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RESEARCH **Open Access**

Biochemical Assessment of Some Trace Elements in Hypertensive Patients

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Abstract

Background: Hypertension is a chronic disease that has been recognized as an important global public health disorder. It is a leading risk factor for stroke, heart failure, kidney diseases, and sudden death; as such its effective management may go a long way in preventing some of these possible complications. In humans, trace elements play key roles in normal metabolic activities that are required for healthy living. It has been hypothesized that trace elements are key to normal heart functions. Thus, deficiency in one or more trace elements may result(s) in or accentuate heart disease(s). This study, therefore, assessed trace elements in hypertensive and control volunteers .

Methods: A total number of two hundred and fifty-six(256) participants comprising of one hundred and sixty-nine (169) hypertensive and eighty-seven (87) normotensive control volunteers participated in this study. Anthropometric data and blood samples were collected from all participants. The blood samples were collected into plain vacutainer and were allowed to clot. The samples were centrifuged and the serum from each sample was aspirated and analyzed for trace elements {Selenium (Se), Copper (Cu), Zinc (Zn), Iron (Fe)} using atomic absorption spectrophotometer and calcium using Cobas C-111.

Results: There was no significant difference ($p>0.05$) between the mean age and weight of the participants. However, the mean body mass index (BMI), systolic, and diastolic blood pressure in hypertensive volunteers were significantly higher ($p<0.05$) than the controls. The mean Cu and Fe were higher ($p<0.05$) in hypertensive volunteers whereas the mean Zn, Se, and calcium were not different ($p>0.05$) between the two groups that participated in this study. There were positive associations between body mass index, systolic blood pressure ($p<0.05$), and Cu whereas negative correlations existed between body mass index, Zn, and Se, among hypertensive volunteers.

Conclusion: From this study, it appears that high blood pressure among Nigerian population is associated with elevated serum copper (Cu) and iron (Fe) trace elements. These may play a part in accentuation of hypertension in some of the volunteers if not properly monitored. Also hypertensive individuals also presented an increased body mass index (BMI) which could also complicate effective management of hypertension .

Keywords: Hypertension, Trace element, Body Mass Index, Blood pressure

1.0 INTRODUCTION

High blood pressure is a non-communicable disease that is characterized by continuous elevation of the blood pressure in the blood vessels. It is also known as arterial hypertension [1, 2]. Hypertension is an important public health problem all over the world and is one of the biggest health challenges in the 21st century [3], with a prevalence affecting about 13% of the world population [4]. Complications from high blood pressure result in about 12.8% (57 million) disability-adjusted life years (DALYs) and 3.7% (7.5 million) deaths worldwide [5, 6]. Nigeria with a population of over 190 million [7] has a high prevalence of hypertension and this hugely contributes to the overall burden in Africa [8]. Some studies previously reported a more than 11% prevalence of hypertension among adults in Nigeria [2, 9-12]. Adeloye *et al.,* [13] also estimated a prevalence of 28% hypertensive cases among Nigerians aged at least 20 years in 2010, while the prevalence was up to 50% in many community-based studies [14-16].

Essential trace elements of the human body include zinc (Zn), ıron (Fe), copper (Cu), selenium (Se), chromium (Cr), cobalt (Co), iodine (I), manganese (Mn), and molybdenum (Mo) [17, 18]. Although these elements account for only 0.02% of the total body weight, they play significant roles, such as active centers of enzymes or as trace bioactive substances [17, 18]. Some trace elements serve as a cofactor in certain enzymatic reactions that play significant roles in human metabolism [19]. They are recognized as essential mediators for the development and progression of cardiovascular disease (CVD), although there is no concrete evidence for the direct relationship between the metals and progression of the disease [20].

In addition to this, trace elements are necessary for biological processes in human health, an overabundance or a deficiency may lead to various diseases [21]. Minute changes in the concentration of some trace metals in the human body can trigger abnormal metabolic processes which later develop into life-threatening diseases [22].

