

## Original article

# Serum Total and Free Calcium in Hypertension

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### Abstract:

**Introduction:** Hypertension is a chronic condition of concern due to its role in causation of coronary heart disease, stroke and other vascular complications. Calcium metabolism is supposed to be linked with the pathophysiology of hypertension, and various studies have shown mixed results. The present study was planned to measure serum total and free calcium levels in hypertensive patients.

**Settings and Design:** A case-control study involving 80 subjects. Subjects were grouped into 40 healthy controls and 40 cases of hypertension.

**Results:** Both serum total and free calcium levels were decreased, in hypertensive subjects as compared to controls.

**Conclusions:** Decreased serum calcium levels suggest that calcium plays a crucial role in the pathogenesis of hypertension.

**Key-words:** Hypertension, total calcium, free calcium.

**Introduction:** An elevated blood pressure is probably the most important public health problem in developed countries. Industrialization, urbanization, and associated lifestyle changes has led to an epidemiologic transition. The high rate of undetected and therefore untreated hypertension is one of the major concerns<sup>(1)</sup>. Peripheral resistance is one of the determinants of arterial pressure. It is widely accepted that the increase in peripheral resistance that characterizes the established phase of hypertension results from an increase in active tension in the vascular smooth muscle<sup>(2)</sup>. Calcium plays a key role in vascular smooth muscle function. Calcium influx through receptor and voltage-operated calcium channels is thought to initiate vascular contraction; and the fall in the intracellular free calcium concentration is thought to result in relaxation or

vasodilatation. Therefore, how the vascular smooth muscle cell handles calcium is critical to vascular tone and blood pressure<sup>(3)</sup>.

Serum free (ionized) calcium reflects true calcium status of the body in health and disease. It is biologically active and tightly regulated by calcium binding hormones. Serum total calcium is the sum of 3 forms, ionized or free (50%), protein-bound (40%) and soluble form, complexes with anions such as bicarbonate and phosphate. Total calcium is thus greatly influenced by protein concentration, especially albumin<sup>(4)</sup>.

Some of the previous studies have shown conflicting results. Some have reported that serum total calcium was not different between hypertensive and normotensive groups, but serum ionized calcium levels were low<sup>(5, 6)</sup>. A recent study in U.S. showed

increased serum total and free calcium levels in hypertensive adults<sup>(7)</sup>.

The present study measures both serum total and free calcium in hypertension in an attempt to further resolve the controversy and extend our understanding of the pathophysiology of hypertension.

**Materials and Methods:**

**Selection of subjects:** In all 80 subjects were included for the study. These were grouped into 40 healthy controls and 40 clinically newly diagnosed hypertensive patients attending the medicine outdoor patient department of a teaching hospital in Pune.

**Inclusion criteria:** Subjects between the age group of 20-60 years were selected. The criteria for diagnosis of hypertension were systolic pressure of  $\geq 140$  mm of Hg and diastolic pressure of  $\geq 90$  mm of Hg.

**Exclusion criteria:** Hypertensive patients who were already on anti-hypertensive treatment were excluded from the study. Both the groups were examined systematically to exclude any disease or factors known to cause hypertension. Subjects with any underlying condition or taking any drug known to

alter serum calcium levels have been excluded from the study.

Samples from cases were collected before institution of anti-hypertensive treatment. Approval from the Institutes Ethics Committee was obtained and informed consent from all the subjects was taken.

**Analytical method:** Fasting blood sample collected from the antecubital vein without tourniquet into two separate containers:

1. 3 ml plain conical centrifuge capped tube filled with heparin- for estimation of free  $Ca^{++}$  for the purpose of anaerobic sampling which is a pre-requisite or crux of estimation of free  $Ca^{++}$ .

2. Plain bulb- estimation of total  $Ca^{++}$ .

Modified Arsenazo method was used for total calcium estimation<sup>(8)</sup>.

Ion Selective Electrode (ISE) by AVL 9180 Electrolyte Analyzer for estimation of free calcium<sup>(9)</sup>.

The samples were processed immediately after serum separation on the semi-autoanalyzer, Erba chem.

**Statistical analysis:** The results were expressed as mean  $\pm$  S.D. Comparison of control and test group was done by unpaired 't' test.

*Indian Journal of Basic & Applied Medical Research*

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**Results:** Table1: Demographic profile and test parameters of subjects

| Parameter                               | Normotensive Controls<br>(n=40) | Hypertensive Cases<br>(n=40) |
|---|---------------------------------|------------------------------|
| Age (years):                            |                                 |                              |
| Males                                   | 46 ± 5 (n=17)                   | 43 ± 4 (n= 24)               |
| Females                                 | 45 ± 5 (n=23)                   | 47 ± 3 (n=16)                |
| Systolic BP (mm of Hg)                  | 119 ± 6                         | 144 ± 5                      |
| Diastolic BP (mm of Hg)                 | 76 ± 5                          | 94 ± 4                       |
| Serum Total Ca <sup>++</sup> (mmol/L)   | 2.49± 0.26                      | 2.29±0.17**                  |
| Serum Free Ca <sup>++</sup> ( mmol/ L ) | 1.25 ± 0.07                     | 1.18 ± 0.10**                |

Statistical analysis shows decreased free Ca<sup>++</sup> and decreased total Ca<sup>++</sup> levels in cases as compared to controls.

\*\*P<0.001 compared to controls-highly significant

**Discussion:**

The present study revealed decrease in both serum total and free calcium. This is in agreement with researchers who have studied only ionized calcium which was found to be decreased<sup>(10,11)</sup>. Some have studied only serum total calcium levels and found it to be lowered in hypertensive subjects<sup>(12,13)</sup>. Booloo Sharma et al who studied serum calcium and magnesium levels in hypertension showed calcium levels to be low in hypertensives<sup>(14)</sup>. In a recent study by Hazari M A et al, there was no significant difference in serum calcium levels between normotensive and hypertensive groups<sup>(15)</sup>.

An association between serum total calcium and hypertension is plausible, including a direct effect on vasculature by enhanced vascular resistance, alteration in extracellular binding of calcium,

interaction between serum calcium, and other cations such as sodium, potassium and magnesium, renal vasoconstriction causing kidney dysfunction and hyperactivity of renin-angiotensin system from hyperparathyroidism<sup>(7)</sup>.

Low serum ionized calcium levels in hypertensives reflect increased levels of intracellular ionized calcium. Increased intracellular calcium may be due to reduced calcium extrusion via an ATP-dependent pump, and decreased vascular smooth muscle membrane stability. Also, intracellular calcium serves as a second messenger in excitation-contraction coupling for vascular smooth muscle cells; causing contraction. This explains why abnormal cellular metabolism and subsequent elevated intracellular concentration of calcium could contribute to hypertension<sup>(16)</sup>.

**Limitations of the study:** The serum total calcium levels were not corrected for the albumin levels and the small sample size.

**Conclusions:**

From the present study, it can be concluded that, abnormal cellular ion transport resulting in altered membrane control over intracellular calcium may be related to hypertension.

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Date of submission: 20 February 2013  
Date of Provisional acceptance: 17 March 2013  
Date of Final acceptance: 28 April 2013  
Date of Publication: 03 June 2013  
Source of Support: Nil ; Conflict of Interest: Nil