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Role of Serum Calcium Levels in Newly Diagnosed Patients with Primary Hypertension: A Cross-Sectional Observational Study

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Abstract: ***Background: Hypertension is a major global health problem and a leading risk factor for cardiovascular morbidity and mortality. Emerging evidence suggests that abnormalities in calcium metabolism may contribute to the pathogenesis of essential hypertension. This study aims to identify relationship between serum calcium levels and blood pressure. Objectives: To evaluate serum calcium levels in newly diagnosed primary hypertensive patients and to determine the correlation between serum calcium, corrected serum calcium, and grades of hypertension. Methods: This observational cross-sectional study was conducted in the Departments of General Medicine and Biochemistry, Government Multispeciality Hospital, Sector-16, Chandigarh. A total of 140 newly diagnosed primary hypertensive patients aged 18–55 years were enrolled over 18 months. Detailed clinical evaluation, blood pressure measurement, serum calcium estimation, serum albumin estimation, and corrected calcium calculation were performed. Correlations between calcium parameters and blood pressure indices were analyzed using Spearman correlation. Results: A significant inverse relationship was observed between serum calcium levels and blood pressure parameters. Systolic blood pressure demonstrated a strong negative correlation with serum calcium ($r = -0.86$, $p < 0.001$) and corrected calcium ($r = -0.86$, $p < 0.001$). Diastolic blood pressure also showed significant negative correlations with serum calcium ($r = -0.80$, $p < 0.001$) and corrected calcium ($r = -0.79$, $p < 0.001$). Furthermore, stage of hypertension exhibited strong negative correlations with serum calcium ($r = -0.87$, $p < 0.001$) and corrected calcium levels ($r = -0.88$, $p < 0.001$). Conclusion: Lower serum calcium and corrected calcium levels are significantly associated with higher blood pressure and advanced stages of hypertension. These findings suggest a potential role of altered calcium metabolism in the pathophysiology of primary hypertension and warrant further prospective studies.***

Keywords: Primary hypertension, Serum calcium, Corrected calcium, Essential hypertension

1. Introduction

Hypertension is one of the most prevalent non-communicable diseases worldwide and remains a leading cause of cardiovascular morbidity and mortality. It is defined as a persistent elevation of arterial blood pressure, with systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in adults according to the Joint National Committee (JNC-8) guidelines (James et al., 2014). Hypertension is a major risk factor for coronary artery disease, heart failure, stroke, peripheral vascular disease, and chronic kidney disease. Owing to its largely asymptomatic nature, it is often referred to as the "silent killer." The global burden of hypertension continues to rise due to increasing life expectancy, urbanization, obesity, unhealthy dietary habits, and sedentary lifestyles.

Primary (essential) hypertension accounts for nearly 90–95% of all cases of hypertension and results from a complex interaction of genetic, environmental, neuro-hormonal and metabolic factors. Despite extensive research, the exact pathophysiological mechanisms underlying primary hypertension remain incompletely understood. Identification of potentially modifiable factors involved in blood pressure regulation is therefore important for improving prevention and treatment strategies.

Calcium is the most abundant mineral in the human body and is essential for numerous physiological functions. Approximately 99% of total body calcium is stored in bones and teeth, while the remaining 1% is present in extracellular fluids and soft tissues. Calcium homeostasis is tightly regulated by parathyroid hormone, vitamin D, and calcitonin (Resnick, 1999). In addition to its role in skeletal integrity, calcium plays a critical role in neuromuscular transmission, blood coagulation, hormone secretion, and cellular signaling pathways. Calcium ions act as important intracellular messengers and are involved in the regulation of vascular smooth muscle contraction and cardiac function.

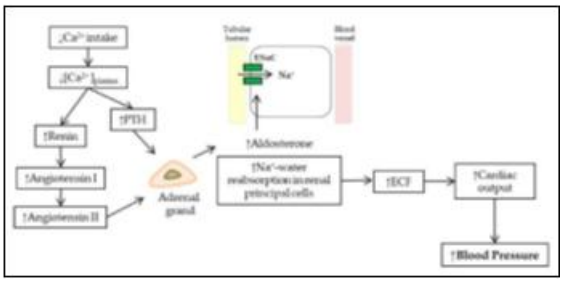

Figure 1: Mechanisms involved in the rise of blood pressure via an increase in cardiac output in low calcium intake

