

Zinc and Copper Levels among Hypertensive Subjects in Port Harcourt, Nigeria

Abstract

Hypertension is a serious medical condition that is increasingly affecting increasing number of individuals globally. This study investigated the levels of copper and zinc, and the copper/zinc ratio among hypertensive subjects in Port Harcourt. A total of 200 subjects, aged between 30 and 70 years, were involved in the study, comprising 100 hypertensive subjects and 100 apparently healthy control subjects. Five (5ml) of venous blood were collected from each subject and put into plain bottle for the determination of copper and zinc using atomic absorption spectrometry (AAS). The data generated were analyzed using SPSS version 23. The mean copper and zinc levels were significantly higher in the hypertensive subjects compared to the control, as well as the systolic and diastolic blood pressure values. The levels of these parameters were significantly higher in male hypertensives compared to the female subjects. The results from this study show that there is an increased level of copper and zinc in hypertension, and these increases are more in men hypertensive subjects than in female hypertensive subjects. The assessment of the levels of copper and zinc, and copper/zinc ratio in hypertension is recommended in order to help in the management of the condition.

Keywords: Zinc, Copper, copper/zinc ratio, hypertension, Port Harcourt, Nigeria

Introduction

Hypertension (sometimes referred to as high blood pressure), is generally defined as systolic blood pressure of 140 mmHg or higher and/or diastolic blood pressure of 90 mmHg or higher [1]. When the heart pumps blood for circulation, blood pushes against the walls of the artery through which they flow. This push creates a pressure on the arterial walls.

Commented [DL1]: it

Blood pressure is usually measured as systolic and diastolic blood pressures. Systolic blood pressure is the pressure in the arteries when the heart beats, while diastolic pressure is the pressure in the arteries when the heart rests [2]. Primary hypertension (also called Essential hypertension) is the most prevalent type, and affects 90-95% of hypertensive patients, while secondary hypertension makes up about 5-10% of the hypertensive patients [1]. The pathogenesis of primary hypertension is multifactorial and complex; Genetic factors, environmental factors, such as sedentary lifestyle, stress, smoking, obesity, salt (sodium) sensitivity, and alcohol intake, are significant factors. Hyperactivity of the renin-angiotensin-

aldosterone system and sympathetic nervous system, abnormal production of natriuretic peptides, and deficiency in endothelial vasodilatation substances are also contributory factors. Secondary hypertension is hypertension that is caused by an underlying condition with a known cause, such as chronic kidney disease, aortic or kidney artery stenosis, or endocrine problems including elevated levels of aldosterone, cortisol, or catecholamine [3]. It is important to recognize secondary hypertension from primary hypertension, because it is treated differently to essential hypertension, by treating the underlying cause of the elevated blood pressure [1]. Generally, hypertension is a chronic condition that is marked by elevated blood pressure [4]. It is often called ‘the silent killer’ because it shows no early symptoms [1].

Trace elements are necessary for the optimal physiological processes in human health; excess or deficiency may lead to various diseases [5]. Therefore, changes in the levels or concentrations of these trace elements in the human body can trigger abnormal metabolic processes which can lead to life-threatening disease conditions. Copper and zinc are two important trace elements that are part of the antioxidant enzymes. It is therefore necessary to study the levels of these elements in hypertension.

This study evaluated the levels of copper and zinc among subjects with hypertension.

B. Methodology

(i) Study Design

Commented [DL2]: Mention the normal range of Zinc and Copper

Commented [DL3]: Ethical permission? Required

A total of 200 subjects, aged between 30 and 70 years, were involved in this study, involving 100 subjects with hypertension (who were attending clinic) and 100 apparently healthy control subjects. The sample size was determined using GPower version 3.1.9.2.

For each subject, blood pressures were recorded twice, and the mean of two readings was calculated for each patient. The age, weight, and height, were also measured, and the body mass index (BMI) calculated for each subject.

(ii) **Sample Collection**

Five (5) millilitres of venous whole blood was collected with minimum stasis from each subject into vacuum tubes. Special care was taken to avoid haemolysis of the blood samples during handling and the blood separated immediately from whole blood by centrifuging to get the serum. The serum was put into a clean plain bottle.

