

# Study of Serum Calcium in Essential Hypertension and its Co-Relation with Severity of the Disease.

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## ABSTRACT

**Background:** Hypertension is one of the leading causes of death and disability among adults all over the world and emerging health problem in India. Over 90% of patients with high blood pressure have Essential Hypertension. Alterations in the intracellular free Calcium regulation as well as disturbances of extracellular calcium homeostasis have been observed in patients with essential hypertension. **AIM:** To study the levels of serum Calcium in patients with primary hypertension and to correlate the serum Calcium levels with severity of disease. **Methods:** Information for the study was collected from patients admitted to BLDEDU'S Shri B.M Patil Medical college Hospital and Research center, Vijayapura from November 2016 to June 2018. Patients were screened and who met inclusion criteria where studied. Serum calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and results were obtained and Comparative Study was done. **Results:** In our study mean age in hypertensive patients was  $50.80 \pm 19.38$  and in controls it was  $43.19 \pm 19.171$ . There was no significant difference of serum calcium was obtained in relation to age in both the Stage of Hypertension. There was no significant difference in relation to gender. In total Hypertensives cases mean  $\pm$  SD of S. Calcium was  $8.408 \pm 1.07$  mg/dl while in normotensives cases it was  $9.190 \pm 0.7827$  mg/dl. In all Stage I Hypertensive case mean  $\pm$  SD of S. Calcium was  $8.626 \pm 0.6012$  mg/dl ( $p = 0.032$ ) while in Stage II Hypertensive it was  $8.190 \pm 1.3668$  mg/dl ( $p = 0.0001$ ). This results were significantly low than normotensives. But comparing both Stage of Hypertension mean was lower in stage II but it is not significantly low. So level of S. Calcium has inverse relation with Hypertension severity. **Conclusion:** In patients of Essential hypertension mean serum Calcium levels were found to be low in comparison to Normotensives. Further, Stage II Hypertensive patient has more reduced levels of serum calcium than Stage I, hence low Serum Calcium levels were associated as the severity of the disease increases.

**Keywords:** Primary Hypertension, Serum Calcium.

## INTRODUCTION

Hypertension is defined as systolic BP measurement of 130 mm Hg or higher or any diastolic BP measurement of 80 mm Hg or higher. Clinically, hypertension might be defined as that level of blood pressure at which the institution of therapy reduces blood pressure related morbidity and mortality.<sup>[1]</sup>

Hypertension is one of the leading causes of the global burden of disease. Approximately 7.6 million deaths (13-15% of the total) and 92 million disability-adjusted life years worldwide were attributable to high blood pressure in 2001.<sup>[2]</sup> The WHO rates Hypertension as one of the most important causes of premature death worldwide.<sup>[3]</sup>

There is strong positive and continuous correlation between BP and the risk of cardiovascular disease (myocardial infarction, heart failure), renal disease, stroke and mortality. This correlation is more robust with systolic than with diastolic Blood Pressure.<sup>[4]</sup>

Hypertension is due to specific causes in a small fraction of cases, but in the vast majority of individuals ( $\approx 90-95\%$ ), its etiology cannot be determined; therefore, the essential hypertension term is employed.<sup>[5]</sup> Essential hypertension is currently understood as a multifactorial disease arising from the combined action of many genetic, environmental, and behavioral factors.<sup>[6]</sup>

Calcium plays crucial role in various cellular function. Thus, extracellular calcium concentrations are maintained within an exquisitely narrow range through a series of feedback mechanisms.<sup>[7]</sup> Humans with essential hypertension and genetic animal models of hypertension is shows low serum ionized calcium, increased urinary calcium excretion, and increased parathyroid hormone (PTH) concentration.

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Calcitriol metabolism and bone mineralization are also altered in hypertension. These alterations in systemic calcium metabolism may be linked to factors responsible for the elevated blood pressure.