Impacts of trace metals are closely associated with each other [23]. For instance, it has been reported previously that high amounts of copper and zinc can interfere with the bio-availability and storage of iron [24-26]. Low iron enhances the absorption of zinc while zinc has been shown to cause anaemia secondary to decreased absorption of copper [23]. Disturbance in the metabolism of one trace metal may affect the others, and a pathophysiological process may be elicited [23].

It has been reported by Lehto *et al.,* [27] that trace elements such as selenium, copper, and zinc play significant roles in blood pressure regulation. It is, therefore, possible that any alteration in the physiological levels of these essential trace elements may affect the blood pressure and lead to the development of hypertension and vascular disease, including alteration in serum cholesterol and triglyceride levels.

2.0 METHODOLOGY

2.1 Ethical Consideration

Approval for this study was obtained from the College of Medicine of the University of Lagos (CMUL/ HREC/02/19/501) prior to the commencement of the fieldwork. Informed consent was sought and obtained from each of the volunteers prior to participating in this study.

2.2 Study Design and Participants Selection

A cross-sectional case-control, observational study was conducted on patients recruited randomly from the Department of Medicine (Nephrology and Cardiology units) of Lagos University Teaching Hospital (LUTH). A total number of two hundred and fifty-six (256) participants comprising of one hundred and sixty-nine (169) hypertensive and eighty-seven (87) normotensive control volunteers were recruited into this study. 5ml of venous blood specimen was collected from the antecubital vein of each volunteer using aseptic procedure into clean, dry plain specimen bottles. Each sample in the specimen bottles was allowed to clot undisturbed for 2 hours and centrifuged at 4,000 revolutions per minute (rpm) for 5 minutes to obtain serum. The serum was stored immediately at -20°C until required for analysis.

2.3 Inclusion Criteria

Individuals who have been diagnosed with hypertension with no other comorbidities at the time of this study were included. Apparently healthy age matched normotensive individuals whose consent had been obtained were included as control. Diagnosis of hypertensive participants was established by the clinicians based on the repeated blood pressure measurements of the patients that

were ≥140/90mmHg. Hypertensive participants were recruited based on previous diagnosis of high blood pressure made by the physicians (medical history), and or the use of antihypertensive medications.

2.4 Exclusion Criteria

Individuals with hypertensive urgency, hypertensive emergency, secondary hypertension, diseases of the liver and kidney, diabetes mellitus, post-myocardial infarction, congestive heart failure were all excluded from this study. Female pregnant volunteers were also excluded from this study.

2.5 Laboratory Analysis

Serum selenium (Se), zinc (Zn), copper (Cu), and iron (Fe) were measured using Buck 210 atomic absorption spectrophotometer (AAS) while calcium (Ca) was estimated using Cobas C-111 auto analyzer.

2.6 Statistical Analysis

All data obtained from this study were analyzed using the STATA statistical package (Stata Corps version 16). Test of normality was performed using Shapiro wilk and Kolmogorov-Smirnov tests. Normally distributed continuous variables were reported as mean ± standard deviation. The independent data were analyzed using the unpaired student "t' test for comparison of the mean. Pearson's correlation coefficient (r) was used to determine the relationship between the mean of the variables. The level of statistical significance was set at $p<0.05$.

Table 1. Demographic characteristics and blood pressure of the participants

Variables	Hypertensive Mean±SD n=169	Controls Mean±SD n=87	t-test	p-value
Age (Year)	54.17±12.46	54.61±10.31	0.29	0.776
Systolic BP (mmHg)	134±16	114±14	9.73	<0.001*
Diastolic BP (mmHg)	90±10	72±10	13.46	<0.001*
Height (m)	1.68±0.10	1.69±0.10	0.57	0.570
Weight (Kg)	73.15±16.00	69.37±13.90	1.87	0.063
BMI (Kg/m^2)	26.04±6.25	24.38±4.88	2.16	0.032*

* Indicates significant probability, BP – Blood Pressure, BMI – Body Mass Index.

