Original Contribution

Serum Calcium Levels in Patients with Essential Hypertension: A Cross-Sectional Study in a Tertiary Hospital of Bangladesh

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The exact cause of essential hypertension remains unclear. There is evidence to suggest that the development of essential hypertension is causally related to serum calcium levels. This study was designed to assess the status of serum calcium level in patients with essential hypertension and compared with healthy control. The research study was cross-sectional observational in nature. This study was done at the Department of Physiology in Sylhet MAG Osmani Medical College, Sylhet, Bangladesh. The duration of the research period was one year. All the known case of hypertension and newly diagnosed hypertensive patients were selected and compared with age-sex matched apparently healthy individual. Age below 18 years, pregnant women and patients taking supplementary calcium therapy were excluded from this study. Blood pressure was measured by auscultatory method; aneroid sphygmomanometer and standard stethoscope were used. Automated chemistry analyzer Vitrose-350, USA was used to estimate serum calcium level. Standard operating procedure strictly followed. There were 62 hypertensive (both known case of hypertension and newly diagnosed cases) were selected in hypertensive group (Group A) and 62 age-sex matched apparently healthy individuals were selected in normotensive group (Group B). The mean age of hypertensive and normotensive subjects was not statistically significant (p=0.814). There were 27(43.5%) male and 35(56.5%) female in hypertensive group, 32(51.8%) male and 30(48.4%) female in normotensive group. The distribution was statistically not significant (p=0.472). The mean value of the systolic blood pressure (SBP) was 146.45±5.82 mm Hg and the mean value of the diastolic blood pressure (DBP) was 92.90±7.66 mm Hg in hypertensive group. The mean value of the SBP was 112.74±6.88 mm Hg and the mean value of the DBP was 74.52±5.33 mm Hg of the normotensive group. The difference in mean blood pressure (BP) between the two groups was highly significant (p<0.001). The mean value of the serum calcium level was 8.59±0.55 mg/dl in hypertensive group and 9.12±0.93 mg/dl in normotensive group, which was statistically significant (p <0.001) between two groups. Serum calcium was significantly lower in hypertensive group than normotensive group. There was a negative correlation of the serum calcium level with both systolic and diastolic blood pressure.

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Key words: Systolic blood pressure, Serum calcium, Diastolic blood pressure, Linear correlation

Introduction

Hypertension is one of the most common cardiovascular disorders in the world, with a high rate of morbidity and mortality[1]. As per the latest guidelines provided by the International Society of Hypertension, an individual is classified as hypertensive if their systolic blood pressure (SBP) is 140 mm Hg or higher and/or their diastolic blood pressure (DBP) is 90 mm Hg or higher study[2]. Based on the underlying pathophysiology, there are two forms of hypertension: primary and secondary. Primary hypertension, also known as essential idiopathic hypertension, is the term used to describe an increase in blood pressure (BP) in the absence of established reasons such as renovascular disease, renal failure, pheochromocytoma, hyper-aldosteronism and others.

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Approximately 95.0% of all cases of hypertension are of the essential kind, which is the most prevalent form[3]. According to estimates, 26.0% of adults have hypertension, and by 2025, that number is predicted to increase to 29.0%[4]. Numerous epidemiological researches revealed a strong correlation between blood pressure (BP) and electrolyte levels as well as between blood pressure (BP) and salt intake[5]. A higher intracellular calcium concentration immediately raises blood pressure (BP) above normal by increasing peripheral resistance and by raising serum sodium levels through the renin-angiotensin-aldosterone pathway to increase vascular blood volume[6]. The relationship between the intracellular and extracellular calcium levels is inverse, and this relationship is mediated by stimulating parathyroid hormone release[7]. Lower serum calcium levels have been linked to an increased number of newly diagnosed hypertension patients, according to Subhash and Ramanathan[8]. Restoring calcium levels significantly lowers both systolic and diastolic blood pressure. In Bangladesh, the number of hypertension patients is rising rapidly, particularly among the younger generation. Previous research demonstrates a causal link between the onset of essential hypertension in several ethnicities and the serum calcium level. The cause of Bangladesh's population's rapid rise in essential hypertension is being investigated. Furthermore, there is not enough study done in this area on the relationship between systemic blood pressure (BP) and serum electrolyte levels. This study therefore aims to compare the blood calcium level status in individuals with essential hypertension with healthy control.

