



Study of Serum Calcium and Potassium Level in Newly Detected Hypertensives and its Correlation with the Severity of the Disease

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Abstract

Background and Objectives: Serum Calcium and serum potassium are two important elements in regulating cardiovascular functions. Alteration in these have been shown to be associated with hypertension. Serum calcium levels are found to be significantly reduced in hypertension, however serum potassium levels have been found to be variable in hypertensive patients. **Methods:** This study was conducted in tertiary care hospital which is a case control study in which newly detected patients with essential hypertension are enrolled. Serum calcium and serum potassium were estimated in all the patients at the time of study. Serum potassium levels were correlated with age, gender, grades of hypertension and ECG changes. **Results:** A total of 75 patients were studied, 50 were cases and 25 controls. majority were in the age group of 46 to 55 years, mean ages among the cases and controls were 49.52 ± 4.67 years and 51.80 ± 9.61 years respectively. Mean systolic (SBP) among the cases and controls were 165.40 ± 10.93 mm Hg and 127.92 ± 10.01 mm Hg and the mean diastolic blood pressures (DBP) were 96.80 ± 7.13 mm Hg and 77.04 ± 5.29 mm Hg respectively. serum calcium levels were significantly lesser among the cases of hypertension (8.05 ± 0.41 mg/dL) compared to controls (8.68 ± 0.34 mg/dL) who did not have hypertension ($P < 0.05$). Serum potassium levels did not vary among the cases (4.51 ± 0.42 mmol/L) and controls (4.64 ± 0.48 mmol/L) ($P > 0.05$). Corrected serum calcium levels were decreased in patients with newly detected hypertension compared with controls. However serum potassium level did not show any difference between cases and controls. Significant negative correlation was found between corrected serum calcium levels and systolic and diastolic blood pressure. **Conclusion:** Corrected serum calcium levels were reduced in patients with essential hypertension and significant negative correlation was seen between corrected serum calcium levels and systolic and diastolic blood pressures but no correlation was found with serum potassium levels.

Keywords: Serum Calcium, serum potassium, Decreased Levels in Essential Hypertension, Systolic and Diastolic Pressure.

Introduction

Elevated blood pressure is a major risk factor for coronary heart disease, heart failure, cerebrovascular disease, peripheral vascular disease, renal failure, atrial fibrillation and total mortality as well as loss of cognitive function and increased incidence of dementia. The degree of blood pressure lowering related linearly to risk reduction ^[1].

Approximately 78 million or 1 in 3 adults in United States have high blood pressure defined as systolic blood pressure 140 mm hg or more, or diastolic blood pressure of 90 mm hg or greater on taking antihypertensive. Men have higher percentage of hypertension than woman until the age of 45. Between 45 and 60 years of age men and woman have similar percentages of hypertension. After 64 years of age higher percentage of woman have diagnosed as hypertension ^[1].

Numerous risk factors and markers for development of hypertension have been identified including increasing age,

ethnicity, family history of hypertension, genetic factors, lower education and socio-economic status, greater weight, lower physical activity, tobacco use, psychosocial stressors, sleep apnoea and dietary factors (increased fats, high sodium intake, lower potassium intake, excessive alcohol intake)

Data suggest that controlling dietary life style risk factors can prevent a large proportion of incident of hypertension in woman. Young woman who adapts healthy practices such as maintaining normal weight, eating a healthful diet, exercising daily, drinking moderate amount of alcohol, and limiting use of over the counter analgesics can greatly reduce the risk of hypertension.

Patient with concomitant chronic kidney disease constitute a high-risk group for focused blood pressure treatment. Both for the prevention of cardio vascular disease and to slow progression of end stage renal disease. Patient with obesity, metabolic syndrome and diabetes also represent high risk group for treatment. High blood pressure occurs in more than two thirds of the patients with type II diabetes and its development coincides with the development of

hyperglycaemia. In patients with diabetes and hypertension confers an enhanced risk of cardiovascular disease [1].

Isolated systolic hypertension carries at least as much risk as diastolic blood pressure for the outcomes of total cardiovascular mortality and stroke. Evidence supports treatment of systolic hypertension even in older adults. Isolated systolic hypertension thus appears to represent distinct pathophysiological state in which elevated blood pressure reflects reduced arterial elasticity not necessarily associated with increased peripheral resistance. Systolic blood pressure remains the most useful clinical predictor of risk [1].