Several studies have suggested an association between calcium metabolism and hypertension (Resnick, 1999; Villa-Etchegoyen et al., 2019). Abnormalities in calcium homeostasis, including reduced serum calcium levels, increased intracellular calcium concentration, and increased urinary calcium excretion, have been reported in hypertensive individuals. Increased intracellular calcium in vascular smooth muscle cells promotes vasoconstriction and increases peripheral vascular resistance, thereby contributing to elevated blood pressure (Zemel, 2001). Furthermore, low calcium levels may stimulate the renin–angiotensin–aldosterone system and parathyroid hormone secretion, both of which have been implicated in blood pressure regulation (Resnick, 1999; Villa-Etchegoyen et al., 2019).

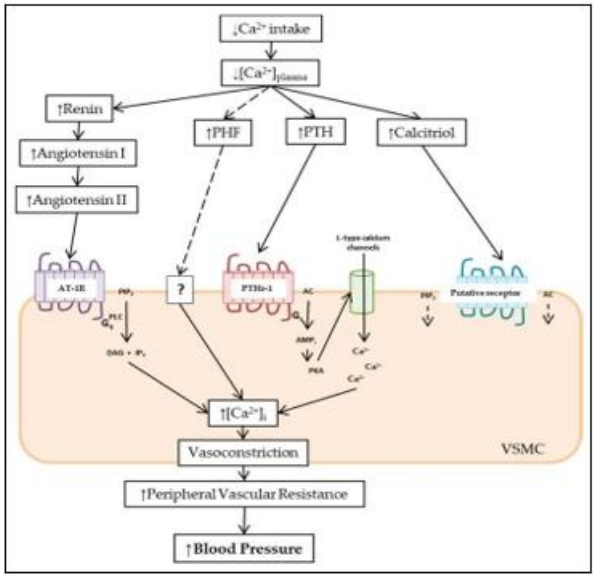

Figure 2: Calcium Intake and Renin–Angiotensin–Aldosterone System

Although previous studies have explored the relationship between calcium metabolism and hypertension, the findings have been inconsistent and data from the Indian population remain limited. Understanding this relationship may provide insight into the pathogenesis of hypertension and identify potential preventive or therapeutic targets. Therefore, the present study was undertaken to evaluate serum calcium levels in newly diagnosed patients with primary hypertension and to determine the correlation between serum calcium, corrected serum calcium, and grades of hypertension.

2. Materials and Methods

Study Design and Setting

This observational cross-sectional study was conducted in the Departments of General Medicine and Biochemistry, Government Multispeciality Hospital, Sector-16, Chandigarh. A written and informed consent was taken from all the patients. The defined guidelines of central ethics committee for biomedical research on human subjects by ICMR and guidelines as per Helsinki

Declaration were strictly adhered to in the project. The study was carried out over a period of 18 months.

Study Population

A total of 140 newly diagnosed primary hypertensive patients aged 18–55 years were enrolled consecutively.

Inclusion Criteria

- Newly diagnosed primary hypertension.
- Age between 18 and 55 years.

Exclusion Criteria

- Patients receiving antihypertensive treatment.
- Secondary hypertension.
- Pregnancy.
- Vitamin D or calcium supplementation.
- Drugs known to affect blood pressure.
- Alcohol or substance abuse.

Blood Pressure Measurement

Blood pressure was measured using an automated oscillometric sphygmomanometer. Two readings were recorded five minutes apart in a seated position, and the average value was used for analysis. Hypertension staging was performed according to JNC-8 recommendations.

Laboratory Evaluation

Venous blood samples were collected for serum calcium and serum albumin estimation. Serum calcium was measured using the Arsenazo III method on a fully automated XL-1000 analyzer. Corrected serum calcium was calculated using the standard albumin correction formula.

Corrected serum calcium = serum calcium + 0.8 (normal albumin – serum albumin)

Statistical Analysis

Data were analyzed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation. Spearman correlation analysis was performed to determine relationships between serum calcium parameters and blood pressure variables. A p-value <0.05 was considered statistically significant.

3. Results

A total of 140 newly diagnosed primary hypertensive patients were included in the study. All participants fulfilled the inclusion criteria and underwent detailed clinical and biochemical evaluation.

