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Serum Total Calcium and Calcium/Phosphorus Ratio in Primary Hypertension and Correlation with Disease Severity: A Case-Control Study

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A B S T R A C T

***Objectives*:** This study aimed to assess serum total calcium and calcium/phosphorus ratio in patients with primary hypertension and correlate these parameters with blood pressure. ***Methods*:** This prospective comparative study included 50 newly diagnosed primary hypertension patients and 50 age- and sex-matched normotensive controls. Serum calcium was measured using arsenazo III reagent and serum phosphorus using ammonium molybdate reagent. Additional investigations included CBC, RFT, LFT and abdominal ultrasound. ***Results*:** The mean age was 44.06±11.74 years and 54% were males. Mean serum calcium (8.7±0.5 vs 9.1±0.6 mg/dL) and phosphorus (2.9±0.7 vs 3.5±0.4 mg/dL) were significantly lower, while calcium-phosphorus ratio was significantly higher (3.20±0.73 vs 2.63±0.30) in cases vs controls ($p<0.05$). Serum calcium negatively correlated ($r=-0.391$) and calcium-phosphorus ratio positively correlated ($r=0.530$) with blood pressure ($p<0.05$). ***Conclusion*:** Serum calcium and calcium-phosphorus ratio show significant alterations in primary hypertension, correlating with blood pressure severity. Monitoring and managing these parameters may be considered in hypertension management.

Keywords: Essential hypertension; calcium; phosphorus; association.

INTRODUCTION

Primary or essential hypertension remains a major modifiable risk factor for cardiovascular morbidity and mortality worldwide, with a steadily rising prevalence [1]. Despite extensive research, the complete pathophysiology of primary hypertension is still not fully elucidated. Alterations in calcium homeostasis have emerged as one potential mechanism contributing to the development of hypertension [2].

Calcium plays a crucial role in regulating vascular smooth muscle tone and peripheral vascular resistance through its effects on vascular smooth muscle contraction and relaxation [3]. Disturbances in calcium metabolism, such as increased intracellular calcium, reduced extracellular calcium, and alterations in calcium-regulating hormones like parathyroid hormone (PTH) and vitamin D have been reported in essential hypertension [4].

Observational studies have found lower serum total and ionized calcium levels in hypertensive individuals compared to normotensives [5, 6]. This hypocalcemia is postulated to increase intracellular calcium, leading to increased vascular tone and blood pressure [7]. Vitamin D deficiency, commonly seen in hypertensives, may also contribute by stimulating PTH secretion and activating the renin-angiotensin-aldosterone system (RAAS) [8].

The calcium-phosphorus ratio, influenced by dietary intake, intestinal absorption and renal excretion of these minerals, is another parameter of interest in hypertension. Phosphorus has been inversely associated with blood pressure in some studies [9, 10]. The interplay between calcium and phosphorus may thus impact cardiovascular risk. However, data on the calcium-phosphorus ratio in essential hypertension is limited.

Correcting calcium and phosphorus abnormalities could potentially aid in optimizing blood pressure control and reducing cardiovascular risk in hypertensive patients. However, the relationship between these parameters and blood pressure is not thoroughly characterized in the Indian population.

Hence, the present study aimed to compare serum total calcium, phosphorus, and the calcium-phosphorus ratio between primary hypertensive patients and normotensive controls and examine their correlation with blood pressure severity. The results could pave the way for considering these accessible biochemical markers in the comprehensive evaluation and management of essential hypertension.

Objectives:

1. To study the levels of serum total calcium and calcium/phosphorus ratio in patients with primary hypertension compared to normotensive controls.
2. To correlate serum total calcium and calcium/phosphorus ratio with blood pressure severity in hypertensive patients.

Methods

This prospective comparative study was conducted at Chigateri General Hospital and Bapuji Hospital attached to JJM Medical College, Davangere between August 2022 and August 2023. The study included 50 patients newly diagnosed with primary hypertension aged over 18 years of either sex. Age- and sex-matched normotensive individuals were recruited as controls (n=50). Informed consent was obtained from all participants.

Patients with chronic kidney disease, chronic liver disease, known secondary hypertension, primary parathyroid disorders, pregnancy, or those on calcium/vitamin D supplements and medications affecting calcium-phosphorus metabolism were excluded.

After detailed history taking and physical examination, the following investigations were done for all subjects:

- Blood pressure (BP) measurement in sitting position after 10 minutes rest
- Serum total calcium: measured by arsenazo III method
- Serum phosphorus: measured by ammonium molybdate method
- Complete blood count (CBC)
- Renal function tests (RFT)
- Liver function tests (LFT)
- Fasting blood glucose
- Serum electrolytes
- Ultrasound of abdomen and pelvis

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.

