

Original article:

Serum albumin levels and Calcium imbalance in Hypertension

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ABSTRACT:

Introduction: Systemic hypertension is global disease responsible for significant mortality and morbidity. Essential or primary hypertension accounts for the majority of people with hypertension. Although our understanding of the pathophysiology of essential hypertension has grown a lot, its etiology still remains hypothetical. Few studies in literature have found some correlation with serum calcium levels and blood pressure of the individuals.

Materials and Methods: A total 200 patients, 100 newly diagnosed essential hypertensive and 100 normotensive patients were included in the study. A detailed history and clinical profile was taken. Blood sample was collected and serum calcium, serum albumin were determined and corrected calcium was calculated and the results were tabulated and appropriate statistical analysis was done.

Results: The mean total serum calcium and corrected calcium levels were significantly lowered in essential hypertensive compared to the normotensive individuals. There was no correlation between total serum and corrected calcium levels against systolic and diastolic blood pressure. There was also no difference in serum total and corrected calcium levels among different subsets in essential hypertensive group.

Conclusion: Essential hypertension still remains the most common form of hypertension present worldwide causing significant mortality and morbidity. Despite increased advances in medicine and large number of studies done in context with the cause of essential hypertension, its etiology still remains obscure and hypothetical. Even though studies have shown some correlation of calcium fractions with hypertension, the aetiology is still unclear.

Keywords: Albumin, Calcium and Hypertension.

INTRODUCTION:

Globally, nearly 40% of adults of age 25 and above were diagnosed with hypertension. People who had hypertension increased from 600 million in 1980 to nearly 1 billion in 2008. Its prevalence is highest in Africa and lowest in Americas. It is responsible for nearly 45% of mortality due to heart disease and 51% of mortality due to cerebrovascular accidents.¹ Affecting 1 billion people worldwide, systemic hypertension is considered to be the most common, easily diagnosable risk factor for many of the cardiovascular and cerebrovascular diseases. Because of increasing the aging of population in developed and developing countries, the burden of hypertension is rising globally and is estimated to affect 1/3rd of the world's population by 2025 that is around 1.5 billion people.² Although our

understanding of the pathophysiology of essential hypertension has increased, the etiology still remains hypothetical. Various studies have shown that essential hypertension is associated with disturbed calcium metabolism like increased cytosolic calcium and decreased serum calcium levels and also increased urinary excretion of calcium in patients with primary hypertension.^{3,4,5}

In this study total serum calcium levels and corrected serum calcium levels of essential hypertension patients is compared and correlated with matched normotensive controls. Also the calcium levels are compared and correlated within the various subsets of hypertensive population viz., age, sex, alcohol, smoking, lifestyle, body mass index (BMI).

MATERIAL AND METHODS:

This study was carried out in the Department of General Medicine and in collaboration with Department of Biochemistry during the period of March 2017 to october 2017. This study was a cross sectional study with 100 cases of newly detected essential hypertensive and 100 controls of normotensive individuals. Cases and controls were selected randomly from those who attended the outpatient department of general medicine.

GUIDELINES FOR MEASURING BLOOD PRESSURE:⁶

A. Posture:

1. The person must be seated comfortably, with the legs uncrossed, and the back and arm supported, in a way that the upper arm is at the level of the heart (the mid-point of the sternum).
2. The person should relax and instructed not to talk during the procedure and readings should be taken after 5 minutes of posturing.
3. For patients who are over 65, diabetic or receiving anti-hypertensive therapy, check for postural changes by taking readings immediately and 2 minutes after the patient stands

B. Circumstances:

- i. No caffeine for preceding hour
- ii. No smoking for preceding 15 minutes.
- iii. No exogenous adrenergic stimulants like phenylephrine in nasal decongestants or eye drops for papillary dilation.
- iv. A quite, warm setting.
- v. Home readings taken under various circumstances and 24 hour ambulatory recordings may be preferable.

II EQUIPMENT:

Mercury sphygmomanometer is the most standard method of eliciting blood pressure.