Correlation of Serum Calcium Levels with Blood Pressure

The relationship between serum calcium levels and blood pressure parameters was assessed using Spearman correlation analysis. A statistically significant negative correlation was observed between serum calcium levels and systolic blood pressure ($r = -0.86$, $p < 0.001$). Similarly, corrected serum calcium levels demonstrated a strong negative correlation with systolic blood pressure ($r = -0.86$, $p < 0.001$). These findings indicate that lower calcium levels were associated with higher systolic blood pressure values.

Diastolic blood pressure also showed significant inverse correlations with serum calcium and corrected serum calcium levels. Serum calcium demonstrated a negative correlation with diastolic blood pressure ($r = -0.80$, $p < 0.001$), while corrected serum calcium showed a similar negative correlation ($r = -0.79$, $p < 0.001$). Thus, lower calcium levels were associated with higher diastolic blood pressure measurements.

Correlation of Serum Calcium with Severity of Hypertension
The stage of hypertension was analyzed in relation to serum calcium and corrected serum calcium levels. A strong negative correlation was observed between stage of hypertension and serum calcium levels ($r = -0.87$, $p < 0.001$). Likewise, corrected serum calcium levels demonstrated a significant negative correlation with hypertension stage ($r = -0.88$, $p < 0.001$). Lower calcium concentrations were associated with greater hypertension severity.

Table 1: Correlation between Blood Pressure Parameters and Calcium Levels

Variable	Calcium Parameter	Spearman's rho	p-value
Systolic Blood Pressure	Serum Calcium	−0.86	<0.001
Systolic Blood Pressure	Corrected Calcium	−0.86	<0.001
Diastolic Blood Pressure	Serum Calcium	−0.80	<0.001
Diastolic Blood Pressure	Corrected Calcium	−0.79	<0.001
Stage of Hypertension	Serum Calcium	−0.87	<0.001
Stage of Hypertension	Corrected Calcium	−0.88	<0.001

Table 2: Observations and Results

	Name	Median (Q1-Q3)	Min-Max
1	AGE	44.00 (38-51)	18-55
2	BMI	23.85 (22.30-26.22)	19.00-40.30
3	Systolic BP	160 (150-170)	142-232
4	Diastolic BP	98 (90-104)	82-130