Meta analysis have shown that magnitude of blood pressure reduction determines reduction in cardiovascular risk more than drug choice and that long term control usually requires combination therapy [1].

Increased consumption of potassium may lower the BP particularly in blacks compared to whites, even though the American society of hypertension recommends an increase in potassium intake of 4.7 grams daily. In 2013 AHA lifestyle guidelines finds the strength of evidence insufficient to establish the relationship between increased dietary potassium or lower BP or altered risk for coronary heart disease or heart failure or cardiovascular mortality [1].

Blood pressure is defined as the lateral pressure exerted by the blood column against unit area of the vessel wall. It is measured in millimetres of mercury (mmHg) [2].

There are multiple mechanisms by which potassium may control BP. Here, we will focus on mechanisms mediated by renal tubular K⁺ channels in the distal tubules. However, it should be taken into account that other tubular segments also contribute to potassium excretion. For example, recent studies by Wang *et al.* revealed that the activities of NKCC2 (Na⁺-K⁺-Cl⁻ cotransporter) and Kir1.1 (also known as ROMK [renal outer medullary K⁺ channel]) are elevated on a low-Na⁺, high-K⁺ diet. Furthermore, renal vascular potassium channels could be involved in the regulation of BP. For instance, small changes in serum potassium can cause endothelium-dependent vasodilation by hyperpolarizing the endothelial and vascular smooth muscle cells. The high-K⁺ diet might also improve the vascular integrity on increased tension, as a result of hypertension. K⁺ supplementation prevented the usual thickening of the arteriolar walls of the kidneys in hypertensive rats. Similarly, even during the development of severe hypertension, the high-K⁺ diet promoted a substantial reduction of wall thickening in either very large or small arteries. It is well recognized that higher levels of sodium intake are associated with elevated BP. Importantly, the effect of high sodium on BP is dependent on diet composition, specifically on the potassium content. It is clear that high dietary potassium is associated with a decrease in BP, particularly in the presence of a high-sodium diet [3].

The level of potassium intake can affect blood pressure. The effect varies with the direction (low potassium intake raises the blood pressure, and high potassium intake lowers the blood pressure) and magnitude of change in potassium intake [4].

No significant difference in serum calcium level was found between normotensive and hypertensive groups; and no correlation was found between calcium levels and the blood pressure. Also the difference in serum calcium levels in hypertensive group on calcium channel blockers and those on antihypertensive other than calcium channel blockers was insignificant [5].

Serum sodium was much higher in hypertensives, and it also had a favourable relationship with BP. On the other hand, serum potassium levels were considerably lower in hypertensives, negatively associated with BP [6].

The corrected serum calcium levels were significantly lowered in newly detected essential hypertensive patients. The

corrected serum calcium levels have a significant negative correlation with the level of systolic blood pressure in newly detected essential hypertensive patients. The corrected serum calcium levels have a significant negative correlation with the diastolic blood pressure also in newly detected essential hypertensive patients. The corrected serum calcium levels showed no significant correlation with gender, BMI, life style, smoking, alcohol intake and family history of hypertension [7].

Within the limitations of the present study, it was found that serum sodium levels and serum potassium were significantly associated with the risk of development of hypertension. Higher BMI also has been found to be associated with hypertension. Therefore changing lifestyles and making people aware of the adverse effects of an increase in BMI and electrolyte imbalance causing hypertension and its complications may go long way in preventing this development in the population [8].

Patients with drug-related hypokalaemia (ie, therapy with a non-potassium-sparing diuretic) should receive potassium supplementation. In patients with asymptomatic hypertension, an effort should be made to achieve and maintain serum potassium levels of at least 4.0 mmol/L. Low serum potassium levels in asymptomatic patients with uncomplicated hypertension should not be regarded as inconsequential. Dietary consumption of potassium-rich foods and potassium supplementation should be instituted as necessary [9].

Objectives of the Study

1. To estimate the level of Serum calcium and potassium levels in patients with newly detected hypertension.
2. To correlate the Serum calcium and potassium levels with blood pressure and its severity.

Materials and Methods

Source of Data: Patients visiting Medicine outpatient department and inpatients admitted in the Medicine ward of tertiary care centre in north Karnataka were enrolled in study after considering the inclusion and exclusion criteria.

Method of Collection of Data: Before collecting Data from patients. Informed Written informed consent from the patients will be obtained.