TECHNIQUE

1. Check blood pressure in both arms during first examination.
2. Minimum of 2 readings should be taken at an interval at least 1 minute and the average of those 2 readings is taken as the value. If there is a difference between the first and second reading of more than 5 mm hg, another set of readings should be estimated.
3. Mercury column should be deflated slowly by 2 mm/s and the initial and final korotoff sounds are taken as the systolic and diastolic blood pressure of the person.

4. Both the subject and the examiner shouldn't talk during the procedure.

Inclusion criteria:

1. Patients with newly detected essential hypertension.
2. Patients above the age of 18 years.
3. Both sexes are included.

Exclusion criteria:

1. Chronic renal failure.
2. Diabetes mellitus.
3. Heart disease.
4. Liver disease.

Patient who fulfilled the criteria were enrolled into the study and hypertensive and normotensives were marked as cases and controls respectively and grouped as Group A and Group B respectively.

ESTIMATION OF SERUM CALCIUM was done by Arsenazo III Method⁷

ESTIMATION OF SERUM ALBUMIN was done Albumin BCG Method⁸

CORRECTED SERUM CALCIUM LEVEL:

Serum Calcium (mg/dl) + {0.8 [4.0 – Serum albumin (g/dl)]}

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver2.11.1 were used for analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

+ Suggestive significance (P value: 0.05 < P < 0.10)

* Moderately significant (P value: 0.01 < P ≤ 0.05)

** Strongly significant (P value: P ≤ 0.01)

RESULTS:

- ❖ A total of 200 individuals were randomly selected. They were divided into two groups, group A and group B.
- ❖ Group A was the study group which included 100 newly detected essential hypertensive patients. Group B was the control group which included 100 normotensive individuals.
- ❖ In Group A, 45 (45%) were males and 55 (55%) were females and in Group B, 26(55%) were males and 24(45%) were females.
- ❖ The mean age in group A was 53.47±10.04 years and the mean age in group B was 48.25±6.45 years.
- ❖ In Group A, 73 (73%) were non-smokers and 27 (27%) were smokers and in Group B, 33 (73%) were non-smokers and 17 (27%) were smokers.
- ❖ In Group A, 80 (80%) were non alcoholics and 20 (20%) were alcoholics and in Group B, 85 (85%) were non alcoholics and 15 (15%) were alcoholics.
- ❖ 72% (72) patients in group A had a sedentary lifestyle.
- ❖ The prevalence of family history of hypertension among hypertensive individuals was 16% (16).

- ❖ The mean systolic blood pressure of group A and group B were 166.06±14.02mmHg and 125.62±6.49 mm hg while the mean diastolic blood pressures were 97.62±5.38 mm hg and 80.70±5.21 mmHg respectively.
- ❖ The mean total serum calcium and corrected serum calcium levels in group A were 8.75±0.53mg/dl while the mean total serum calcium and corrected serum calcium levels in group B were 9.00±0.45mg/dl 8.87±0.40 mg/dl respectively. The calcium levels were significantly lowered in group A when compared with group B.
- ❖ There was no correlation noted between the total and corrected serum calcium levels as against the systolic blood pressure.
- ❖ There was no correlation noted between the total corrected serumcalcium levels as against the diastolic blood pressure.
- ❖ There was no significant difference in the total and corrected serum calcium levels with age, sex, BMI, life style, smoking, alcohol, family history of hypertension in newly detected essential hypertensive patients.

Table 1: Serum calcium levels in two groups studied

Lower Serum calcium is significantly more associated with Group A with P<0.001**

Serum calcium	Group A		Group B	
	No	%	No	%
<8.5	36	36.0	9	9.0
8.5-9.5	54	54.0	78	78.0
>9.5	10	10.0	13	13.0
Total	100	100.0	100	100.0

** Strongly significant (P value: P≤0.01)

Table 2: Corrected calcium levels in two groups studied

Lower corrected calcium levels is significantly more associated with Group A with P<0.001**

Corrected calcium	Group A		Group B	
	No	%	No	%
<8.5	48	48.0	12	12.0
8.5-9.5	47	47.0	81	81.0
>9.5	5	5.0	7	7.0
Total	100	100.0	100	100.0

