Research Article

Correlation of Serum Zinc with Blood Pressure in Hypertensive Individuals

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Abstract

Background: Hypertension is one of the leading causes of mortality and morbidity worldwide. Trace elements deficiencies are believed to be related with development of hypertension and associated complications.

Objective: To explore the correlation of serum zinc with blood pressure in hypertensive individuals.

Methods: This study was conducted at the Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from March 2020 to February 2021. A total of 100 adult subjects were selected purposively, among them 50 were diagnosed cases of hypertension and 50 were normotensive healthy adults as control group. Their blood pressure (BP) was measured and body mass index (BMI) was calculated accordingly. Serum zinc and serum lipid profile [Total Cholesterol (TC), High Density Lipoprotein- Cholesterol (HDL-C), Low Density Lipoprotein- Cholesterol (LDL-C) and Triglyceride (TG)] of the study subjects were measured. Data were analyzed and compared by statistical tests.

Results: The mean(±SD) age was 46.9±12.7 years in hypertensive patients and 43.1±8.5 years in control group. Male subjects were predominant in both groups. Majority of the hypertensive patients were found over-weight. Mean(±SD) levels of serum TC, LDL-C, TG were significantly high ($p<0.05$) and mean serum HDL-C level was significantly low ($p=0.018$) in hypertensive group. Mean(±SD) serum zinc level was significantly low ($p=0.020$) in hypertensive group. In hypertensive group, serum zinc had significant negative correlation with systolic blood pressure [SBP ($r= - 0.620$, $p<0.001$)] and diastolic blood pressure [DBP ($r= - 0.446$, $p=0.001$)].

Conclusion: The serum zinc level is significantly low in hypertensive individuals. Serum zinc has a negative correlation with systolic and diastolic blood pressures in hypertensive individuals.

Keywords: Blood Pressure; Correlation; Hypertension; Zinc

1. Introduction

Hypertension is a condition in which the blood vessels have persistently raised pressure [1]. Hypertension refers to the systolic blood pressure ≥140 mmHg and/or the diastolic blood pressure ≥90 mmHg, measured on two separate occasions [1]. During recent years hypertension has become a global health problem; about 1.13 billion people worldwide have hypertension [1]. In South Asia, prevalence of hypertension was 27% [2]. Dyslipidemia and overweight are the most common comorbidities associated with hypertension [3,4]. Hypertension is a major risk factor for cardiovascular disease, cerebrovascular disease and chronic kidney disease [3,4]. Hypertension is divided into two classes: primary or essential hypertension and secondary hypertension. Majority of the patients suffer from essential hypertension, which is of unknown aetiology [1]. Risk factors for essential hypertension include- high salt intake, low trace elements (zinc, magnesium and potassium) in diet, low physical activity, smoking and stress [1] [5]. Only 5-10% patients of hypertension have secondary hypertension [1]. That may be influenced by pre-existing chronic diseases [3,4]. Trace elements are accepted as essential for optimum human health and

well-being [5,6]. Trace elements influence fluid and electrolyte balance; regulate acid-base balance and neuromuscular functions [6]. Zinc, a potent antioxidant is the second most abundant intracellular trace element [7]. Zinc is essential for enzymatic action of superoxide dismutase (SOD), which disables free radicals [8]. Free radicals are considered as triggering factor for hypertension [6]. Zinc deficiency is involved in growth retardation, immunodeficiency and increased cardiovascular mortality [9], that affects 31% of world's population [10]. It was reported that, zinc deficiency causes increased reabsorption of renal sodium in distal convoluted tubules of kidney, which results in elevated blood pressure [8,11]. In recent years a couple of previous studies have explored the relationship between serum zinc with hypertension; however the results were conflicting and inconsistent. Few studies had shown a high serum zinc level in hypertensive patients [12-14]. While low serum zinc level in hypertensive individuals were revealed in other studies [11,15-17]. On the other hand, few reports observed no significant association of zinc and hypertension [18] [19]. Recently zinc deficiency has been reported as an independent risk factor for the development of hypertension [11,17,20]. Some studies have shown; zinc deficiency hampers hepatic lipid metabolism that results in atherosclerosis, dyslipidemia, insulin resistance and obesity [21-23]. A recent clinical study suggests that zinc supplementation with dietary management helps in reducing weight and insulin resistance [21]. It was also reported that zinc supplementation may be beneficial as a therapeutic strategy in hypertension and dyslipidemia [24,25]. There is scarce evidence to explore the correlation of serum zinc with hypertension. Therefore, the aim of this current study was to explore the correlation of serum zinc with blood pressure in hypertensive individuals.

