

Correlation analysis of serum calcium level with the blood pressure among patients with essential hypertension in rural population of Himachal Pradesh

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Abstract

Introduction: A high blood pressure that doesn't have a known secondary cause is called as essential hypertension, is a leading cause of death worldwide. Calcium supplementation known to reduce the blood pressure in normal healthy individuals.

Objective: The present study aims towards analysing the correlation between serum calcium level with the blood pressure among patients with essential hypertension.

Methods: 30 cases of essential hypertension patients as cases and 30 suitable healthy age sex matched individuals with normal blood pressure as controls, as per JNC-8 guidelines were recruited in study. Serum calcium level and blood pressure was analysed in all patients.

Results: Systolic Blood Pressure in control group was 111.1 ± 7.570 and in cases was 158.1 ± 9.066 . Diastolic Blood Pressure in control group was 72.80 ± 6.183 and in cases was 92.33 ± 6.456 . Serum calcium in control group was 9.207 ± 0.7249 and in cases was 8.130 ± 0.4843 .

Conclusion: Patients with lower calcium level tends to have raised blood pressure and vice versa. Thus, routine dietary restriction salt in hypertensive individuals can help in better management of hypertension.

Keywords: Hypertension, calcium, blood pressure, diet

Introduction

Hypertension remains the leading cause of death worldwide and one of the world's great public health problems ^[1]. Systemic hypertension is commonly recognised risk factor for various diseases like myocardial infarction, cardiovascular diseases, heart failure, and

peripheral artery disease. Hypertension have global prevalence of one billion individuals. Globally, it has been estimated that one-third of population going to be affected hypertension by 2025 as a result of rising obesity and population ageing in industrialised and developing nations [2]. Hypertension (HTN) is defined as having a SBP of 130mmHg or higher and/or a DBP of greater than 80mmHg. To distinguish it from secondary hypertension, which occurs as a result of identified reasons such as renal artery stenosis, essential hypertension is also referred to as primary hypertension. According to an estimate, 90% to 95% of all hypertension is caused by an unknown reason, thus vast majority of hypertension is primary or essential hypertension [3]. According to the 2017 ACC/AHA guideline, a SBP of 130 mmHg or a DBP of 80 mmHg is considered hypertension [4]. According to the 2018 ESC and ESH guidelines, hypertension is defined as office SBP of 140 mmHg and/or DBP of 90 mmHg, which is equivalent to a 24-hour ambulatory blood pressure measurement average of 130/80 mmHg or a home blood pressure measurement average of 135/85 mmHg [5]. If blood pressure is less than 140/90 mmHg, the JNC-8 advises commencing pharmacologic therapy in individuals with chronic renal disease and diabetes. When blood pressure is less than 150/90 mmHg in the general population over the age of 60, therapy to decrease blood pressure should begin. Because of the risk of cardiovascular events associated with BP 140/90 mmHg, the latter suggestion did not receive unanimous approval from all panel members [6]. Until recently the strong evidence pointed to a positive relationship between raised Ca and blood pressure. There is evidence that abnormalities of calcium homeostasis at both an organ and cellular level plays a role in the pathogenesis of human and experimental hypertension. Clinical experimental and epidemiologic studies showed that Ca not only mediates arterial smooth muscle contraction but excess of Ca can also cause an increase in peripheral vascular resistance leading to essential hypertension. Ca entry blockers such as verapamil and nifedipine which reduce the influx of Ca into the arterial smooth muscle cell have been successfully used in the management of these patients. An increase in leucocyte, RBC and platelet cytosolic calcium levels has been reported in some hypertensives [7]. However increased calcium levels also have a direct vasoconstrictive effect. In some cases, hypertension can be treated by correcting hypercalcemia [8]. The positive effect of a calcium-rich diet (> 1000 mg calcium daily) in decreasing blood pressure may be due to parathormone suppression with a subsequently decreased calcium content in the vascular smooth muscle cells. A calcium-rich diet inhibits lipogenesis in the fat tissue; thus, additionally improving the cardiovascular risk profile [9-11]. Additional studies are needed to resolve these seemingly conflicting observations. Therefore, present study was conducted with aims towards analysing the correlation between serum calcium level with the blood pressure among patients with essential hypertension.

Material and Methods

Study design: This study is a cross sectional study, with cases and controls enrolling 30 cases of essential hypertension patients as cases and 30 suitable healthy age sex matched individuals with normal blood pressure as controls, as per JNC-8 guidelines. Cases will be selected from those who visited hypertension clinic, outpatient department and those who were admitted in wards during the study period. Controls will be selected from those who attended medical outpatient department for minor ailments and healthy volunteers.