In hypertensive patients there is a defect in excreting the digitalis like natriuretic factor which inhibits ouabain sensitive Na<sup>+</sup>-K<sup>+</sup>ATPase causing intracellular sodium accumulation. This increased intracellular sodium causes intracellular calcium accumulation in the vascular smooth muscle cells leading to an increase in contractility.<sup>[8]</sup>

Many researchers even recommend a regular consumption of the recommended daily levels of dietary calcium to combat with hypertensive disorders.<sup>[9]</sup> 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.

**MATERIALS AND METHODS**

This Comparative study included inpatients at tertiary care center, Vijayapur between November 2016 to June 2018, who were diagnosed as primary hypertension. Patients with primary hypertension were included in the studied and patients with secondary hypertension were excluded. A Study of serum total calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and results were obtained. Serum Calcium was done in every patient of primary hypertension and other routine investigations to rule out secondary hypertension are done. After considering the inclusion and exclusion criteria, all patients will be interviewed as per the prepared proforma and then complete clinical examination and laboratory investigations was done.

**Inclusion Criteria:**

1. Patients with newly detected or untreated primary hypertension.
2. The classification of blood pressure in adults as PER JNC8.<sup>[2]</sup>
3. Patients whose age is above 18 yr are included. Both sexes are included.

**Exclusion Criteria:**

1. Patients already on antihypertensive drugs
2. On drugs that alters calcium levels
3. Patients with renal disease (also nephrosis, nephritis)
4. Pregnant females
5. With Endocrine disorders like Diabetes Mellitus, Thyroid and Parathyroid disorder,
6. Patients with Acute Diarrhoeal disease, steatorrhoea
7. Ischemic Heart Disease

**Statistical analysis:**

1. Mean +/- SD<sup>2</sup>

2. Statistical tests like students t test / Mann whitney U test.

It was done using Software SPSS version 17

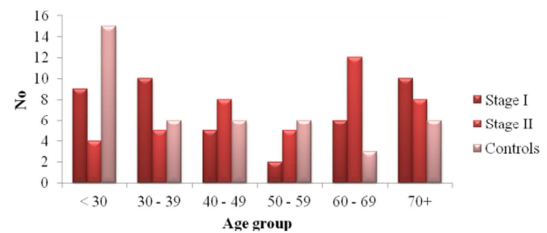
**RESULTS**

A Study of serum total calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and following results were obtained.

**Age distribution:**

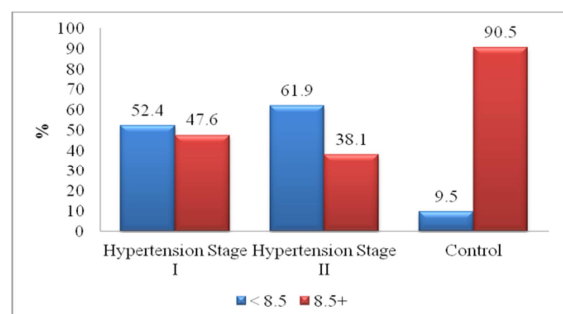
**Table 1: Distribution Of Cases By Age**

Age (years)	Stage I		Stage II		Controls	
	N	%	N	%	N	%
< 30	9	21.4	4	9.5	15	35.71
30 - 39	10	23.8	5	11.9	6	14.28
40 - 49	5	11.9	8	19.04	6	14.28
50 - 59	2	4.7	5	11.9	6	14.28
60 - 69	6	14.28	12	28.57	3	7.1
70+	10	23.8	8	19.04	6	14.28
Total	42	100	42	100	42	100



**Figure 1: Distribution of Cases by Age**

Here number of male and female cases were same in all 3 groups which was 23 and 19 respectively and were compared. In the study history of smoking and/or tobacco chewing in Stage I hypertensives was 50% and in stage II hypertensives it was 31%. History of alcohol consumption in Stage I hypertensives and in stage II hypertensives was same 19%. Family history of essential hypertension in Stage I hypertensives was 52.4% and in stage II hypertensives it was 38.1%. So, history of smoking and/or tobacco chewing was associated most followed by family history of essential hypertension.