2. Materials and Methods

This cross sectional study was conducted at the Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from March 2020 to February 2021. A total of one hundred (100) adult subjects (age >18 years) of both sexes were selected purposively, among them 50 (fifty) subjects were diagnosed cases of hypertension with or without drugs (Group I) and 50 (fifty) subjects were normotensive healthy adults as control group (Group II). All study subjects were selected from out-patient department (OPD), Department of Internal Medicine, BSMMU, Dhaka, Bangladesh. Patients having diabetes mellitus, ischemic heart disease, chronic kidney disease, chronic liver disease, patients with a history of recent stroke/infection/diarrhea, patients with any types of malignancy, patient receiving zinc supplement/lipid lowering agent or receiving medication influencing serum zinc level (such as- thiazide or loop diuretics, aminoglycosides, amphotericin B, cyclosporine, cisplatin etc) and obese/pregnant/lactating subjects were excluded from the study. The study was approved by the Ethical Review Committee, BSMMU, Dhaka, Bangladesh.

2.1 Study procedure

Informed written consent was taken from each study subject prior to enrollment. The relevant history and clinical examination findings were recorded. Diagnosis was confirmed by blood pressure (BP) measurement. In case of new patients, two readings from separate day or home reading for three consecutive days with average reading were used to diagnosis of the patients. For blood pressure

measurement, the subjects were asked to sit in an armed chair for 15 minutes in a quiet room with comfortable room temperature. The mercury manometer was placed his/her arm at heart level. Then BP was recorded in all subjects using a standard sphygmomanometer having a cuff size of 25 cm × 12.5 cm. The BP was recorded 2 times by auscultatory method and the mean value was taken for analysis. Those who were already diagnosed previously as a case of hypertension were included with present BP measuring along with elaborative drug and lifestyle history (exercise, calorie intake etc). The height, weight, waist circumference of the study subjects were measured and body mass index (BMI) was calculated accordingly. BMI was categorized [normal weight: BMI 18.5-22.9 kg/m^2; overweight: BMI 23.0-24.9 kg/m^2; obese: BMI ≥25 kg/m^2] according to the World Health Organization (WHO) Asia-Pacific guidelines [26]. Then serum zinc and serum lipid profile [Total Cholesterol (TC), High Density Lipoprotein- Cholesterol (HDL-C), Low Density Lipoprotein- Cholesterol (LDL-C) and Triglyceride (TG)] of all study subjects were estimated.

2.2 Collection and analysis of Blood samples

Following standard procedure, 6 ml venous blood was collected from each patient in the morning after 8-12 hours overnight fasting. Collected blood sample was kept in upright position for 30 minutes. Blood was centrifuged at 3000 rpm in room temperature (22˚C - 24˚C) for 5 minutes. Separated serum was stored in -20˚C temperature until analysis was done.

2.3 Analytic Method

Serum zinc and serum lipid profile (TC, HDL-C, TG) were estimated by automated biochemistry analyzer by using the principle of photometric technique. All biochemical tests were performed at the Biochemistry Laboratory, Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka, Bangladesh.

2.4 Reference Values

The reference normal value used in this study was according to the Biochemistry Laboratory, Department of Biochemistry and Molecular Biology, BSMMU, Dhaka, Bangladesh.

Serum zinc: 65-118 µg/dl

Lipid profile:

- Serum Total Cholesterol (TC) <200 mg/dl = Desirable, 200-239 mg/dl = Borderline high, ≥240 mg/dl = High
- Serum LDL Cholesterol (LDL-C) <100 mg/dl = Optimal, 100-129 mg/dl = Near optimal/ Above optimal, 130-159 mg/dl = Borderline high, 160-189 mg/dl = High, ≥190 = Very high.
- Serum HDL Cholesterol (HDL-C) <40 mg/dl = Low, ≥60 mg/dl = High
- Serum Triglyceride (TG) <150 mg/dl = Normal, 150-199 mg/dl = Borderline high, 200-499 mg/dl = High, ≥500mg/dl = Very high.