Methods

This was a cross-sectional study, carried out in the Department of Physiology in collaboration with the Department of Medicine at Sylhet MAG Osmani Medical College Hospital, Sylhet. Ethical permission was taken from the ethical committee of Sylhet MAG Osmani Medical College (Memo no: SOMC/2021/59 Date: 06/11/2021). Total study duration was one year, from January 2021 to December 2021. Patients came to the outpatient department (OPD) of Department of Medicine for the treatment of elevated blood pressure (BP) was the study population. Patients with previously or newly diagnosed hypertension were selected in the hypertensive group. Age and sex matched apparently healthy and normotensive hospital staffs were selected as normotensive group and considered as co. Person below 18 years age, patients on calcium supplementation therapy and pregnant women were excluded from the study. Sixty two subjects were included in hypertensive group and 62 subjects were included in normotensive group. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and serum calcium level were the study variables. Informed written consent was taken and detailed physical examination of all participants was done. The clinical history of the subjects was noted. BMI (Body mass index) were calculated from the height and weight of the subjects. Subjects' blood pressure (BP) was measured and recorded. A standard sphygmomanometer and stethoscope were used for BP measurement. BP was measured three times at ten minutes interval. Average value was recorded. With all aseptic precautions, blood sample were collected for biochemical analysis. Thyroid stimulating hormone (TSH) assay was done to exclude thyroid disorder. Serum creatinine and urine routine examination were done to exclude chronic kidney disease. Fasting lipid profile was done to exclude dyslipidemia. Automated chemistry analyzer Vitrose-350, USA, was used to estimate serum calcium level. Each 1 gm/dl reduction of serum albumin concentration lowers the total calcium concentration approximately by 0.8 mg/dl without affecting the ionized calcium concentration. Thus the calcium level was corrected in patients with low serum albumin levels. The following equation was used to correct serum calcium level:

Corrected calcium (mg/dl) = Measured calcium (mg/dl) ± 0.8 (4.0-serum albumin [gm/dl])

Quantitative data were expressed as mean±SD (Standard Deviation) and comparison was done by using unpaired 't' test. Qualitative data were expressed as frequency and percentage and compared by Chi-Square (χ^2) test. Linear regression analysis was done to compare the relationship between serum calcium level and blood pressure of the subjects. The p value of <0.05 was considered statistically significant.

Results

Mean age of the hypertensive group was 47.06±11.59 years and normotensive group was 45.08±12.97 years. The difference was not

significant between the groups (p>0.05) (Figure 1). The gender distribution of the subjects was showed in Figure 2. The distribution was found similar between the study groups (p>0.05).

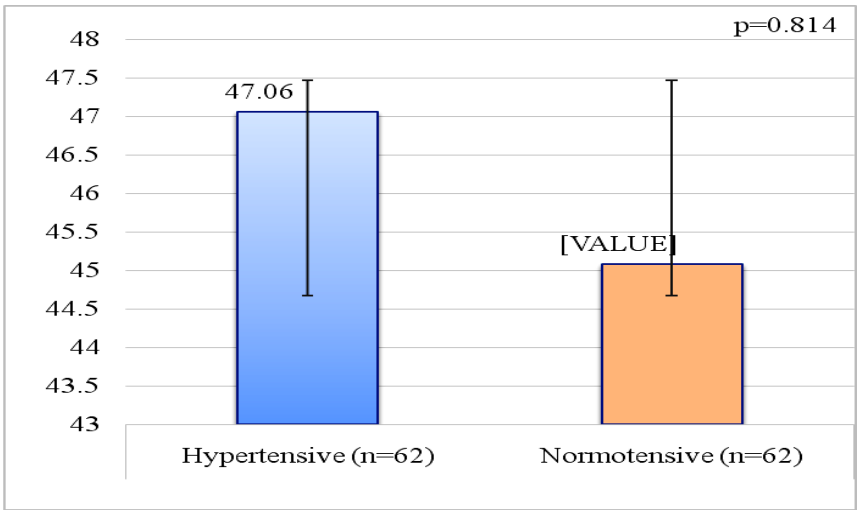

Figure 1: Age distribution of the subjects (years)