**Figure 2: Graphical Distribution Of Cases By Normal And Low Serum Calcium In Different Stages Of Hypertension**

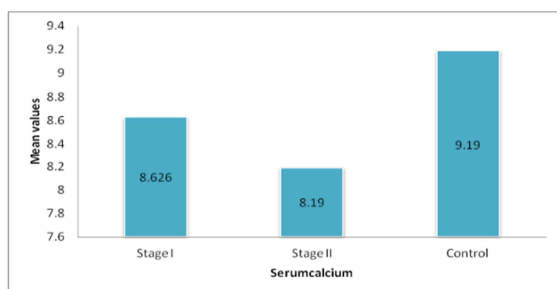
In the study S Calcium value of 8.5 – 11 mg/dl is taken normal.

Out of 42 cases of Stage I Hypertension 22 (52.4%) has low S. Calcium. Out of 42 cases of Stage II Hypertension 26 (61.9%) has low S. Calcium level. Out of 42 controls only 4 (9.5%) has low S. Calcium level.

Here, overall >50 % of Hypertensive cases has low S. Calcium level. And number of cases with low S. Calcium were more in Stage II than in Stage I group.

**Table 2: mean s. Calcium in cases having low s. Calcium**

S. Calcium(mg/dl)	Mean	
< 8.5	Hypertension Stage I	Hypertension Stage II
	8.182±0.18	7.34±0.58



**Figure 3: Mean Serum Calcium in All Patients in Each Group**

In all Stage I Hypertensive case mean ± SD of S. Calcium was 8.626 ± 0.6012

In all Stage II Hypertensive case mean ± SD of S. Calcium was 8.190 ± 1.3668

In all normotensives cases mean ± SD of S. Calcium was 9.190 ± 0.7827

Here, study shows average Serum Calcium is low in Hypertension. And when comparing all cases of Stage I and Stage II Groups, average S. Calcium is Normal in Stage I and Low in Stage II. But in comparison to control group both Stages has low S. Calcium Level. Here Serum calcium level was compared between male and female in all cases and Different stages, too. There was no statistically significant difference of S. Calcium level was observed between male and female hypertensive cases

**Table 3: comparison of serum calcium between hypertension stage i, stage ii and control groups**

Hypertension	Serum calcium		Krisal wallis test
	Mean	Std. Deviation	
Stage I	8.626	0.6012	P = 0.001*
Stage II	8.190	1.3668	
Control	9.190	0.7827	
Total	8.669	1.0494	
Comparison between		Significant value	
Stage I and Stage II		P=0.126	
Stage I and Control		P=0.032*	
Stage II and Control		P=0.0001*	

\*P value is 0.05 which is statistically significant

Hence, low Serum Calcium level in hypertensive patient is statistically Significant in comparison to controls. Low Serum Calcium level in Stage I hypertension and Stage II Hypertension is statistically Significant in comparison to controls.

But low calcium level in all cases of Stage I is not statistically significant when compare with Stage II. But the mean value is much low in Stage II and when cases with low Serum calcium are compared it is statistically significant.

## DISCUSSION

Hypertension is one of the leading causes of death and disability among adults all over the world and emerging health problem in India 41. Essential hypertension is a heterogeneous disorder, with different patients having different causal factors that lead to high Blood Pressure, Alterations in the intracellular free Calcium regulation as well as disturbances of extracellular calcium homeostasis have been observed in patients with essential hypertension.<sup>[4]</sup>

Considering the above study was conducted in BLDEDU's Shri BM Patil Medical College and Research centre over a period of 2 year in which A Study of serum calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and the results were obtained and compared. Lian IA and Asberg A<sup>[10]</sup>, did a study which has concluded that Unadjusted Total calcium has better diagnostic accuracy than commonly used adjustment formulas, so clinician should stop use of this formulas. In our study corrected S. Calcium levels were not obtained and compared.