2.5 Statistical Analysis

All data were analyzed by the computer software Statistical Packages for Social Sciences (SPSS) version-26. Quantitative data were expressed as mean with standard deviation (±SD), qualitative data were expressed as frequency and percentage. The statistics used to analyze the data was descriptive statistics. Unpaired t-test, Chi-squared (χ^2) test and Pearson's correlation coefficient test were performed to analyze

the data. A p value <0.05 was assigned for statistical significance.

3. Results

This cross-sectional study was carried out to explore the correlation of serum zinc with hypertension. A total of 100 Bangladeshi adults of both sexes (male 60 and female 40) were selected. Among them 50 individuals were hypertensive (Group I) and 50 individuals were normotensive in control group (Group II).

Table-I shows the age distribution between hypertensive and normotensive participants. The mean(±SD) age of hypertensive individuals (Group I) was 46.9±12.7 years and that was 43.1±8.5 years in control group (Group II). In both groups maximum participants were in age group 31-40 years. The age difference was not statistically significant between the groups (p=0.080).

Age Group	Group I (n=50)	Group II (n=50)	p value
	No. (%)	No. (%)	
21-30	2(4%)	0(0%)	
31-40	20(40%)	24(48%)	
41-50	12(24%)	17(34%)	
51-60	7(14%)	7(14%)	
>60	9(18%)	2(4%)	
Total	50(100%)	50(100%)	
Mean±SD	46.9±12.7	43.1±8.5	0.080 ns
Range	27 –75	32 – 65	
p value reached from Unpaired t-test; ns = not significant			

Table 1: Comparison of age between two groups (N=100).

Table-II shows the gender distribution between the groups. In hypertensive group; 33(66%) patients were male and 17(34%) patients were female. In control group; 27(54%) subjects were male and 23(46%) subjects were female. Male participants were predominant in both groups. But there was no significant difference in gender distribution between the groups (p=0.221).

Gender	Group I (n=50)	Group II (n=50)	p value
	No. (%)	No. (%)	
Male	33(66.0%)	27(54.0%)	
Female	17(34.0%)	23(46.0%)	0.221 ns
Total	50(100.0%)	50(100.0%)	
Figures in the parentheses indicate corresponding percentage; p value reached from Chi-squared test (c2); ns = not significant			

Table 2: Gender distribution between two groups (N=100).

Table-III shows the comparison of blood pressures (BP) between the groups. It was found that mean (±SD) systolic blood pressure (SBP) and mean(±SD) diastolic blood pressure (DBP) were significantly high in hypertensive group compared to control group (p<0.001).

Blood pressure (mmHg)	**Group I (n=50)**	**Group II (n=50)**	**p value**
	Mean±SD	**Mean±SD**	
Systolic blood pressure (SBP)	139.6±16.9	115.1±8.8	<0.001[s]
Diastolic blood pressure (DBP)	96.2±12.7	76.7±7.1	<0.001[s]
p value reached from Unpaired t-test; s = significant			

Table 3: Comparison of blood pressure between the groups (N=100).

Regarding body mass index (BMI) categories; it was observed that, majority of the study subjects were overweight (BMI: 23.0-24.9 kg/m^2) in both groups [40(80%) and 29(58%)]. But overweight individuals were significantly higher in hypertensive group compared to control group (p=0.017) (Table- IV). In this study, obese (BMI ≥25 kg/m^2) individuals were excluded from the study.

Body Mass Index [BMI (kg/m^2)]	**Group I (n=50)**	**Group II (n=50)**	**p value**
	No. (%)	**No. (%)**	
Normal weight (BMI: 18.5-22.9 kg/m^2)	10(20%)	21(42%)	**0.017[s]**
Overweight (BMI: 23.0-24.9 kg/m^2)	40(80%)	29(58%)	
Total	50(100%)	50(100%)	
Figures in the parentheses indicate corresponding percentage; p value reached from Chi-squared Test (χ^2); s = significant; BMI was categorized according to the World Health Organization (WHO) Asia-Pacific guidelines [26].			

Table 4: Distribution of the study subjects by body mass index (BMI) categories (N=100).

Lipid profile analysis of the study subjects revealed that, mean(±SD) levels of serum total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and triglyceride (TG) were significantly high in hypertensive group compared to control group (p<0.05). While, mean(±SD) serum high density lipoprotein- cholesterol (HDL-C) level was significantly low in hypertensive group compared to control group (p=0.018) (Table-5).