Data was analyzed using IBM SPSS software v23.0. Continuous variables were expressed as mean ± 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 100 participants with a mean age of 44.06±11.74 years. Males constituted 54% 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 (28% vs 12%, $p=0.01$). As expected, mean systolic and diastolic BP values were significantly higher in hypertensives compared to controls ($p<0.01$).

Table 1: Baseline characteristics of cases and controls

Parameter	Cases (n=50)	Controls (n=50)	P-value
Age (years)	47.3±11.2	41.1±12.5	0.066
Male gender, n (%)	29 (58%)	25 (50%)	0.422
BMI (kg/m2)	24.25±3.71	22.09±1.82	0.04*
Family history of HTN	14 (28%)	6 (12%)	0.01*
Smoking	18 (36%)	16 (32%)	0.673
Alcoholism	14 (28%)	14 (28%)	1.00
Systolic BP (mmHg)	159.2±14.7	108.1±6.7	<0.01*
Diastolic BP (mmHg)	106.0±6.4	72.4±3.7	<0.01*

BMI: Body mass index; HTN: Hypertension; BP: Blood pressure *Statistically significant (p<0.05)

The biochemical parameters of cases and controls are compared in Table 2. Mean serum total calcium (8.7±0.5 vs 9.1±0.6 mg/dL) and phosphorus (2.9±0.7 vs 3.5±0.4 mg/dL) levels were found to be significantly lower in hypertensives compared to normotensives (p<0.01). On the other hand, the calcium-phosphorus ratio was significantly higher in the hypertensive group (3.20±0.73 vs 2.63±0.30, p<0.01).

Table 2: Comparison of biochemical parameters between cases and controls

Parameter	Cases (n=50)	Controls (n=50)	P-value
Serum total calcium (mg/dL)	8.7±0.5	9.1±0.6	<0.01*
Serum phosphorus (mg/dL)	2.9±0.7	3.5±0.4	<0.01*
Calcium-phosphorus ratio	3.20±0.73	2.63±0.30	<0.01*

*Statistically significant (p<0.05)

Serum calcium showed a significant negative correlation with systolic BP (r= -0.391, p<0.01), whereas the calcium-phosphorus ratio positively correlated with systolic BP (r= 0.530, p<0.01) in hypertensive patients, as depicted in Table 3. The correlation of these parameters with diastolic BP followed a similar trend (data not shown).

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	-0.391	0.01*
Calcium-phosphorus ratio	0.530	0.01*

*Statistically significant (p<0.05)

Among hypertensives, 12 patients (24%) had severe hypertension (systolic BP ≥180 mmHg and/or diastolic BP ≥110 mmHg). The mean serum calcium was lower (8.4±0.5 vs 8.8±0.5 mg/dL) and mean Ca:P ratio was higher (3.72±0.74 vs 3.02±0.64) in severe hypertensives compared to those with non-severe hypertension, although statistical significance was not reached, likely due to the small number of severe hypertensives.

DISCUSSION

This study found that compared to normotensive controls, patients with primary hypertension had significantly lower serum total calcium and phosphorus levels and a higher calcium-phosphorus ratio. Furthermore, serum calcium negatively correlated, while the Ca:P ratio positively correlated with blood pressure in the hypertensive group, suggesting an association of these parameters with hypertension severity.

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 [6]. Touyz*et al*., also reported hypocalcemia along with lower potassium and magnesium levels in hypertensives [5].

The mechanism linking lower serum calcium with higher blood pressure could be the compensatory increase in intracellular calcium concentration in vascular smooth muscle cells, leading to increased contractility and vascular tone. This is supported by studies showing elevated intracellular calcium levels in hypertensives, which normalize with blood pressure reduction [7, 10].

Vitamin D deficiency, commonly associated with hypertension, may also explain the lower calcium levels by reducing intestinal calcium absorption. Vitamin D is known to have vasculoprotective and antihypertensive effects mediated by inhibition of the RAAS, modulation of inflammatory cytokines, and improvement of endothelial function

[8]. Hence, the low calcium may reflect an underlying vitamin D deficiency in these patients. Estimating 25-hydroxyvitamin D levels would help confirm this hypothesis.

The influence of dietary factors on calcium levels cannot be ruled out. Low dietary calcium intake has been linked to increased risk of hypertension in some populations. As this study did not assess dietary calcium intake, further studies accounting for dietary factors are needed to establish the independent association between serum calcium and hypertension.