** Strongly significant (P value: P≤0.01)

Table 3: Comparison of Serum Calcium and Corrected calcium levels in two groups studied

	Group A	Group B	P value
Serum calcium	8.75±0.53	9.00±0.45	<0.001**
Corrected calcium	8.62±0.61	8.87±0.40	0.001**

Table 4: Comparison of Serum calcium levels and corrected calcium levels according different clinical in Group A

* There was no significant difference in the total and corrected serum calcium level with sex, life style, smoking, alcohol, family history of hypertension in newly detected essential hypertensive patients

Variables	Serum Calcium levels	Corrected Calcium levels
Gender		
* Male	8.73±0.54	8.62±0.62
* Female	8.75±0.53	8.63±0.59
* P value	0.955	0.938
Smoking		
* No	8.70±0.53	8.58±0.60
* Yes	8.88±0.52	8.57±0.61
* P value	0.145	0.225
Alcohol		
* No	8.76±0.55	8.62±0.62
* Yes	8.73±0.47	8.66±0.59
* P value	0.852	0.793
Life style		
* Non-sedentary	8.69±0.54	8.58±0.59
* Sedentary	8.81±0.52	8.66±0.62
* P value	0.246	0.502
Family History		
* No	8.78±0.53	8.65±0.63
* Yes	8.58±0.53	8.46±0.47
* P value	0.158	0.250

Table 5: Pearson correlation between study variables with Serum calcium levels in two groups studied

- There was no correlation noted between the total and corrected serum calcium levels as against the systolic blood pressure.
- There was no correlation noted between the total and corrected serum calcium levels as against the diastolic blood pressure. P<0.001**

Pair	Group A		Group B	
	r value	p value	r value	p value
SBP vs Serum calcium levels	-0.149	0.139	-0.116	0.252
SBP vs Corrected calcium levels	-0.173	0.085+	-0.156	0.122
DBP vs Serum calcium levels	-0.115	0.253	-0.034	0.738
DBP vs Corrected calcium levels	-0.135	0.181	-0.024	0.815

DISCUSSION:

Hypertension still seems to be one among the top risk factors, reversible risk factors which are easily detectable for most of the common diseases (cerebrovascular accident, myocardial infarction arrhythmias like atrial fibrillation etc..) responsible for mortality and morbidity.² There is enough evidence now to say that there is some relationship between calcium physiology and hypertension but whether it is secondary association or whether altered calcium metabolism is the reason behind or is it the cause for essential hypertension is still unclear. There are various trials which show that the increased levels of intracellular calcium decrease to normal levels due to treatment with antihypertensive drugs, so it is known that there is some direct effect of calcium ions on vascular tone in the peripheral vessels.⁹

TOTAL SERUM CALCIUM AND CORRECTED SERUM CALCIUM LEVELS:

In our study the mean serum calcium level and mean corrected calcium level in group (essential hypertensive) were 8.75±0.53 and 8.62±0.61 and in group B (normotensives) were 9.00±0.45 and 8.87±0.40. The mean total and corrected calcium levels were significantly decreased in essential hypertensive when compared to normotensives which was statistically revealed by a p value of <0.001 and 0.001 respectively.

Our study was supported by K.Sudhakar et al⁵ in the total and corrected calcium levels were decreased in males and females in hypertensive group compared to normotensive group. Study done by AR Folsom¹⁰ et al observed that mean serum levels of ultra filterable calcium (p=0.01), ionized calcium (p=0.09), and complex calcium (p=0.04) and level of protein-bound calcium (p=0.07) were lower in hypertensive group. Erne P, Bolli P., et al⁹ and Touyz, R.M.³, et al also reported a decrease in total serum calcium levels in hypertensive subjects. Study by Strazzullo P et al¹¹. also showed that total serum calcium levels were lowered in hypertensive group. Fu Y, Wang S., et al¹² ., in their study demonstrated that in the hypertensive group there was lower plasma calcium levels and higher cytosolic calcium levels when compared to the normotensive subjects. Study conducted by McCarron DA and Resnick LM¹³ , LaraghJH.,et al¹⁴ , showed that ionized calcium levels were lower in essential hypertensive group compared to similar total calcium levels in hypertensive and normotensive groups. Studies by Harlan WR., et al¹⁵ , Rolf Jorde., et al¹⁶ . and KestelootH., et al¹⁷ ., showed that direct and positive correlation between serum total calcium levels and arterial pressure which is in contrast with our study. This paradoxical correlation is probably due to the failure of them to correct for hemoconcentration that attends hypertension which is because of an increase in serum albumin concentration to which most of the calcium is bound.