Lipid profile (mg/dl)	**Group I (n=50)**	**Group II (n=50)**	**p value**
	Mean±SD	**Mean±SD**	
Total cholesterol (TC) (mg/dl)	178.2±48.7	154.5±36.4	**0.007[s]**
High density lipoprotein- cholesterol (HDL-C) (mg/dl)	35.5±10.6	40.9±11.6	**0.018[s]**
Low density lipoprotein-cholesterol (LDL-C) (mg/dl)	119.9±37.1	105.7±27.5	**0.031[s]**
Triglyceride (TG) (mg/dl)	176.80±96.1	128.9±47.8	**0.002[s]**
p value reached from Unpaired t-test; s= significant			

Table 5: Comparison of serum lipid profile between two groups (N=100).

In this study it was observed that, mean(±SD) serum zinc level was significantly low in hypertensive group compared to control group (84.9±22.9 µg/dl versus 96.0±24.2 µg/dl, p=0.020) (Table-6).

	Group I (n=50)	Group II (n=50)	p value
	Mean±SD	Mean±SD	
Serum zinc (µg/dl)	84.9±22.9	96.0±24.2	**0.020**[s]
p value reached from Unpaired t-test; s = significant			

Table 6: Comparison of serum zinc between the groups (N=100).

Figure-1 shows that serum zinc had significant moderate negative correlation with systolic blood pressure (SBP) in hypertensive group (r= - 0.620, p<0.001). The Pearson's correlation was statistically significant (p<0.001).

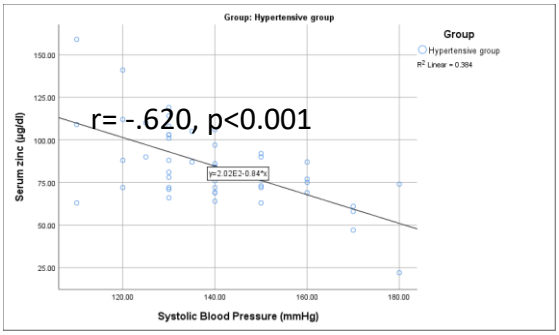

Figure 1: Scatter diagram showing the correlation of serum zinc with systolic blood pressure (SBP) in hypertensive group.

Figure 2 showed that serum zinc had significant moderate negative correlation with diastolic blood pressure (DBP) in hypertensive group (r= - 0.446, p=0.001). The Pearson's correlation was statistically significant (p=0.001).

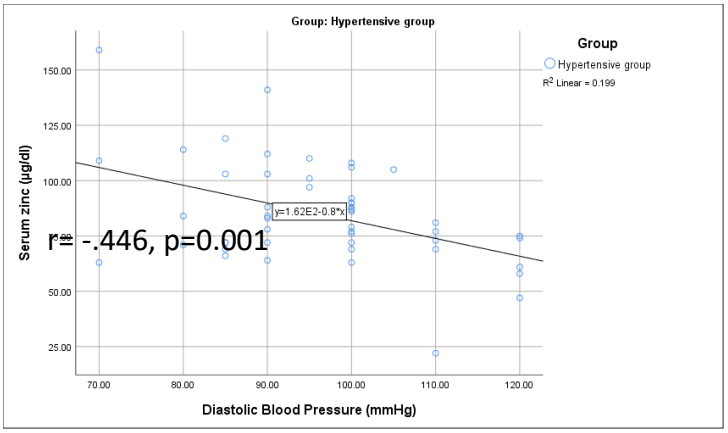

Figure 2: Scatter diagram displaying the correlation of serum zinc with diastolic blood pressure (DBP) in hypertensive group.

4. Discussion

Hypertension is the leading cause of mortality and morbidity worldwide [1]. Deficiencies of trace elements are closely related with development of hypertension and associated complications [5,25]. It was reported that, zinc deficiency is associated with development and adverse clinical outcomes of essential hypertension [20,25]. Serum zinc is the potential biomarker for prediction of zinc status in human body [22,23,27]. Estimation of serum zinc in hypertensive patients may be helpful for management of hypertension [22,27]. In this context, this study was intended to explore the association of serum zinc with hypertension among Bangladeshi adults. A total of 100 adult subjects of both sexes were selected; among them 50 were hypertensive patients (Group I) and rest 50 subjects were normotensive as control group (Group II). The mean age of hypertensive individuals (Group I) was 46.9±12.7 years and that was 43.1±8.5 years in control group (Group II). The difference was not statistically significant (p=0.080). Similar finding was observed in a couple of previous study [25,27].

