

A HOSPITAL BASED STUDY TO ASSESS THE SERUM TOTAL CALCIUM AND SERUM CALCIUM PHOSPHORUS RATIO IN ESSENTIAL HYPERTENSION AND ITS ASSOCIATION WITH SEVERITY OF DISEASE: AN PROSPECTIVE STUDY

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ABSTRACT

Background: Hypertension is an increasingly important medical and public health burden globally. Essential hypertension is associated with altered calcium metabolism. The aim of this study to assess the serum total calcium and serum calcium phosphorus ratio in essential hypertension and its association with severity of disease. **Materials & Methods:** This was a hospital based prospective study done on 60 subjects, of which 30 cases of essential hypertension satisfying inclusion and exclusion criteria visiting medicine OPD and admitted in Government Medical College, Dausa, Rajasthan, India and 30 age and sex matched normotensive controls during six-month period. Serum calcium was measured using arsenazo III reagent and serum phosphorus using ammonium molybdate reagent. Correlations were assessed using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant. **Results:** The study comprised of 60 participants with a mean age of 48.7±10.5 years. Males constituted 56.66% of the study population. Family history of hypertension was significantly more common in cases (26.66% vs 12%, p<0.05*). As expected, mean systolic and diastolic BP values were significantly higher in hypertensives compared to controls (p<0.05*). Serum calcium showed a significant negative correlation with systolic BP (r= -0.387, p<0.01), whereas the calcium-phosphorus ratio positively correlated with systolic BP (r= 0.536, p<0.01) in hypertensive patients. **Conclusion:** According to our research, serum calcium levels and essential hypertension are correlated, and there is an inverse link between disease severity and serum calcium levels. Compared to normotensive controls, patients with primary hypertension had a considerably higher calcium-phosphorus ratio.

INTRODUCTION

Hypertension is a common medical condition defined as systolic blood pressure (BP) ≥140 mmHg and/or diastolic BP ≥90 mmHg.^[1] A major hazard to world health, the prevalence of hypertension has been steadily rising over the past few decades, particularly in low- and middle-income nations.^[2] The large impact of lifestyle interventions, such as physical activity, eating habits, and body weight management beyond hereditary endowment, on blood pressure has been confirmed by growing epidemiological research.^[3]

Along with other cations, calcium is one of the most prevalent mineral elements that are widely involved in a variety of bodily functions. As such, its role in hypertension has drawn a lot of attention. About half

of the calcium in serum is ionized, 40% is bound, mostly to albumin, and 10% is bound to anions.^[4] Serum total calcium is the sum of the three types and is least impacted by variations in measurement or physiological changes. Therefore, total serum calcium is routinely used in clinical practice to represent calcium status in the human body.^[5]

Essential hypertension is associated with altered calcium metabolism. Changes in the regulation of intracellular free Calcium and disturbed extracellular calcium homeostasis are noted in patients diagnosed with primary hypertension. Extracellular calcium provides calcium ions for the maintenance of intracellular calcium levels, blood coagulation, bone mineralization and plasma membrane potential. It is widely accepted that the increase in peripheral vascular tone that characterizes the established phase

of hypertension is due to increased active tension in the smooth muscle cells. Calcium influx through receptor and voltage-gated calcium channels initiates vascular contraction and the fall in the intracellular free calcium concentration results in relaxation or vasodilatation.^[6]

In hypertensive patients there is a defect in excreting the digitalis like natriuretic factor which inhibits ouabain sensitive Na⁺-K⁺ATPase causing intracellular sodium accumulation. The vascular smooth muscle cells accumulate intracellular calcium as a result of the elevated intracellular sodium, which increases contractility.^[7] Many researchers even recommend a regular consumption of the recommended daily levels of dietary calcium to combat with hypertensive disorders.^[8] In a country like India, people tend to have a diet rich in sodium and poor in potassium and calcium, this change in diet can change hypertension course and progress. The aim of this study to assess the serum total calcium and serum calcium phosphorus ratio in essential hypertension and its association with severity of disease.