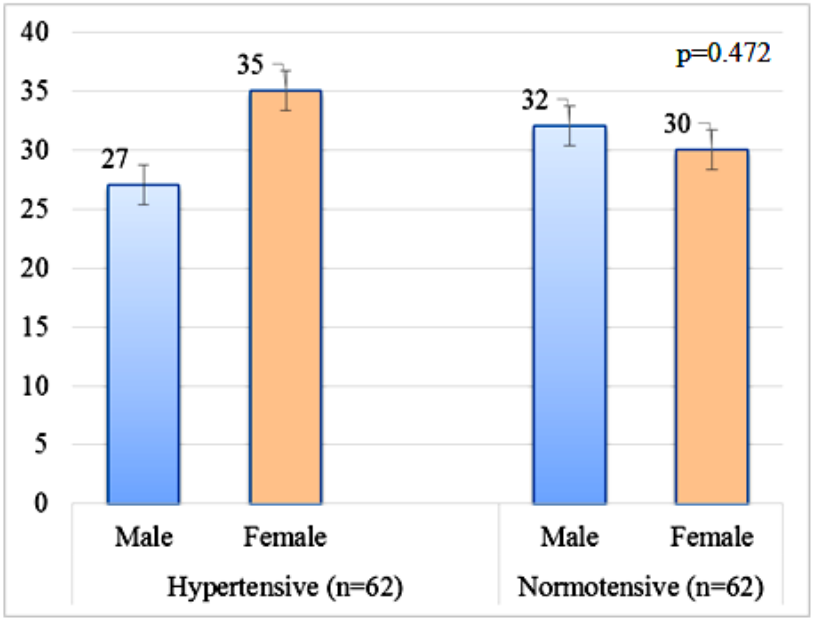

Figure 2: Gender distribution of the subjects

The mean BMI was found 24.56±2.81 kg/m^2 and 23.19±2.49 kg/m^2 in hypertensive and normotensive group respectively. BMI was found significantly higher in hypertensive group than that of normotensive group (p=0.005). The mean value of the pulse was found equal between two study groups. The mean systolic blood pressure (SBP) was 146.45±5.82 mm Hg in hypertensive group and 112.74±6.88 mm Hg in normotensive group. The mean of the diastolic blood pressure (DBP) was 92.90±7.77 mm of Hg in hypertensive group and 74.52±5.33mm of Hg in normotensive group. Both the SBP and DBP were significantly higher (p<0.001) in hypertensive group than that of the normotensive group (Table I). Comparison of mean serum calcium level between the study groups and sub-groups (newly diagnosed and previously hypertensive patients) presented in Table II. Mean serum calcium level was 8.59±0.55 mg/dl in hypertensive group and 9.12±0.93 mg/dl in normotensive group. The difference was statistically

significant (p <0.001) between two groups. However sub-group analysis, mean serum calcium was 8.43±0.57 mg/dl in newly diagnosed cases and 8.66±0.53 mg/dl in previously diagnosed cases. Newly diagnosed hypertensive patients (n=19) and previously diagnosed hypertensive patients (n=43) were not found significant difference (p=0.074). Distribution of subjects of different calcium level showed in Table III. Serum calcium level was more below normal in hypertensive group (n=28) than normotensive group (n=11). Whereas, 49(79.0%) normotensive subjects had normal serum calcium level and 34(54.8%) hypertensive subjects had normal serum calcium level. Only 2(3.2%) subjects of normotensive group had serum calcium level above normal. The distribution was statistically significant (p <0.001). There was a moderate negative (R = -0.331) correlation observed between serum calcium level and systolic blood pressure. The fitted regression model for serum calcium was -7.4229±195.32. The overall regression result was found statistically significant; R^2 = 0.1096, F (1,122) = 15.018, p<0.001. It was found that the serum calcium level significantly predicted the systolic blood pressure (B = -0.331, p <0.001, 95% CI: -11.215 to -3.631) (Figure 3). There was a weak negative (R = -0.246) correlation observed between serum calcium level and diastolic blood pressure. The fitted regression model for serum calcium was -3.4513±114.27. The overall regression result was found statistically significant; R^2 = 0.06, F (1,122) = 7.826, p=0.006 (Figure 4).