In our study mean age in hypertensive patients was 50.80 ± 19.38 and in controls it was 43.19 ± 19.171. There was no significant difference was obtained in relation to age in both the Stage of Hypertension but Jorde.,et al.<sup>[11]</sup> has noticed that there was a significant decrease in serum calcium with increasing age in men as age increases there is significant decrease in S. C alcium levels while in women it increases with age

In our study while comparing S. Calcium values in different groups with each other, the observation was that overall > 50 % of Hypertensive cases has low S. Calcium level. And number of cases with low S. Calcium were more in Stage II than in Stage I group. Out of 42 controls only 4 (9.5%) has low S. Calcium level. In total Hypertensives cases mean ± SD of S. Calcium was 8.408 ± 1.07 mg/dl while in normotensives cases it was 9.190 ± 0.7827 mg/dl hence difference of 0.782 ± 0.2873.

G. Ranjani,<sup>[12]</sup> showed similar difference of S. Calcium levels in which Hypertensive Patient has mean Serum Calcium of 8.9160 ± 0.62529 mg/dl and 9.7042 ± 0.79350 mg/dl in normotensives and

difference was 0.7882 0.16821 mg/dl which were statistically significant as in our study.

K. Sudhakar et al,<sup>[13]</sup> They the study first of all in Indian population, serum calcium levels were measured in 117 subjects and 77 first degree relatives. Serum Calcium levels were decreased in hypertensive which were statistically significant.

Strazzullo P et al.<sup>[14]</sup> showed there is elevated fractional urinary calcium excretion in cases of Primary hypertension and had obtained significant reduction in Total S. Calcium levels, but no significant reduction in Ionized calcium levels.

Tillman DM and Semple PF,<sup>[15]</sup> 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

In all Stage I Hypertensive case mean  $\pm$  SD of S. Calcium was  $8.626 \pm 0.6012$  mg/dl ( $p = 0.032$ ) while in Stage II Hypertensive it was  $8.190 \pm 1.3668$  mg/dl ( $p = 0.0001$ ). This results were significantly low than normotensives. But comparing both Stage of Hypertension mean was lower in stage II but it is not significantly low. So level of S. Calcium has inverse relation with Hypertension severity.

Kamlesh Jha M,<sup>[16]</sup> support this observation of inverse relation between Calcium levels and Severity of disease. But they have studied Ionised Calcium. In Stage I hypertensives mean was  $2.30 \pm 0.072$  mmol/l which was significantly lower ( $p < .0001$ ) than that of normotensives, but in comparison to Stage II hypertensives it was significantly higher ( $p = .009$ ) where mean serum calcium level was  $2.25 \pm 0.09$  mmol/l

There are difference studies which showed that calcium supplementation can alter outcome of disease or not. Jolma at al, a study in rats showed increased dietary Calcium reduce the development of hypertension there will be the improved vasorelaxation after Calcium supplementation in NO deficient hypertension. On human populations also several similar studies are done for dietary supplementation in England, Oregon, Indiana showed reduction in Blood pressure.

The findings have been highly variable across various studies but the largest study (TOHP) - Trials and Hypertension Prevention Study found no significant blood pressure lowering at 600mg per day. Based on the data and experience available, calcium supplementation on increased Dietary intake of calcium rich foods can be recommended non-specifically for prevention of hypertension, and in osteoporosis it will have. Therefore, intake be maintained at 1.0 to 1.5 gm per day is recommended through dietary intake on supplements for both adolescent and Adults.

## CONCLUSION

### The study concludes:

Hypertensive cases are found to have low S. Calcium level. And number of cases with low S. Calcium were more in Stage II than in Stage I group. Average Serum Calcium is low in Hypertensive patients. And when comparing all cases of Stage I and Stage II Groups, average S. Calcium is Normal in Stage I and Low in Stage II. But in comparison to control group both Stages has statistically significant low S. Calcium Level.

Low Serum Calcium level in Stage I hypertension and Stage II Hypertension is statistically Significant in comparison to controls.

Our study shows there is correlation between Serum Calcium levels and essential hypertension and also shows Severity of disease and Serum calcium has inverse relationship.

### Limitation of the study:

1. Sample size was small
2. Ionized Calcium, Parathyroid Hormons and Serum renin levels were not done due to constrains
3. Patients with having low Calcium levels are not studied for Effect of Calcium supplements as this is not a follow up study.

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