Measurement of Blood Pressure: Patients were informed to refrain from smoking or drinking tea or coffee for at least 30 minutes before measuring blood pressure. Blood pressure was measured in the Right arm of the subject in sitting position after resting for 10 minutes. 2 readings were recorded using Sphygmomanometer and mean of these readings was noted as a final blood pressure. The JNC 8 criteria for establishing hypertension was followed.

Table 1: JNC 8 Classification of Blood Pressure for Adults

Blood Pressure Classification	SBP (mmHg)	DBP (mmHg)
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	≥160	≥100

Study Duration: 18 months.

Inclusion Criteria

- Patients with newly detected hypertension.
- Patients aged between 25-55 years are included.

Exclusion Criteria

- Patients with renal failure.
- Pregnancy.
- Patients on calcium supplements.
- Patients having Thyroid and parathyroid disorders.
- Patients with Diabetes mellitus.

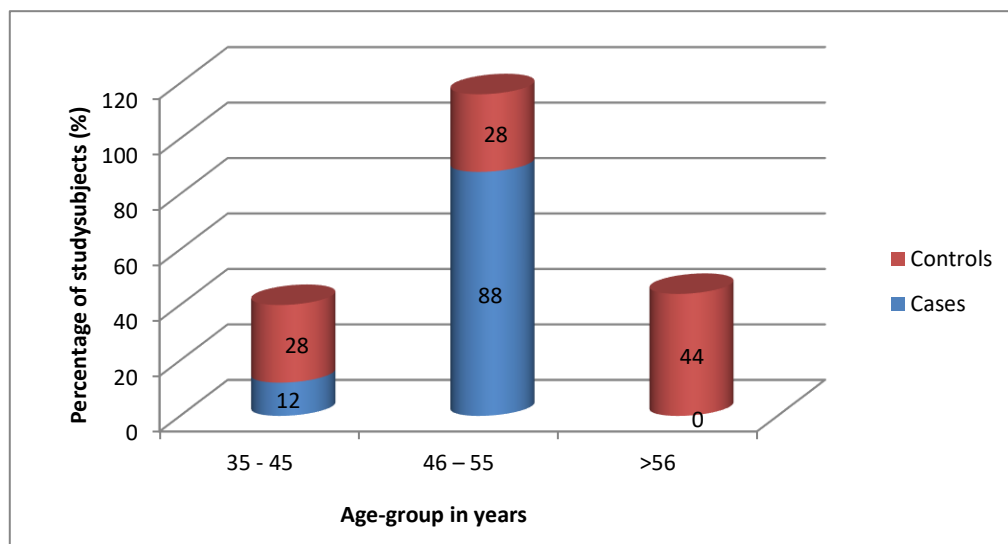
A total 75 cases 50 cases of newly detected hypertension satisfying inclusion and exclusion criteria visiting medicine OPD and admitted in inpatient department of tertiary care centre in north Karnataka and 25 age and sex matched normotensive controls were taken up for study. The sample size is estimated based on 1% significance level and 90% power.

Sample Size

Results

Table 2: Distribution of study subjects according to age group among the cases and controls

Age group in years	Cases n (%)	Controls n (%)	Total n (%)
35 – 45	06 (12.0)	07 (28.0)	13 (17.3)
46 – 55	44 (88.0)	07 (28.0)	51 (68.0)
>56	00 (0.0)	11 (44.0)	11 (14.7)
Total	50 (100.0)	25 (100.0)	75 (100.0)