Table I: Comparison of the groups based on the physical findings (N=124)

Parameter	Hypertensive (n=62)	Normotensive(n=62)	p value (unpaired 't' test)
	Mean±SD	Mean±SD	
BMI (Kg/m^2)	24.56±2.81	23.19±2.49	0.005
Pulse (beats/minute)	76.68±4.02	77.15±3.36	0.483
SBP (mm Hg)	146.45±5.82	112.74±6.88	<0.001
DBP (mm Hg)	92.90±7.66	74.52±5.33	<0.001

Table II: Comparison of serum calcium level between the study groups (N=124)

Groups	Subject	Serum Calcium level (mg/dl)	p value (unpaired 't' test)
		Mean±SD	
Study group	Hypertensive (n=62)	8.59±0.55	<0.001
	Normotensive (n=62)	9.12±0.93	
Sub-group	Hypertensive (n=19)	8.43±0.57	0.074
	Normotensive (n=43)	8.66±0.53	

Table III: Distribution of the subjects based on the difference on serum calcium status (N=124)

Serum calcium level	Hypertensive (n=62)	Normotensive (n=62)	p value (χ^2 test)
	n (%)	n (%)	
Below normal (<8.5 mg/dl)	28 (45.2)	11 (17.7)	<0.001
Normal (8.5-10.5 mg/dl)	34 (54.8)	49 (79.0)	
Above normal (>10.5 mg/dl)	-	02 (03.2)	

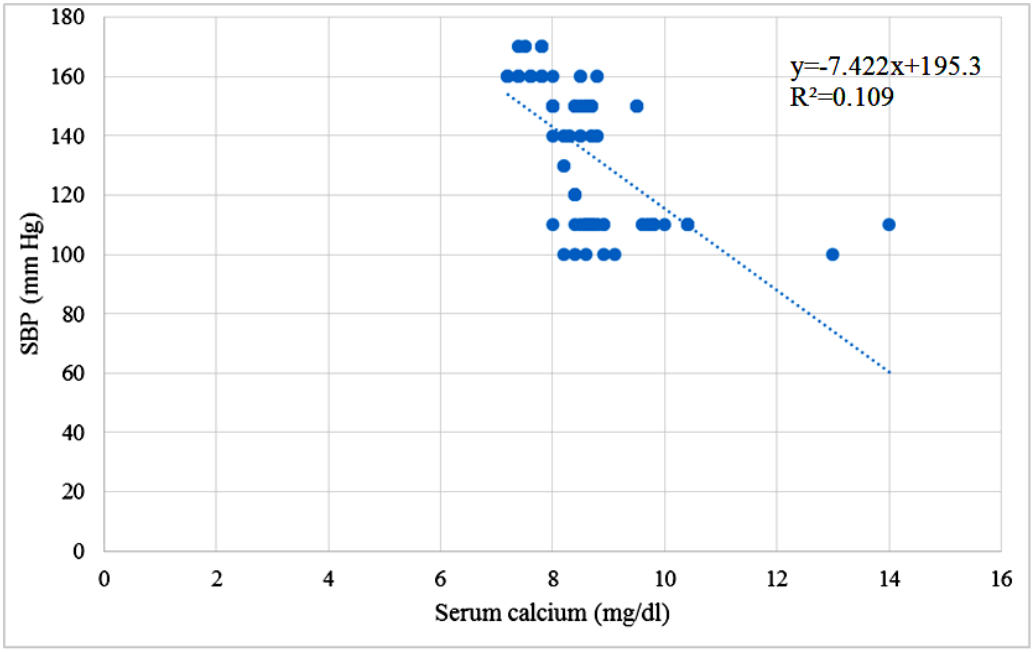

Figure 3: Scatter diagram showing significant negative correlation of serum calcium level with systolic blood pressure