Commented [DL4]: Mention the location of collection of sample from home or hospital

(iii) **Sample Analysis**

Samples were digested according to the method adopted from a earlier study [6]. Briefly, 1ml each of the serum, was taken into Pyrex flask separately. Then, 3ml of freshly prepared mixture of concentrated nitric acid and hydrogen peroxide (HNO_3 - H_2O_2) (2:1 v/v) were added the sample and stood for 10minutes. Small amount of anti-bumping was also added. The mixture was heated following a one – stage digestion programmed at 80% of the total power in a sharp light- up (Dial) domestic microwave oven with maximum heating power of 800 w for 3 minutes after this the digestion flasks were cooled. It was heated until the volume reduced to two third of its original volume and its colour became clear and turned yellowish and all its components digested.

The resulting solutions were evaporated to semidried mass to remove excess acid. The worked-up samples were allowed to cool. The solution was carefully filtered using whattman filter paper of 0.2mm. After which the digested sample was introduced into 50ml volumetric flask and make it up to the mark with distilled water. The sample is stored in a sample bottle and kept below 4°C before analysis. A blank extraction was carried out through the complete procedure using triply distilled water. Digested samples and reagent blank were analyzed for copper (Cu) and zinc (Zn) by Atomic absorption Spectrophotometer (AAs) using acetylene flame at wave length of 217nm. The atomic Absorption spectrophotometer was calibrated using zinc standard solution and copper standard solution before measurement.

Calculation

$$\text{Concentration} = \frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \times \text{concentration of standard}$$

(iv) Statistical Analysis

Data from this study were analyzed using Statistical Package for Social Sciences (SPSS) version 23. Comparison of means was done using t-test and ANOVA, with p-values less than or equal to 0.05 being considered statistically significant. Results were expressed as mean \pm Standard deviation.

C. RESULTS

Table 1: Demographic Information

The data from this study indicate that demographic data shown below:

Male	Female	Age (yrs)
------	--------	-----------

Hypertensives	58	42	52± 3
Control	64	36	54+_2

Table 2: Comparison of Biochemical parameters

The table below shows the comparison of the levels of copper and zinc among the subjects. The hypertensives had significantly higher copper levels and significantly lower zinc levels. The copper/zinc ratio is also significantly raised in the hypertensive subjects.

	Copper (µg/ml)	Zinc (µg/ml)	Cu/Zn	SP (mmHg)	DP (mmHg)
Hypertensives Subjects	1.34± 0.09	0.85± 0.08	1.58± 0.14	159.83± 16.37	92.17± 6.25
Control Subjects	1.16± 0.07	1.08± 0.07	1.08± 0.06	107.80± 7.97	72.85± 4.48
p-value	<0.001	<0.001	<0.001	<0.001	<0.001
t-value	10.31	14.910	21.460	18.634	16.829

Table 3: Comparison of Biochemical Parameters According to Sex

The male hypertensives had significantly higher copper levels compared to the female subjects.

However, there were no significant differences in zinc levels and the cu/zn ratio.

	Copper (µg/ml)	Zinc (µg/ml)	Cu/Zn	SP (mmHg)	DP (mmHg)
Female	1.31± 0.08	0.83± 0.06	1.58± 0.14	159.29± 12.30	92.25± 6.46
Male	1.37± 0.09	0.87± 0.08	1.59± 0.14	160.32± 19.53	92.10± 6.16
p-value	0.014	0.103	0.778	0.810	0.926
t-value	2.530	1.658	0.283	0.241	0.093

D. Discussion

This study evaluated the levels of copper and zinc, as well as the copper/zinc ratio among hypertensive subjects.

The blood pressures of the hypertensives were significantly higher than the control subjects. The significantly raised systolic and diastolic blood pressures of the hypertensive subjects is understandable because of the consistently higher than normal pressure of blood flowing in their system, which is a major characteristic of hypertension [7].

The mean serum zinc and copper levels were significantly higher in hypertensive subjects compared to control subjects. This finding agrees with an earlier study [8], which reported a similar observation among patients with hypertension. Increased levels of zinc favours the activity of the enzyme, carbonic anhydrase which eventually predisposes to the development of hypertension [9].