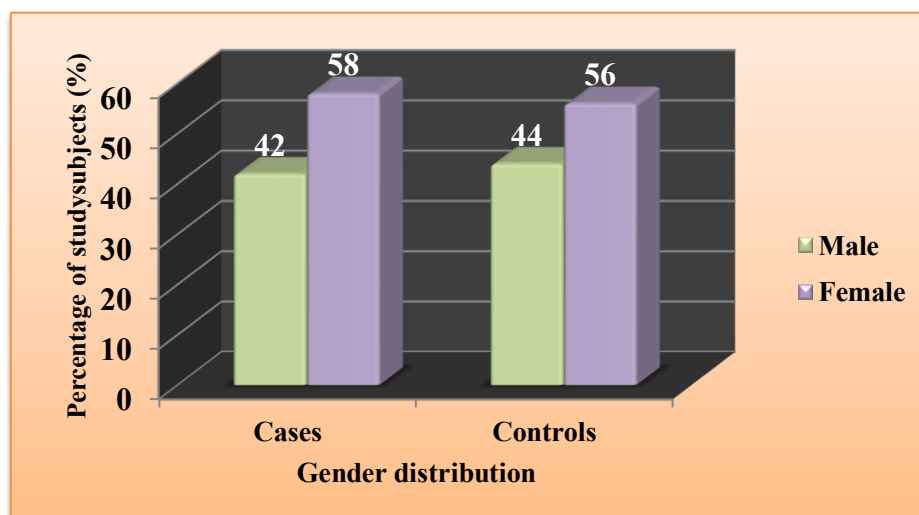


Graph-1: Age group distribution

Among the cases, majority were in the age group of 46 to 55 years, however, among the controls, most of them were aged above 56 years. Though the proportions appeared to be distributed unequally among the groups, the mean ages among the cases and controls were 49.52 ± 4.67 years and 51.80 ± 9.61 years respectively. The difference in means were not significant among the cases and controls (t-value [95% CI]: -1.39 [-5.55 to 0.99]) ($P > 0.05$)

Table 3: Distribution of study subjects according to gender among the cases and controls

Gender	Cases n (%)	Controls n (%)	Total n (%)
Male	21 (42.0)	11 (44.0)	32 (42.7)
Female	29 (58.0)	14 (56.0)	43 (57.3)
Total	50 (100.0)	25 (100.0)	75 (100.0)

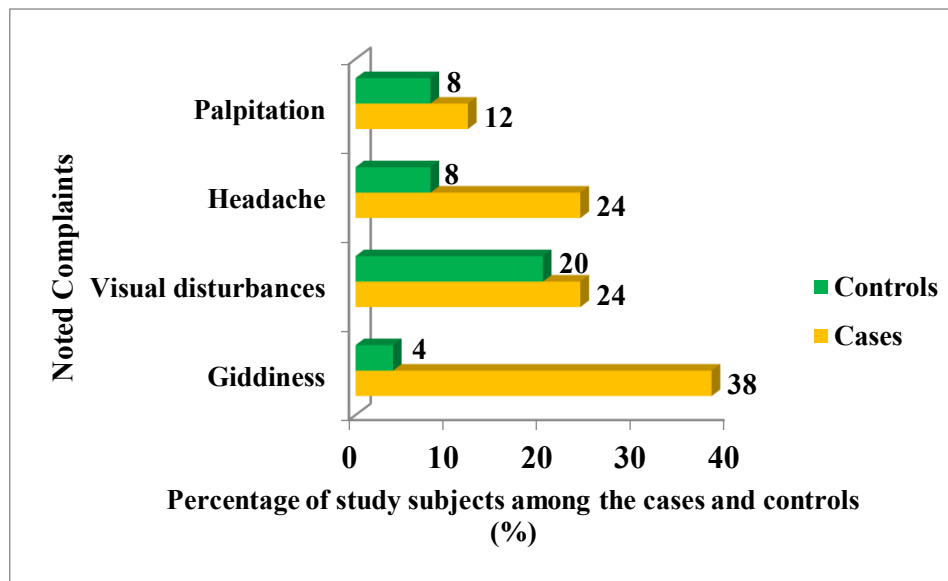


Graph-2: Gender-wise distribution among cases and controls

Nearly equal proportions among the cases and controls were males and females, with male proportions being 42.0% vs 44.0% and female proportions being 58.0% vs 56.0% among the cases and controls respectively ($P>0.05$).

Table 4: Distribution of study subjects according to the presence of complaints

Complaints	Cases n (%)	Controls n (%)	Total n (%)
Yes	08 (16.0)	08 (32.0)	16 (21.3)
No	42 (84.0)	17 (68.0)	59 (78.7)
Total	50 (100.0)	25 (100.0)	75 (100.0)