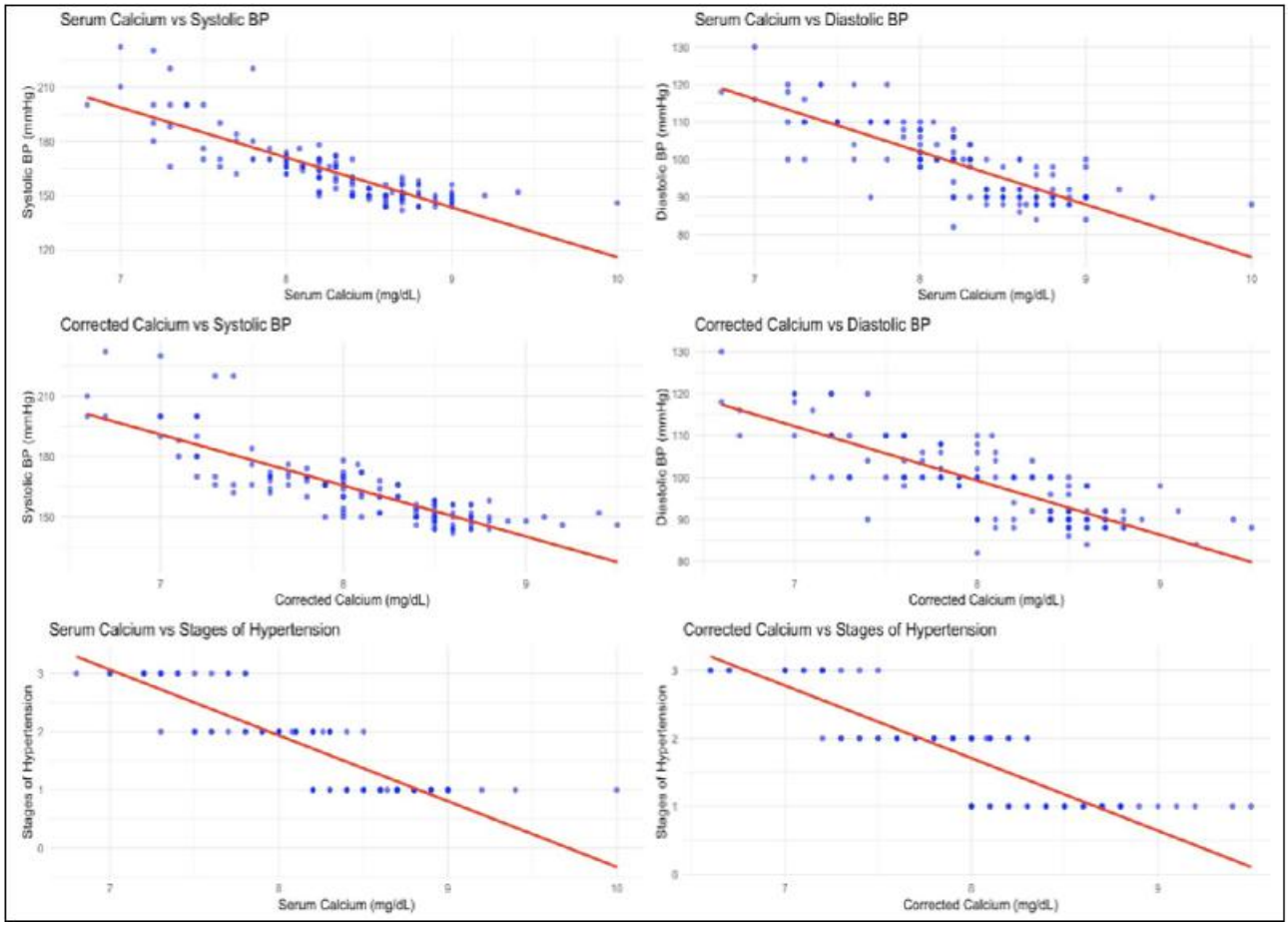

Figure 3: Correlation between serum calcium levels and BP, Stages of Hypertension

Serum calcium and corrected serum calcium showed significant inverse correlations with systolic blood pressure, diastolic blood pressure, and hypertension stage. The strongest association was between corrected calcium and hypertension stage ($r = -0.88$, $p < 0.001$).

4. Discussion

The present study demonstrated a strong inverse relationship between serum calcium levels and severity of hypertension. Patients with higher blood pressure values and more advanced stages of hypertension exhibited significantly lower serum calcium and corrected calcium levels.

These findings support previous observations suggesting that disturbances in calcium metabolism contribute to the development and progression of essential hypertension (Sudhakar et al., 2004; Villa-Etchegoyen et al., 2019). Calcium plays a fundamental role in vascular smooth muscle contraction (Zemel, 2001). Reduced extracellular calcium may stimulate parathyroid hormone secretion and activation of the renin–angiotensin–aldosterone system, leading to increased intracellular calcium concentration and vasoconstriction (Resnick, 1999).

The observed negative correlations between systolic blood pressure and serum calcium ($r = -0.86$) as well as corrected calcium ($r = -0.86$) indicate a strong biological association. Similar relationships were observed for diastolic blood pressure and hypertension stage. These results are consistent with earlier studies reporting altered calcium homeostasis among hypertensive individuals (Sudhakar et al., 2004; Villa-Etchegoyen et al., 2019).

The findings suggest that serum calcium may potentially serve as a biomarker of hypertension severity. Furthermore, dietary calcium optimization and correction of calcium imbalance may represent adjunctive approaches in hypertension management (Villa-Etchegoyen et al., 2019). However, given the multifactorial nature of hypertension, calcium metabolism should be considered within a broader framework of cardiovascular risk assessment.

5. Limitations

The study had several limitations:

1) Relatively small sample size.
2) Cross-sectional design prevented assessment of causality.
3) Cytosolic calcium, urinary calcium, parathyroid hormone, and renin levels were not measured.
4) Calcium supplementation was not evaluated.
5) Single-center hospital-based design may limit generalizability.

6. Conclusion

Serum calcium and corrected serum calcium levels demonstrate significant negative correlations with systolic blood pressure, diastolic blood pressure, and stages of hypertension. Lower calcium levels are associated with greater hypertension severity, supporting a potential role of altered calcium metabolism in primary hypertension. Future longitudinal studies are required to establish causality and evaluate whether correction of calcium imbalance can improve blood pressure control.

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