Table 2. Comparative analysis of biochemical parameters between hypertensive and control groups.

Variables	Hypertensive Mean±SD n=169	Controls Mean±SD n=87	t-test	p-value
Se (µg/dL)	76.48±5.84	76.03±4.61	0.62	0.536
Zn (µg/dL)	98.98±19.10	97.32±18.96	0.66	0.510
Cu (µg/	94.39±20.11	86.49±18.86	3.04	0.003*
Fe (µg/dL)	99.76±20.61	93.30±23.65	2.26	0.025*
Ca^{2+} (mmol/L)	2.41±0.29	2.45±0.60	0.65	0.517

* Indicates significant probability

3.0 RESULTS

Table 1 showed the mean demographic features and the blood pressure of the participants in this study. The mean values were; age: 54.17±12.46 and 54.61±10.31years; systolic blood pressure 134±16, and 114±14 mmHg; diastolic blood pressure 90±10, and 72±10, (mmHg); weight 73.15±16.00, and 69.37±13.90Kg; and body mass index: 26.04±6.25, and 24.38±4.88 Kg/m^2 for hypertensive and normotensive control volunteers respectively. Table 2 showed the mean serum values of trace elements (Se, Zn, Cu, and Fe) and Ca^{2+} in hypertensive and normotensive participants. The results were as follow: Se: 76.48±5.84, and 76.03±4.61 µg/dL; Zn: 98.98±19.10,and 97.32±18.96µg/dL;Cu:94.39±20.11, and 86.49±18.86µg/dL; Fe: 99.76±20.61, and 93.30±23.65µg/dL for hypertensive and control groups respectively. Also the mean Ca^{2+} (mmol/L) in hypertensive and normotensive control group were 2.41±0.29 (mmol/l) and 2.45±0.60 (mmol/l) respectively. In addition, the comparative analysis (Table 3) of demographic parameters between female and male hypertensive patients were examined. From this table, the mean systolic blood pressure, and diastolic blood pressure were similar in both female and male hypertensive participants. On the other hand, the weight and body mass index were higher among female hypertensive participants (Weight: 75.88±17.21Kg and 68.67±12.70kg) and body mass index; 27.85±6.57Kg/m^2 and 23.07±4.30Kg/m^2).

This may be as a result of increased adipose tissue mass

Table 3. Comparative analysis of demographic parameters of hypertensive patients by sex

Variables	Female Mean±SD n=105	Male Mean±SD n=64	t-test	p-value
Systolic	134±15	133±17	0.38	0.706
Diastolic (mmHg)	89±10	91±11	0.67	0.502
Weight (Kg)	75.88±17.21	68.67±12.70	2.90	0.004*
BMI (Kg/m^2)	27.85±6.57	23.07±4.30	5.18	<0.001*

* Indicates significant probability, BMI – Body Mass Index.

The comparative analysis of the trace elements and calcium (Se, Zn, Cu, Fe, and Ca^{2+}) between female and male hypertensive volunteers was presented in Table 4. From this table, the mean serum trace elements for female and male hypertensive volunteers were all similar. Furthermore, the degree of association between the continuous parameters in hypertensive participants was determined (Table 5) using Pearson's correlation coefficient (r). Positive relationships were observed between systolic and diastolic blood pressures (r = 0.688, p<0.001), BMI and weight (r = 0.883, p<0.001), BMI and systolic pressure (r= 0.181, p=0.0036), BMI and Cu (r = 0.0107, p =0.8653), conversely, a negative association was observed between BMI and Zn (r = -0.1072, p=0.871) as well as BMI and Se (r = -007, p = 0.99).