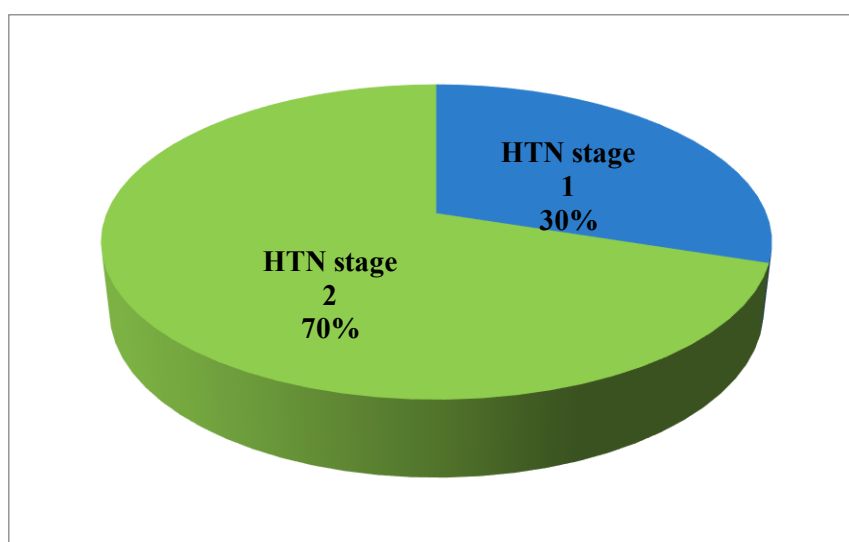


Graph-3: Noted percentages of different complaints among the cases and controls

Most of the study subjects among cases (84.0%) and controls (68.0%) did not have any complaints. Among the cases the most frequent complaint was giddiness (38.0%), headache and visual disturbances (24.0% each). Among the controls the most common complaint was visual disturbances (20.0%).

Table 5: Distribution of study subjects according to stages of hypertension among the cases

Complaints	Frequency (n)	Percentage (%)
HTN stage 1	15	30.0
HTN stage 2	35	70.0
Total	50	100.0



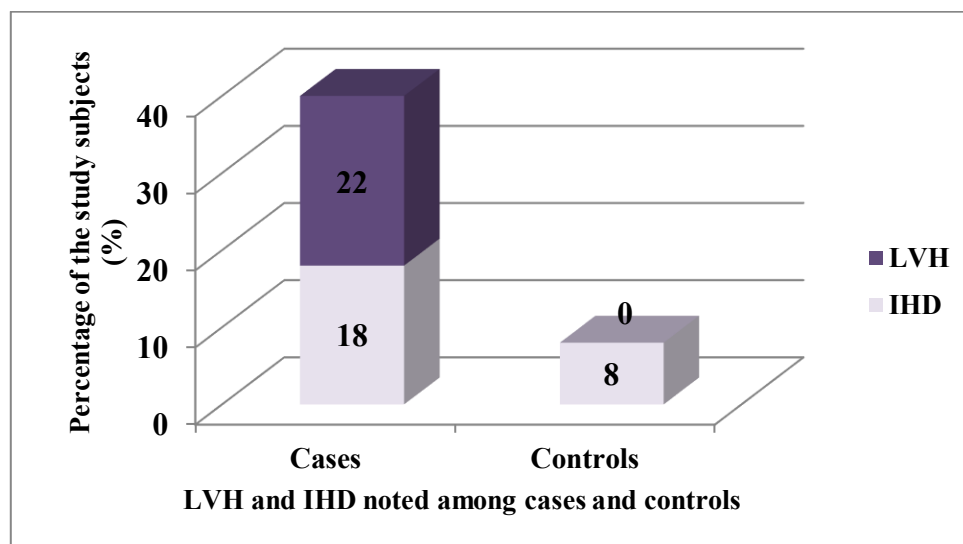
Graph-4: Percentage distribution of study subjects based on stage of HTN among the cases (n=50)

The highest proportions of study subjects among the cases had stage 2 hypertension accounting to 70.0%.

The mean systolic (SBP) among the cases and controls were 165.40 ± 10.93 mm Hg and 127.92 ± 10.01 mm Hg and the mean diastolic blood pressures (DBP) were 96.80 ± 7.13 mm Hg and 77.04 ± 5.29 mm Hg respectively. Both the mean systolic (t-value [95% CI]: 14.38 [32.29 to 42.67]) and diastolic (t-value [95% CI]: 12.26 [16.55 to 22.97]) blood pressures were significantly higher among the cases compared to controls ($P<0.05$).