MATERIALS AND METHODS

This was a hospital based prospective study done on 60 subjects, of which 30 cases of essential hypertension satisfying inclusion and exclusion criteria visiting medicine OPD and admitted in Government Medical College, Dausa, Rajasthan, India and 30 age and sex matched normotensive controls during six-month period.

Inclusion Criteria: Patients with Newly diagnosed Essential hypertension Patients whose age is above 18 years are included Both sexes are included.

Exclusion Criteria:

- Patients who are below 18 years Patients who are on Vitamin D and Calcium supplementation
- Patients with Primary kidney disease/Chronic Kidney disease
- Chronic Liver disease
- Secondary Hypertension
- Pregnancy
- Drugs influencing Calcium and Phosphorus metabolism

Methods:

Patients with acute ischemic stroke admitted in the medicine department within 48 hrs. of onset of symptoms were enquired about presenting complaints, mode of onset of neurological deficit, past history of TIA, hypertension, diabetes mellitus

in detail. Special enquiry about alcoholism, smoking, pregnancy or recent delivery and use of anticoagulants or oral contraceptives was made. Any similar illness in the family was asked. Complete general examination and neurological examination was done. Other systems were examined in detail. Basic investigations such as Haemoglobin, blood cell count, urine for albumin, sugar deposit, blood sugar, urea, serum creatinine, and serum electrolytes, total cholesterol were estimated. Electrocardiography, echocardiography and CT scan of brain were done. Primary hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg on at least two occasions or current use of antihypertensive medication. Severe hypertension was defined as systolic BP ≥ 180 mmHg and/or diastolic BP ≥ 110 mmHg.

Statistical Analysis:

Data was analyzed using IBM SPSS software v23.0. Continuous variables were expressed as mean \pm standard deviation and categorical variables as frequencies and percentages. Means were compared using unpaired t-test. Correlations were assessed using Pearson's correlation coefficient. A p-value < 0.05 was considered statistically significant.

RESULTS

The study comprised of 60 participants with a mean age of 48.7 ± 10.5 years. Males constituted 56.66% of the study population. Baseline characteristics are presented in Table 1. Cases and controls were comparable in terms of age, gender distribution, BMI and history of smoking/alcoholism ($p > 0.05$). Family history of hypertension was significantly more common in cases (26.66% vs 12%, $p < 0.05^*$). As expected, mean systolic and diastolic BP values were significantly higher in hypertensives compared to controls ($p < 0.05^*$).

The biochemical parameters of cases and controls are compared in Table 2. Mean serum total calcium (8.6 ± 0.4 vs 9.3 ± 0.5 mg/dL) and phosphorus (2.7 ± 0.5 vs 3.6 ± 0.4 mg/dL) levels were found to be significantly lower in hypertensives compared to normotensives ($p < 0.05^*$). On the other hand, the calcium-phosphorus ratio was significantly higher in the hypertensive group (3.18 ± 0.82 vs 2.58 ± 0.36 , $p < 0.05^*$).

Serum calcium showed a significant negative correlation with systolic BP ($r = -0.387$, $p < 0.01$), whereas the calcium-phosphorus ratio positively correlated with systolic BP ($r = 0.536$, $p < 0.01$) in hypertensive patients, as depicted in Table 3.