Table 4. Comparative analysis of biochemical parameters of hypertensive patients by sex

Variables	Female Mean±SD n=105	Male Mean±SD n=64	t-test	p-value
Se (µg/dL)	76.11±5.94	77.08±5.65	1.05	0.294
Zn (µg/dL)	99.87±19.38	97.52±18.70	0.77	0.440
Cu (µg/dL)	93.93±20.71	95.14±19.20	0.38	0.706
Fe (µg/dL)	100.33±20.47	98.82±20.96	0.46	0.645
Ca^{2+} (mmol/L)	2.41±0.30	2.42±0.29	0.15	0.880

* Indicates significant probability

Table 5. Correlation of Body mass index with the blood pressure and the trace elements parameters in hypertensive group

Variables	Correlation coefficient (r)	p-value
Systolic vs Diastolic BP	0.688	<0.001*
Systolic BP (mmHg)	0.1812	0.0036*
Weight (Kg) (µg/dL)	0.883	<0.001*
Selenium (Se) (µg/dL)	-0.007	0.990
Copper (Cu) (µg/dL)	0.0107	0.865
Zinc (Zn) (µg/dL)	-0.1072	0.089
Iron (Fe) (µg/dL)	-0.014	0.8232

* Indicates significant level of association

4.0 DISCUSSION

Hypertension has been shown to be an important risk factor for stroke and kidney failure [28] and is highly implicated as a major predisposing factor for various cardiovascular diseases [29, 30], leading to high morbidity and mortality [30].

In this study, the demographic characteristics show no significant difference (p>0.05) in the mean age, and weight of the hypertensive and normotensive participants (Table 1). On the other hand, the mean systolic blood pressure, diastolic blood pressure, and body mass index (BMI) were significantly higher (p<0.05) in the hypertensive group when compared with the control group. This observation with respect to systolic and diastolic blood pressure was in agreement with previous study by Tiwari *et al.,* [31] who reported significantly higher systolic and diastolic blood pressure in hypertensive subjects than normotensive subjects. This observation further gives credence to the fact that the test group was actually hypertensive individuals that were already been managed. An increase in BMI agrees with the previous studies by Jan *et al.,* [32] and Priyanka *et al.,* [33]. A raised BMI suggests that overweight possibly plays a significant role in the development and deterioration of essential hypertension. However, when the demographic characteristics of the test participants were stratified by sex (Table 3), it was observed that the mean weight and BMI were significantly higher (p<0.05) in the female hypertensive group when compared with the male hypertensive group. This observation corroborates the finding by Zhang *et al.,* [34] who reported that obesity-related hypertension was higher in women than in men.

in females compared to males [35]. This observation suggests that females could be at higher risk of developing hypertension than males.

In addition to this, a significant increase in the mean serum copper (Cu) was observed in hypertensive volunteers (Table 2). Observation from this study agrees with previous studies reported by Olatunbosun *et al.,* [36], Ghayour -Mobarhan *et al.,* [37], and Solanki *et al.,* [38]; but at variance with the study by Taneja and Mandal, [39] where decreased level of copper was observed among hypertensive participants in Chandigarh population. This variation could be due to the difference in the study population as well as the sample size of the study. Previous studies have also reported an association between increased in body mass index and increase in body copper levels [40-41]. Copper is an essential metal that plays a critical role in haemoglobin synthesis, immune functions, and as a cofactor for Cu/Zn superoxide dismutase, and ceruloplasmin [20]. Due to the redox-active nature of Cu, it catalyzes the production of highly reactive oxygen species which has the potential to cause oxidative damage to proteins, DNA, lipids, and other molecules. As a result, Cu overload induces tissue injuries, which may lead to diseases or affect the progression of diseases [42-43]. Thus, a significant increase in Cu as observed in this study could elicit a cardio-toxic effect among hypertensive volunteers, and this could be made worse by increase in body mass index since there appears to be a positive association between the two (Table 5). The role of Cu has been implicated in several studies, as elevated level of serum Cu was reported to be an independent risk factor for heart disease [44-45] and hypertension [45]. Also, an increase ($p>0.05$) in serum Zinc (Zn) levels was observed among hypertensive participants when compared with the control group. Our observation in respect of Zn is consistent with the previous study by Taneja and Mandal [39] but inconsistent with the studies reported by Solanki *et al.,* [38] and Tiwari *et al.,* [31] where the mean level of serum Zn was found to be significantly low in the hypertensive individuals as compared with control. This disparity could be due to variation in sample size and study population as their studies had a lower sample size and among the Indian population.