Table 6: Distribution of study subjects according to the status of ECG

Sinus Rhythm on ECG	Cases n (%)	Controls n (%)	Total n (%)
Yes	36 (72.0)	23 (92.0)	59 (78.7)
No	14 (28.0)	02 (8.0)	16 (21.3)
Total	50 (100.0)	25 (100.0)	75 (100.0)

**Graph-5: Percentage distribution of study subjects with LVH and IHD**

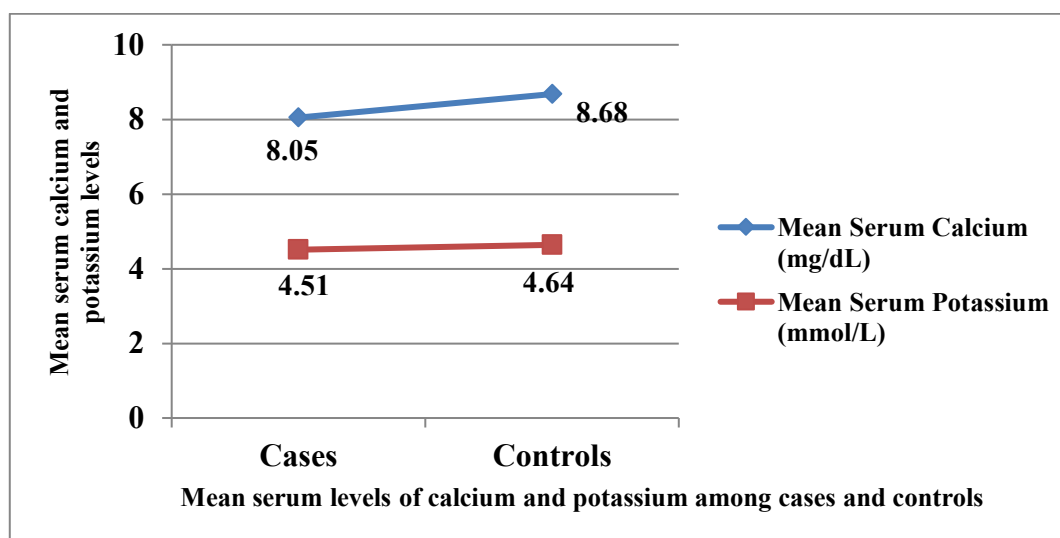
Among all, 72.0% of cases and 92.0% of the controls had normal sinus rhythm on ECG.

Majority of the study subjects among the cases i.e. 22.0% had left ventricular hypertrophy (LVH) and 18.0% had IHD. On the contrary, there were none with LVH and 8.0% of them had IHD among the controls.

Table 7: Comparison of mean values of serum calcium and potassium levels among cases and controls

Variables	Cases (n = 50)	Controls (n = 25)	t-value [95% CI]	P-value
Serum Calcium (mg/dL)	8.05±0.41	8.68±0.34	-6.71 [-0.82 to -0.45]	<0.0001*
Serum Potassium (mmol/L)	4.51±0.42	4.64±0.48	-1.26 [-0.35 to 0.08]	0.21

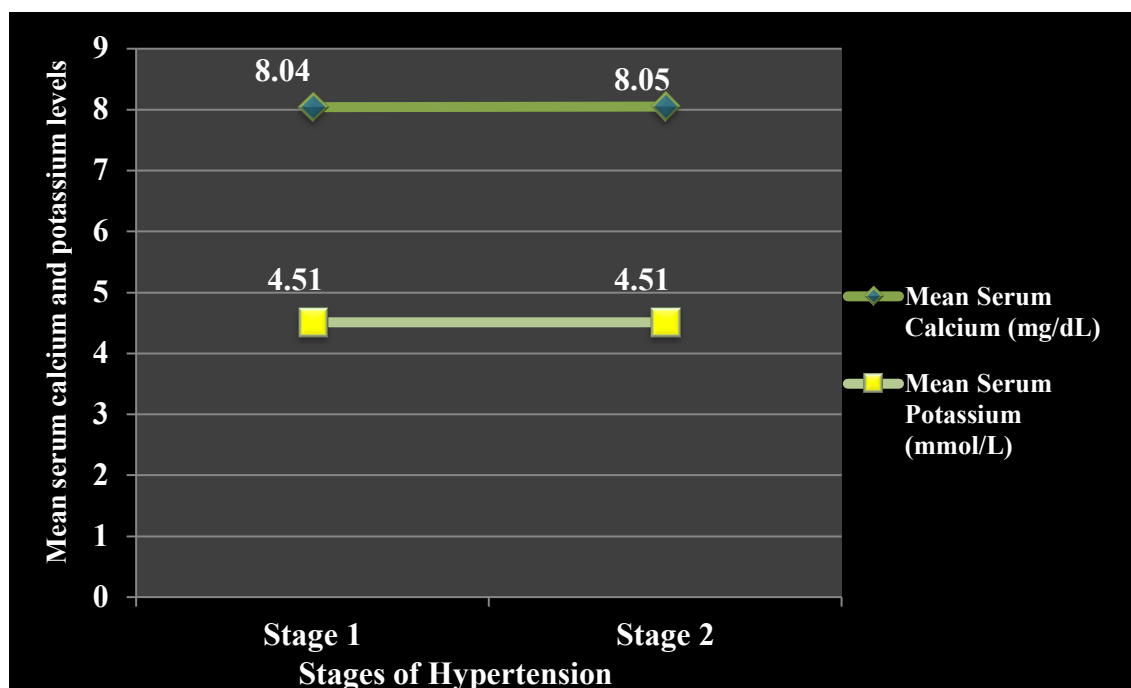
*Indicates statistically significant difference at $P < 0.05$