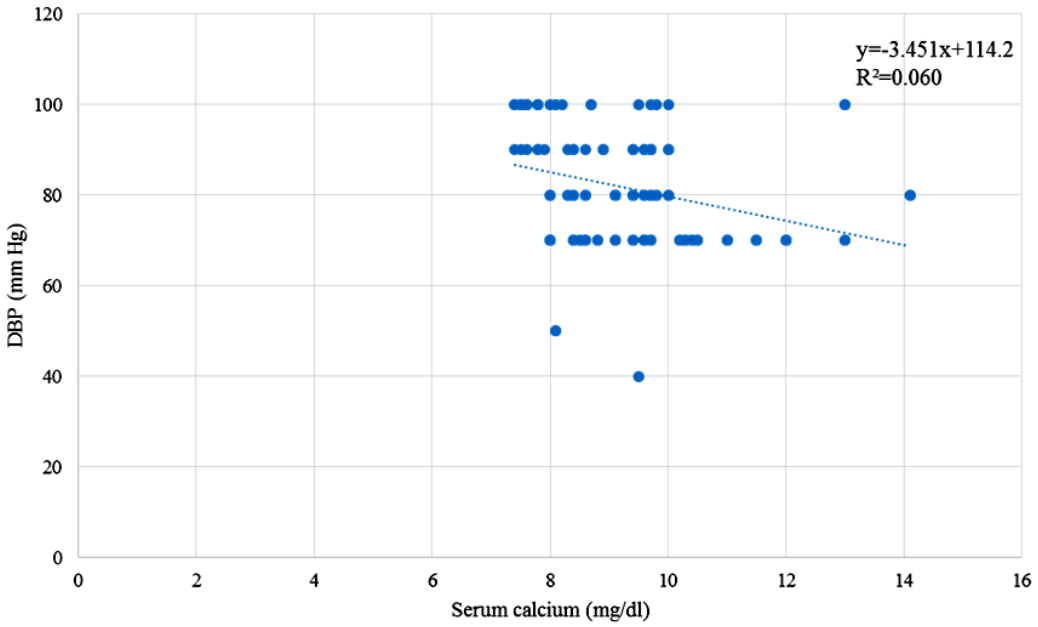

Figure 4: Scatter diagram showing significant negative correlation of serum calcium level with diastolic blood pressure

Discussion

Several reasons have already been identified, including stress, ageing, obesity, and sedentary lifestyles. It has also been shown that a number of electrolytes are responsible for the development of hypertension[3]. Evidence indicated that essential hypertension and abnormal serum electrolyte levels are causally related in people of different countries. In consequence, this investigation was structured to assess the relationship between serum calcium levels and essential hypertension in the individuals of Bangladesh. In present study, all the known and newly diagnosed cases of essential hypertension patients were enrolled in

hypertensive group and age and sex matched apparently healthy individuals were enrolled in the normotensive group. There were 62 hypertensive and 62 normotensive evaluated in this study. Out of 62 hypertensive patients 19 were newly diagnosed and 43 were already being diagnosed as hypertensive patients. The study populations were matched by age and sex. So, probability of variation of study parameter due to age and sex variation could be eliminated. Significantly ($p<0.001$) lower serum calcium levels were seen in hypertension patients compared to normotensive subjects. Distribution of study subjects also showed significantly more (p level below normal reference value). Linear regression analysis showed moderately negative correlation ($R = -0.331$, $p<0.001$) of serum calcium with SBP and weakly negative correlation ($R = -0.246$, $p=0.006$) of serum calcium with DBP in this study. Both Ambwani et al. and Sharma and Sarmah observed lower serum calcium level in hypertensive patients compared to normotensive patients similar to this study[1,9]. Another Indian study found significant reduction of serum calcium level not only in essential hypertensive patients but also in their first degree relatives compared to the normotensive controls[10]. The significant difference also found with the severity of the disease. The more decrease in serum calcium level, more increase in blood pressure[11,12]. Subhash and Ramanathan (2019) found negative correlation between serum calcium and systolic and diastolic blood pressure ($R = -0.289$, $p=0.001$) in their sample of newly diagnosed essential hypertension[8]. Distribution in their study showed that lower than normal serum calcium level (<8.5 mg/dl) more common in stage 2 hypertension than stage 1 hypertension. But according to Hazari et al., there was no significant variation in the blood pressure-related calcium levels between the normotensive and hypertensive groups[13]. The possible mechanism associated with increase blood pressure in low plasma calcium concentration is as follows. When plasma calcium level is decreased the renin is secreted from the juxtaglomerular cell, causing vaso-constrictive affect by activation of angiotensin II (Ag II). Low calcium concentration in plasma, stimulate the release of parathyroid hormone (PTH), parathyroid hypertensive factor (PHF) and synthesis of calcitriol. They stimulate intracellular signaling pathway to raise calcium level inside the cell, lead to increase the vascular resistance, hence increase blood pressure; although the role of parathyroid hormone is still not properly understood[6].

Conclusion

Serum calcium level is significantly lower in the patients with hypertension compared with that of normotensive subjects. It is also found that, serum calcium level is negatively correlated with both systolic and diastolic blood pressure. Therefore, it can be concluded that, serum calcium play an important role in the development of essential hypertension.

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