In this study no significant gender difference was observed between the groups (p=0.221). But male participants were predominant in both groups. These results were consistence with similar previous studies [28,29]. The blood pressure (BP) of the study subjects was measured separately as systolic blood pressure (SBP) and diastolic blood pressure (DBP). The mean(±SD) blood pressures (both SBP and DBP) of hypertensive cases was significantly higher than controls (p<0.001). This finding was supported by related previous studies [25,30,31].

In this current study, 40(80%) individuals were overweight in hypertensive group and 29 (58%) subjects were overweight in control group, according to the World Health Organization (WHO) Asia-Pacific guidelines [26]. A significant more overweight individuals were observed in hypertensive group compared to control group (p=0.017). A recent study showed that there was significant relationship between overweight and obese (BMI: 23.0-24.9 and BMI: ≥25 kg/m^2) with hypertension (p=0.002) [28]. It was reported that, overweight or obese individuals had a 38.5 times higher risk of developing hypertension compared with normal weight individuals (BMI: 18.5-22.9 kg/m^2) [28]. Another previous study compared data from two surveys [The Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD) and National Health and Nutrition Examination Surveys (NHANES)] [32]. They found 80% hypertensive individuals in SHIELD survey and 85% hypertensive individuals in NHANES survey were overweight or obese. While, some related study found micronutrient deficiencies were associated with obesity [33].

In this study, it was observed that mean serum levels of total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and triglyceride (TG) were significantly higher in hypertensive individuals compared to normotensive individuals (p<0.05). The mean level of serum high density lipoprotein-cholesterol (HDL-C) was significantly low in hypertensive patients compared to control subjects (p=0.018). These results were comparable with related previous studies [3,4].

In present study, it was observed that mean serum zinc level was significantly low in hypertensive patients compared to control subjects (p=0.020). This finding was an agreement of a couple of previous

studies [17,28] [34,35,36]. Pearson's correlation coefficient test was performed to observe the correlation of serum zinc with blood pressures (both SBP and DBP) in hypertensive group. It was observed that serum zinc had a significant negative correlation with systolic blood pressure (SBP) (r= - 0.620, p<0.001) and diastolic blood pressure (DBP) (r= - 0.446, p=0.001) in hypertensive individuals. In accordance Bergomi *et al.* found serum zinc was negatively correlated with SBP (r= - 0.401, p=0.002) and DBP (r= - 0.320, p=0.013) [27]. While, Darroudi *et al*. found a weak negative correlation between DBP and serum zinc quartiles (r= - 0.024, p=0.021) [37]. The current study was consistent with these previous studies [27,37].

This study demonstrated that serum zinc level was significantly low in hypertensive individuals. It was also found that serum zinc had significant negative correlation with systolic blood pressure (SBP) and diastolic blood pressure (DBP) in hypertensive patients. The exact mechanisms of association between zinc and hypertension are not yet clearly understood. It was reported that, zinc act as an antioxidant and is essential for enzymatic action of superoxide dismutase (SOD) that disabled free radicals [8]. Any alteration of serum zinc level may affect the activity of SOD, which ultimately lead to vascular endothelial dysfunction [38,39]. On the other hand, zinc have a negative effect on ATP-dependent calcium channel that promotes outpouring of calcium ions (Ca^{+2}) from cell interior [40]. An increased level of calcium ions (Ca^{+2}) in vascular smooth muscle layer caused increased arterial wall tension [41]. These combined effects resulting in development of hypertension. Therefore, estimation of serum zinc level may act as an additional tool in the management of hypertension.

Conclusion

The present study concluded that serum zinc level is significantly low in hypertensive individuals. Serum zinc level has a negative correlation with systolic blood pressure (SBP) and diastolic blood pressure (DBP) in hypertensive patients. Determination of serum zinc level could be helpful for better management of hypertension.

Limitations of the study

This current study has several limitations. First, it was a single center study. Second, the sample size was relatively small. Third, the control group was selected purposively, not age and sex matched. Besides, detailed dietary habit of the participants was not noted in this study.

Recommendations

Further large-scale population based studies are needed to confirm the findings of this current study.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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