CORRELATION OF TOTAL AND CORRECTED SERUM CALCIUM LEVELS WITH SYSTOLIC BLOOD PRESSURE:

In our study we found no correlation between calcium levels and systolic blood pressure of the people in the hypertensive population. AR Folsom et al had conducted a study in which he also found that no correlation between the different calcium fractions and the systolic blood pressure of the individuals. This supports our study.

In contrast to the study done by us, reports by Staessen J, SartorF,¹⁸ Jorde.,¹⁷ and KestelootH.¹⁹ resulted in a favourable correlation between blood pressure and the serum calcium levels. Study by Philips AN., et al²⁰ done identified a positive correlation between the blood pressure both systolic and diastolic and calcium levels this was identified after making adjustments with other fractions like globulin and haematocrit values. Henceforth these different fractions could possibly be the reason for the association between blood pressure and calcium levels of the individuals. Study done by Morris, C.D.et al.,²¹ and Christina Martinez also demonstrated a negative relationship between calcium level and pressure.

CORRELATION OF TOTAL AND CORRECTED SERUM CALCIUM LEVELS WITH DIASTOLIC BLOOD PRESSURE

We also found that there was also no correlation between the calcium levels and corrected calcium levels total and corrected calcium levels when compared with the diastolic blood pressure of the hypertensive individuals (p 0.253 and p 0.181 respectively). This negative correlation between calcium fractions and diastolic blood pressure was also supported by AR Folsom et al.

In contrast to this Jorde., et al.,¹⁶ and Kesteloot H, Geboers J¹⁹ found a positive correlation between calcium levels and the blood pressure especially the diastolic blood pressure of the study people. But studies by Kesteloot H, Joossens JV¹⁷., found there was positive correlation between the calcium levels and both the systolic and diastolic blood pressure in men but in females they found the correlation with diastolic pressure alone.

CORRELATION OF TOTAL AND CORRECTED SERUM CALCIUM LEVELS WITH VARIOUS SUBSETS OF STUDY GROUP (ESSENTIAL HYPERTENSIVE GROUP):

In this study we also correlated serum total and corrected calcium levels with various subsets of essential hypertensive like age, sex, smoking, alcohol, family history, BMI, and lifestyle. There was no significant difference found between the various subsets and calcium levels in our study. AR Folsom et al.¹⁰ and Staessen J, SartorF, et al¹⁸., found that there was no significant difference between total calcium levels and both the sexes. Jorde.,et al¹⁶., observed that there was decrease in serum total calcium level with increasing age in men while there was an increasing trend in women. C Brot., et al²²., observed no difference among smokers and non-smokers with serum ionized calcium levels.

According to K.Sudhakar et al⁵ serum total calcium levels were significantly lowered among first degree relatives of essential hypertensive when compared to normotensives. In an observational study by J.Sundsfjord., R.Jorde., et al²³ there was a positive correlation between BMI and serum calcium level in both the sexes.

CONCLUSION

1. The total and corrected serum calcium levels are significantly lowered in newly detected essential hypertensive patients when compared to normotensive controls.
2. The total and corrected serum calcium levels have no correlation with the level of systolic blood pressure in newly detected essential hypertensive patients.
3. The total and corrected serum calcium levels have no significant correlation with the diastolic blood pressure in newly detected essential hypertensive patients.
4. The total and corrected serum calcium levels showed no significant difference with age, sex, BMI, life style, smoking, alcohol, family history of hypertension in newly detected essential hypertensive patients.

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