameters	(mean±SD)				P-value
	First Trimester	Second Trimester	Third Trimester	Preeclampsia	
Zinc (mg/dl)	99.4±16.3	95.4±17.5	89.2±15.9	79.3±11.5	0.000
Copper (µmol/l)	19.13±4.25	19.80±5.80	25.33±7.5	30.83±12.6	0.000
Zn/Copper	5.51±1.58	5.33±1.99	3.89±1.5	3.09±1.4	0.000

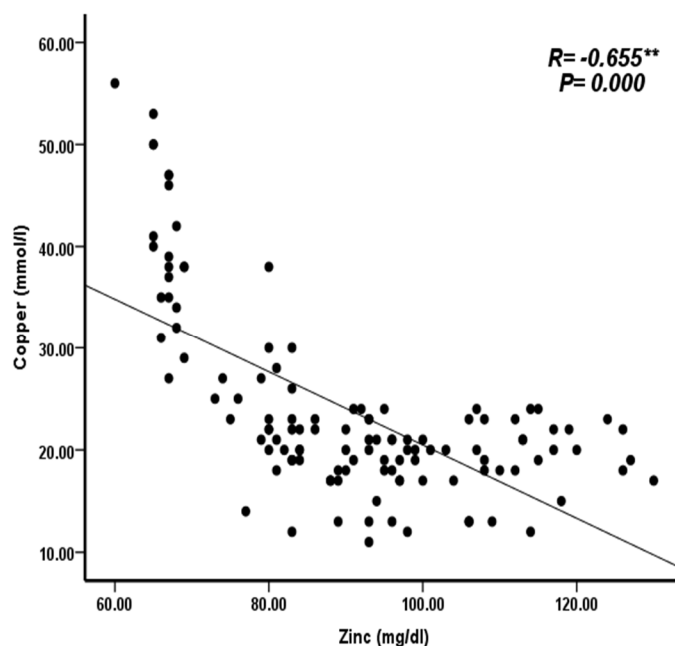


Figure (2): Correlation between zinc and copper levels in the study populations

Discussion:

Our finding (lower zinc level) is in concurrence with (Farzin and Sajadi, 2012) who reported significantly lower levels of zinc in preeclamptic women compared with the controls . (Jain *et al.*,2010) observed significantly lower levels of zinc in women with preeclampsia (25 with mild and 25 with severe preeclampsia) than the normal pregnant controls . (Negi *et al.*, 2012) observed decreased levels of zinc, copper in the umbilical cord blood of preeclamptic and

eclamptic pregnancies. Yet, (Vafaei *et al.*,2015) observed no significant difference in the serum levels of zinc levels in the 40 normotensive pregnancies (controls), 20 mild and 20 severe preeclamptic Iranian women . The current study showed significant higher copper level between cases and controls. (Farzin and Sajadi, 2012, Katz *et al.*, 2015) reported that , an association between high maternal serum copper and preeclampsia .

However, others linked the association with ceruloplasmin activity on a background of a raised serum copper, probably secondary to impaired antioxidant enzymes (Mistry *et al.*, 2013). Our study showed significantly lower of serum zinc and higher of serum copper in preeclampsia compared with normal Sudanese pregnant women, previous Sudanese study reported that, zinc and copper levels were not significantly different between the preeclampsia compared with normal Sudanese pregnant women (Elmugabil *et al.*, 2016). (Al-Shalah *et al.*, 2015) reported that the levels of serum zinc and copper were significantly lower in patients with pre-eclampsia compared to control groups. (Rafeenia *et al.*, 2014) reported that the lower the serum zinc, the higher the serum copper and the lower the zinc/copper ratio in pregnant women with and without pre-eclampsia. Although in our study the serum zinc and zinc/copper were significantly decreased and also the serum copper was significantly increased, supported by (Tabrizi and Pakdel, 2014). The deficiency of trace elements like zinc (Zn), copper (Cu), is thought to be involved in many reproductive events like infertility, congenital disorders, preeclampsia, low birth weight, and stillbirth (Onyegbule *et al.*, 2016) In addition to the known functions and importance of Zn it is reported that Zn is needed for properly developed fetus and the decrease in Zn during pregnancy could also be a physiological response to the increased maternal blood volume (Chitra *et al.*, 2004) It was reported that an increased incidence of preeclampsia in Zn-deficient regions was corrected by Zn supplementation in those regions (Adam *et al.*, 2001) The main findings of this study may suggest that zinc and copper were associated with pathogenesis of preeclampsia. The results findings agreed with a Nigerian study in which they observed a significant decrease

in the serum level of Zn in preeclamptic women when compared to the non-preeclamptic women also they noted a significant difference between the serum copper levels in preeclamptic and non-preeclamptic women (Tabrizi and Pakdel, 2014). In a meta-analysis conducted by Xingxing Song *et al.* to see the associations between serum copper and ratios of Cu/Zn and the preeclampsia (PE) risk in Asian population, they calculated the standardized mean difference and found that PE patients had a higher serum copper level compared with healthy pregnancy controls (Xingxing *et al.*, 2017) and these results are in concordance with the current study. In the present study we found that age group of the study population ranged, similar to age group of other study (Elmugabil *et al.*, 2016).

Conclusion: preeclamptic pregnant had decreased of serum zinc and increased serum copper and, accordingly; assessment of serum levels of these elements as indices of the pathogenesis of preeclampsia is recommended.

Conflict of Interests

The authors declared no conflict of interests.

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