**Graph 6: Mean levels of serum calcium and potassium among cases and controls**

The serum calcium levels were significantly lesser among the cases of hypertension (8.05 ± 0.41 mg/dL) compared to controls (8.68 ± 0.34 mg/dL) who did not have hypertension ($P < 0.05$). Serum potassium levels did not vary among the cases (4.51 ± 0.42 mmol/L) and controls (4.64 ± 0.48 mmol/L) ($P > 0.05$).

Table 8: Comparison of mean values of serum calcium and potassium levels among the cases with stage 1 and 2 hypertensions

Variables	Stage 1 HTN (n = 15)	Stage 2 HTN (n = 35)	t-value [95% CI]	P-value
Serum Calcium (mg/dL)	8.04±0.40	8.05±0.42	-0.09 [-0.27 to 0.24]	0.93
Serum Potassium (mmol/L)	4.51±0.41	4.51±0.43	-0.01 [-0.27 to 0.26]	0.99



Graph 7: Mean levels of serum calcium and potassium among the cases with different stages of hypertension

Among the cases with hypertension, the mean serum calcium levels were 8.04 ± 0.40 mg/dL in stage 1 hypertension and 8.05 ± 0.42 mg/dL in stage 2 hypertension subjects.

Mean serum potassium levels were 4.51 ± 0.41 mmol/L in stage 1 hypertension and 4.51 ± 0.43 mmol/L stage 2 hypertension, values did not vary among the different stages of hypertension ($P > 0.05$).

Discussion

Various epidemiological studies stated that the calcium status of humans with essential hypertension and genetic animal models of hypertension is characterized by low serum total and ionized calcium concentration, increased intracellular calcium, increased urinary calcium excretion, and increased parathyroid hormone (PTH) concentration [9,10].

This study was conducted to observe the serum calcium and potassium level in newly detected hypertensives and its correlation with the severity of blood pressure.

In this study, cases, majority were in the age group of 46 to 55 years, mean ages among the cases and controls were 49.52 ± 4.67 years and 51.80 ± 9.61 years respectively. Most of the study subjects among cases (84.0%) and controls (68.0%) did not have any complaints. Among the cases the most frequent complaint was giddiness (38.0%), headache and visual disturbances (24.0% each). Among the controls the most common complaint was visual disturbances (20.0%).

Mean systolic (SBP) among the cases and controls were 165.40 ± 10.93 mm Hg and 127.92 ± 10.01 mm Hg and the mean diastolic blood pressures (DBP) were 96.80 ± 7.13 mm Hg and 77.04 ± 5.29 mm Hg respectively

The mean serum calcium levels were 8.04 ± 0.40 mg/dL in stage 1 hypertension and 8.05 ± 0.42 mg/dL in stage 2 hypertension subjects.

Serum calcium levels were significantly lesser among the cases of hypertension (8.05 ± 0.41 mg/dL) compared to controls (8.68 ± 0.34 mg/dL) who did not have hypertension ($P < 0.05$).