Table 1: Baseline characteristics of patients

Parameter	Cases (n=30)	Controls (n=30)	P-value
Age (years)	48.7±10.5	43.3±11.6	>0.05
Male gender, n (%)	17 (56.66%)	15 (50%)	>0.05
BMI (kg/m ²)	25.23±3.56	22.39±1.77	>0.05
Family history of HTN	8 (26.66%)	4 (12%)	<0.05*
Smoking	11 (36.66%)	10 (33.33%)	>0.05
Alcoholism	8 (26.66%)	8 (26.66%)	1.00
Systolic BP (mmHg)	156.8±12.8	110.3±6.9	<0.05*
Diastolic BP (mmHg)	105.4±7.2	74.6±4.6	<0.05*

Table 2: Comparison of biochemical parameters between cases and controls

Parameter	Cases (n=30)	Controls (n=30)	P-value
Serum total calcium (mg/dL)	8.6±0.4	9.3±0.5	<0.05*
Serum phosphorus (mg/dL)	2.7±0.5	3.6±0.4	<0.05*
Calcium-phosphorus ratio	3.18±0.82	2.58±0.36	<0.05*

Table 3: Correlation of serum calcium and calcium-phosphorus ratio with systolic blood pressure in hypertensives

Parameter	Pearson's correlation coefficient (r)	P-value
Serum total calcium	-0.387	0.01*
Calcium-phosphorus ratio	0.536	0.01*

DISCUSSION

Hypertension is one of the leading causes of death and disability among adults all over the world and emerging health problem in India. Essential hypertension is a disorder that is heterogeneous, meaning that different patients have different causes of high blood pressure. Patients with essential hypertension have been found to have abnormalities in the regulation of intracellular free calcium as well as disruptions in extracellular calcium homeostasis.^[9] In our study mean age in hypertensive patients was 48.7±10.5 and in controls it was 43.3±11.6. There was no significant difference was obtained in relation to age in both groups. This may be attributed to the fact that most hypertensive patients remain asymptomatic for many years and they seek medical attention only when complication sets in. As expected, participants from age group 40-59 were the highest as they began to develop hypertension related problems like end organ damage during this age. In our study, we observed a slightly increased number of male participants but it was not significant. Therefore, our observation is that both males and females are almost equally affected, especially in the middle age.

Our study showed that 26.66% of the cases had a positive family history of hypertension while 73.33% did not have any family history. Among the control, only 12% had family history of hypertension while 88% of them did not have any positive family history. Although, Sudhakar et al^[10], and Sharma^[11] concluded that serum calcium was decreased in the first-degree relatives of hypertensive individuals as well, we observed that the association of positive family history of hypertension was only slightly stronger with cases, and we did not find it statistically significant (p Value: 0.046)

According to this study, patients with primary hypertension had a greater calcium-phosphorus ratio and considerably lower serum total calcium and phosphorus levels than normotensive controls.

Additionally, there was a negative correlation between serum calcium and blood pressure in the hypertensive group, but a positive correlation between the Ca:P ratio and blood pressure, indicating that these parameters are related to the severity of hypertension.

The inverse association between serum calcium and blood pressure observed in this study is consistent with previous reports. Sudhakar *et al.*, demonstrated significantly reduced serum calcium in both newly diagnosed hypertensives and their first-degree relatives compared to controls.¹⁰ Touyz *et al.*, also reported hypocalcemia along with lower potassium and magnesium levels in hypertensives.^[12]

The compensatory rise in intracellular calcium concentration in vascular smooth muscle cells, which results in greater contractility and vascular tone, may be the mechanism connecting lower serum calcium to higher blood pressure. Research indicates that hypertensives have higher intracellular calcium levels, which return to normal when blood pressure drops.^[13,14]

Tillman DM and Semple PF^[15] showed that there is disturbance of calcium metabolism in hypertension, and although result of Ionized calcium, Total Serum Calcium concentration in the hypertensive was not significant, there was significant correlation between total calcium and systolic pressure.

CONCLUSION

According to our research, serum calcium levels and essential hypertension are correlated, and there is an inverse link between disease severity and serum calcium levels. Compared to normotensive controls, patients with primary hypertension had a considerably higher calcium-phosphorus ratio. The complete care of essential hypertension may involve the monitoring and correction of certain metabolic abnormalities. The pathophysiological relevance of calcium-phosphorus imbalance in hypertension and

the therapeutic advantages of focusing on these pathways require more investigation.

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