Furthermore, a significant increase ($p<0.05$) in the level of serum Fe was observed in hypertensive patients when compared with the control group (Table 2). This observation is in concordance with the previous study by Asaolu *et al.,* [46] who reported a higher value of Fe in hypertensive patients when compared with normal healthy controls. Ramakrishnan *et al.,* [47] and Nagarajrao, [48] also reported an increased level of Fe in cardiovascular disease (CVD) patients when compared with the control group. Several epidemiological studies had shown that the level of body Iron (Fe) stores is positively correlated with the incidence of coronary heart disease (CHD) in human populations [49]. Iron is an important part of haemoglobin and various enzymes in the human body but a higher concentration of free iron is involved in oxidative stress. Its overload leads to free radical damage by the Fenton reaction. This reaction occurs when Fe^{2+} reacts with hydrogen peroxide to generate hydroxyl radicals/ ions and highly reactive intermediates, causing oxidative stress in the cell. These reactive oxygen species are involved in the peroxidation of lipoproteins and in consequence, produce the oxidized low-density lipoprotein (LDL), which along with other factors lead towards the development of atherosclerosis [50-51]. Besides, a non-significant increase ($p>0.05$) in serum selenium (Se) levels was observed among hypertensive participants when compared with the control group. This finding on Se is at variance with previous studies by Mihailović *et al*., [52] and Afridi *et al.,* [53] where significantly lower Se values were reported in hypertensive patients when compared with controls. The possible reason for this observation is sparse, however, it may be due to either genetic diversity between the different study populations. It is also important to note that the non-significant increase in selenium among hypertensive group could have occurred by chance. Moreover, there was no significant difference ($p>0.05$) in serum calcium (Ca^{2+}) between the hypertensive group and the control group (Table 2). This finding agrees with the study by Giassudin *et al.,* [54] who reported a non-significant difference in serum calcium between the hypertensive group and the control group. It is interesting to note that there was no significant difference ($P>0.05$) in any of the measured trace elements when the hypertensive participants were stratified by sex (Table 4); thus suggesting that gender may not have any influence on any of these trace metals.

Moreover, a measure of the degree of association (Table 5) was carried out on the parameters in hypertensive participants using Pearson's correlation coefficient (r). As expected, systolic and diastolic blood pressure correlated

positively ($p<0.05$). However, a careful assessment showed a significant positive association ($p<0.05$) between body mass index (BMI) and systolic blood pressure thus emphasizing the import of increased BMI to the development and complications of high blood pressure [55-56]. In addition to this, BMI correlated negatively with selenium, zinc and iron; this observation suggests that increase in BMI particularly in obesity often associate with risk of low selenium, zinc and iron [40-41]. However Banach *et al.,* [57] reported a contradictory association between obesity and iron. On the other hand, BMI correlated positively with copper. This association agrees with the previous study by Lima *et al.,* [58]. It appears that increase in body mass index (BMI) impacts deleterious effect on different trace elements which could by extension impact negatively on blood pressure. Thus mineral imbalance-a possible consequence of abnormal body mass index in human may therefore contribute significantly to the pathogenesis and progression of essential hypertension.

In conclusion, the outcome of this study showed that hypertension is associated with alteration in some trace elements. A better understanding of this may enhance better management of this group of individuals.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors Contribution

OAE, ITS conceived and designed the study, performed data collection, contributed to data analysis tools, analysis of data and writing of the manuscript; **NCM** contributed to data collection, data analysis tools and manuscript writing.

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