This observation is supported by the study conducted by Dr. Uday. S. Bande *et al.* [11] in 2016, which attempted to focus the serum calcium level among essential hypertensives and to correlate Serum calcium status with the blood pressure where serum calcium levels were measured in 80 cases of essential hypertension which included 37 cases of grade I and 43 cases of grade II hypertension. In cases,

the mean serum calcium level was 8.0020 ± 0.6520 mg/dl where in controls, it was 9.02 ± 0.5077 mg/dl. The result showed that serum Calcium levels were significantly decreased in grade I ($P < .0001$) as well as grade II ($P < .0001$) hypertension cases when compared to age matched normotensive control.

In our study, there was a significant decrease in serum calcium level in newly detected hypertensives which was supported by another study conducted by Touyz, R.M., *et al.* [12] who also reported a decreased serum total calcium concentration in essential hypertensive patients.

In our study, only serum calcium level was observed and correlated with newly detected hypertension. ATPase activity or serum magnesium and intracellular magnesium levels were not observed which was done in the study conducted by Fu Y, Wang S., *et al.* [13] in their study suggested that the hypertensive group consistently demonstrated a significant decreased activity of ATPase studied, with significantly lower plasma calcium and higher cytosolic calcium levels when compared with those in normotensive group ($P < 0.01$ or $P < 0.05$, respectively). No significant differences were found in either plasma Mg^{2+} or intracellular Mg^{2+} level between the two groups.

In the present study, a correlation between calcium levels and systolic blood pressure was attempted and found that the serum calcium level had a significant negative correlation with systolic and diastolic blood pressure ($P < 0.001$ and $P < 0.001$ respectively) which is supported by a study conducted by Ottar Hals [14] who found that pretreatment systolic blood pressure was inversely correlated to serum ionized calcium ($r = -0.44$ and $p = 0.05$) in his.

Another study supporting our study of negative correlation of serum calcium level with blood pressure was conducted by Morris.C.D. *et al.* [15] and Christina Martinez [16], in which there was a clear inverse relationship between calcium and both the prevalence of hypertension and the level of blood pressure.

In our study, the comparison of serum calcium level with gender distribution and first degree relatives was not studied which

was done in a study conducted by K. Sudhakar *et al.*^[17] where the mean total serum calcium levels were significantly ($p < 0.01$) decreased in males and females in hypertensive group when compared with normotensive controls and also in the first-degree relatives ($p < 0.01$) when compared with the controls.

Serum Potassium Levels in Hypertension

Study by Mane, *et al.*^[18] found an increased risk of hypertension individuals with baseline potassium < 4.2 mmol/L.

In Framingham Heart Study^[19] during the follow-up period, 46% of the study sample had a 10 mm Hg increase in systolic BP or a 5 mm Hg increment in diastolic BP, or required treatment with antihypertensive medications. After adjusting for multiple confounders, no association was seen between serum potassium and risk for increase in BP between the baseline and follow-up examinations.

However in our study Mean serum potassium levels were 4.51 ± 0.41 mmol/L in stage 1 hypertension and 4.51 ± 0.43 mmol/L stage 2 hypertension, values did not vary among the different stages of hypertension ($P > 0.05$). Serum potassium levels did not vary among the cases (4.51 ± 0.42 mmol/L) and controls (4.64 ± 0.48 mmol/L) ($P > 0.05$). Serum potassium levels were not statistically significant among cases and controls.

Summary

Hypertension is one of the leading causes of death and disability among adults all over the world. It remains the major risk factor for coronary, cerebral and peripheral vascular disease.

The identification of patients with Hypertension is an important individual and public health issue.

The present study aimed at comparing the serum calcium levels in newly detected hypertensive patients with matched normotensive controls. It also aimed at correlating the serum calcium and serum potassium levels with blood pressure in newly detected hypertensive patients. With inclusion and exclusion criteria, 75 individuals out of which 50 newly detected hypertensive cases and 25 normotensive controls were selected and enrolled in the study.

The serum calcium levels were found to be significantly lowered in cases when compared to controls. Also a significant negative correlation between the calcium levels and both systolic and diastolic blood pressure was noted among the cases. However serum potassium levels did not show any statistical significance among cases and controls.

Conclusion

Serum calcium levels were reduced in patients with essential hypertension and significant negative correlation was seen between serum calcium levels and systolic and diastolic blood pressures, however serum potassium value did not show any statistical significance among cases and controls.

Declarations

Ethics approval and consent to participate

Ethical committee approval was obtained from institute

Conflicts of Interest

There is no conflict of interest regarding the publication of this paper

Funding Statement

None

Authors' contributions

All the authors are equally contributed for concept, study design, data collection, Analysis.

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