The hypertensive subjects in this study had significantly higher levels of copper compared to the control subjects. It has been reported that copper levels are raised in conditions of inflammation [10]. Increased levels of free radicals and oxidative stress are and known contributors to the pathogenesis of hypertension [11]. Raised levels of copper increase the levels of free radicals, which can lead to vascular resistance and hypertension [9].

Both elements, copper and Zinc, are important factors in the function of enzyme superoxide dismutase, an essential antioxidant enzyme (SOD) [8]. Therefore, alterations in the levels of these elements may negatively affect the activity of SOD, which may in turn cause vasculo-endothelial dysfunction in hypertension.

Also, the hypertensive subjects had significantly higher copper/zinc ratio. Elevated copper/zinc levels have been associated with higher risks of cardiovascular mortality [12].

These findings of raised copper and copper/zinc ratio, and significantly low zinc levels in hypertensive subjects attending clinic in our study agree with the work of another study [13], which reported a similar finding.

Commented [DL5]: Make a hypothetical sentence about why there is variation in males and females. What it signifies

References

Commented [DL6]: Increase the number of references

1. Sawicka, K., Szczyrek, M., Jastrzębska, I., Prasał, M., Zwolak, A., Daniluk, J. (2011). Hypertension – The Silent Killer. Journal of Pre-Clinical and Clinical Research., 5(2), 43-46.

2. Desai, A.N. (2020). High Blood Pressure. *Journal of American Medical Association*, 324(12), 1254–1255
3. Mian, M.O., Barhoumi, T., Briet, M., Paradis, P., & Schiffrin, E.L. (2016). Deficiency of T-regulatory cells exaggerates angiotensin II-induced microvascular injury by enhancing immune responses. *Journal of Hypertension*, 34, 97-108.
4. Cheng, L. (2022). Pathophysiology of Hypertension and Its Cause. *Journal of Molecular Pathophysiology*, 11 (9), 01-02
5. Sousa, C., Moutinho, C., Vinha, A. F., Matos, C. (2019). Trace Minerals in Human Health: Iron, Zinc, Copper, Manganese and Fluorine. *International Journal of Science and Research Methodology*, 13 (3), 2-24
6. Memon, A.R., Tasneem, G.K., Hassan, I.A., & Nasreen, S. (2007). Evaluation of Zinc status in whole blood and scalp hair of female cancer patients. *Clinica Chimica Acta*, 10564
7. Oparil, S., Acelajado, M.C., Bakris, G.L., Berlowitz, D.R., Cifková, R., Dominiczak, A.F., Grassi, G., Jordan, J., Poulter, N.R., Rodgers, A., & Whelton, P.K. (2018). Hypertension. *Nature Review Disease Primers*, 4,18014
8. Fatima, T. & Anee, S. (2019). Serum Levels of Magnesium, Copper, Zinc and Iron in Patients with Essential Hypertension. *Scholars International Journal of Biochemistry*, 2(7), 205-208.
9. Kim, M. K., Baek, K. H., Song, K. H., Kang, M. I., Choi, J. H., Bae, J. C., & Oh, K. W. (2012). Increased serum ferritin predicts the development of hypertension among middle-aged men. *American journal of hypertension*, 25(4), 492-497.
10. Lopez de Romanda, D., Olivarez, M., Uauy, R. & Araya, M. (2011). Risks and benefits of copper in light of new insights of copper haemostasis. *Journal of Trace Elements and Medical Biology*, 25, 3-13
11. Mohanty, G, A. (2014). Status of serum levels of copper in essential hypertension. *International Journal of Innovative Pharmaceutical Sciences and Research*, 2(11), 2800-2807
12. Leone, N., Courbon, D., Ducimetere, P. & Zureik, M. (2006). Zinc, copper, and magnesium and risks for all-cause, cancer, and cardiovascular mortality. *Epidemiology*, 17, 308-314.
13. Emokpae, M. A. & Coker, O. (2018). Serum levels of copper, zinc and copper-to-zinc ratio in subjects with uncomplicated hypertension. *Annals of Biomedical Sciences*, 17 (1),