Coming to phosphorus, the hypertensive group demonstrated lower levels compared to normotensives, concurring with some but not all previous reports. Lower phosphorus has been documented in hypertensives by Kesteloo*et al.*, [9] and Ljunghall*et al*., Conversely, Harlan *et al*., found no association between serum phosphorus and blood pressure. These discrepancies could stem from differences in study populations, dietary phosphorus intake, and presence of comorbidities affecting phosphorus levels. The mechanism relating low phosphorus to hypertension is unclear but may involve the stimulation of vascular calcification and reduced arterial compliance.

Despite lower individual calcium and phosphorus values, their ratio was significantly elevated in hypertensives and correlated positively with blood pressure. This suggests that the balance between the two minerals may be more important than their absolute levels in modulating vascular function and blood pressure. An altered Ca:P ratio could influence the calcium-sensing receptor (CaSR) or fibroblast growth factor-23 (FGF-23) pathways involved in mineral metabolism and cardiovascular health. However, limited data exists on the clinical utility of the Ca:P ratio in essential hypertension, warranting further research.

The strengths of this study include the comparative design with age- and sex-matched controls, the focus on newly diagnosed hypertensives to minimize confounding by antihypertensive therapy, and the use of a standardized protocol for blood pressure measurement and biochemical analyses. The limitations include the relatively small sample size, single-center setting, lack of data on dietary mineral intake, and the cross-sectional nature precluding causal inferences.

Larger prospective studies are needed to validate these findings and elucidate the mechanisms linking calcium-phosphorus abnormalities with essential hypertension. If proven, correcting these abnormalities through dietary modifications or supplements could be a simple and inexpensive strategy to optimize blood pressure control and reduce cardiovascular risk in hypertensive patients.

CONCLUSION

This study demonstrates that serum total calcium and phosphorus levels are significantly reduced, and the calcium-phosphorus ratio significantly elevated in patients with primary hypertension compared to normotensive controls. These parameters correlate with blood pressure, indicating a potential association with hypertension severity. Monitoring and correcting these biochemical abnormalities may be considered in the comprehensive management of essential hypertension. Further research is needed to establish the causal role of calcium-phosphorus imbalance in hypertension pathogenesis and the clinical benefits of targeting these pathways.

REFERENCES

1. Kearney, P. M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P. K., & He, J. (2005). Global burden of hypertension: analysis of worldwide data. *The lancet*, *365*(9455), 217-223.
2. Belizan, J. M., Villar, J., Pineda, O., Gonzalez, A. E., Sainz, E., Garrera, G., &Sibrian, R. (1983). Reduction of blood pressure with calcium supplementation in young adults. *Jama*, *249*(9), 1161-1165.
3. Resnick, L. M. (1993). Ionic basis of hypertension, insulin resistance, vascular disease, and related disorders the mechanism of "Syndrome X". *American Journal of Hypertension*, *6*(4S), 123S-134S.
4. Jorde, R., Sundsfjord, J., Fitzgerald, P., &Bønaa, K. H. (1999). Serum calcium and cardiovascular risk factors and diseases: the Tromsø study. *Hypertension*, *34*(3), 484-490.
5. Touyz, R. M., Milne, F. J., Seftel, H. C., &Reinach, S. (1987). Magnesium, calcium, sodium and potassium status in normotensive and hypertensive Johannesburg residents. *South African Medical Journal*, *72*(6), 377-381.
6. Sudhakar, K., Sujatha, M., Babu, S. R., Padmavathi, P., & Reddy, P. P. (2004). Serum calcium levels in patients with essential hypertension and their first degree relatives. *Indian Journal of Clinical Biochemistry*, *19*(1), 21-23.
7. Resnick, L. M., Laragh, J. H., Sealey, J. E., & Alderman, M. H. (1983). Divalent cations in essential hypertension: relations between serum ionized calcium, magnesium, and plasma renin activity. *New England Journal of Medicine*, *309*(15), 888-891.
8. Vaidya, A., & Forman, J. P. (2010). Vitamin D and hypertension: current evidence and future directions. *Hypertension*, *56*(5), 774-779.

9. Kesteloot, H. U. G. O., &Joossens, J. V. (1988). Relationship of serum sodium, potassium, calcium, and phosphorus with blood pressure. Belgian Interuniversity Research on Nutrition and Health. *Hypertension*, *12*(6), 589-593.
10. Elliott, P., Kesteloot, H., Appel, L. J., Dyer, A. R., Ueshima, H., Chan, Q., ...&Stamler, J. (2008). Dietary phosphorus and blood pressure: international study of macro-and micro-nutrients and blood pressure. *Hypertension*, *51*(3), 669-675.