Selection of patients: In individuals with hypertension, a complete history was taken and a

clinical examination was performed. Urine and blood tests were performed as needed. All patients had a fundus evaluation for hypertensive retinopathy. The study was carried out after getting the clearance from the institutional ethical committee and the informed written consent from every individual patient was obtained, and detailed information regarding demographic, family history and a personal history of chronic kidney disease, diabetes, hypertension was taken.

Blood pressure measurement: Within 30 minutes, the participants were not allowed to consume coffee or smoke. Prior to the reading, the participants were asked to sit silently in a room for 5 minutes after emptying their bladders, with one arm bared and supported at the level of the heart and the back against a chair. The blood pressure was measured using a mercury manometer with the proper cuff size. Phase I (appearance) of the Korotkoff sound was used to determine systolic blood pressure, whereas phase V (disappearance) was used to determine diastolic blood pressure. After 30 minutes, two sets of blood pressure measurements were collected. If the blood pressures differed in both arms in a sitting position, the arm with the greater pressure was taken.

Serum calcium analysis: Blood sample for routine investigations were collected from anterior cubital vein in aseptic condition in indoor patients. Serum routine biochemistry was done on fully automated chemistry analyser, Beckmann coulter AU480 based on Spectrophotometric method. For the estimation of total serum calcium, 2 ml of fasting, venous, non-haemolyzed blood sample was withdrawn without the aid of a tourniquet, in a plain sterile bulb. The blood samples were analysed immediately. The estimation of serum calcium was done on a SEIMENS DIMENSION RXL-MAX fully automatic analyser with the kit based on the Modified O-Cresol phthalein Complex one (OCPC) Method of Moorehead and Briggs.

Results :

The mean of participants in control group was 50.93 ± 14.68 years and in cases was 58.30 ± 17.40 years. Sex ratio highlight that in control group, males were 12 (40%) and females were 18 (60%) whereas in cases males were 25 (83.33%) and females were 5 (16.66%). male to female sex ratio in control group was 0.66 and in cases was 5. Family history of hypertension was present in 16 (53.33%) of cases and no family history of hypertension was found in 14 (46.66%) cases. Systolic Blood Pressure in control group was 111.1 ± 7.570 and in cases was 158.1 ± 9.066 . There was significant difference between the two groups (Figure 1). Diastolic Blood Pressure in control group was 72.80 ± 6.183 and in cases was 92.33 ± 6.456 . There was a significant difference between the two groups (Figure 2). Serum calcium in control group was 9.207 ± 0.7249 and in cases was 8.130 ± 0.4843 . There was a significant difference between the two groups (Figure 3). In case group, the correlation analysis of systolic blood pressure vs. calcium revealed a negative correlation of $r=-0.09047$ which was significant. The correlation analysis of diastolic blood pressure vs. calcium revealed a negative correlation of $r=-0.06065$ which was significant. (table 1)

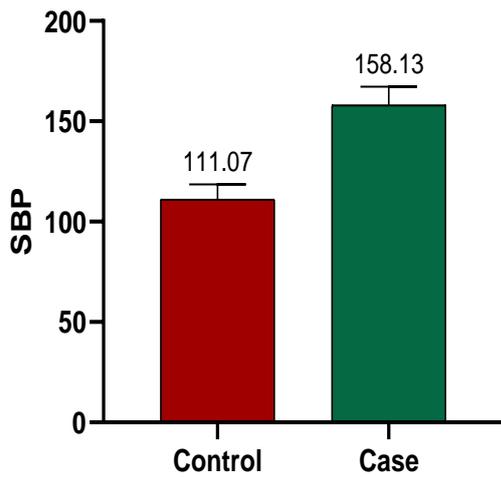


Fig 1: Systolic blood pressure

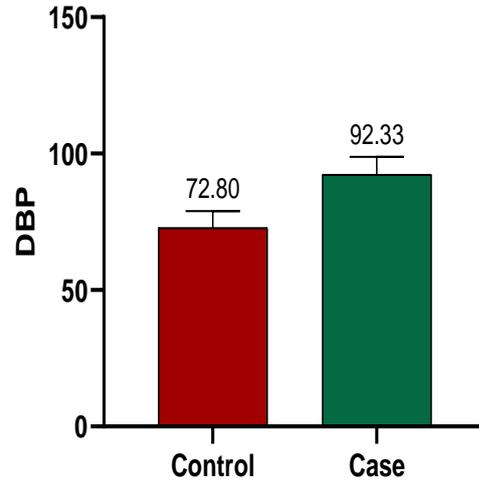


Fig 2: Diastolic blood pressure

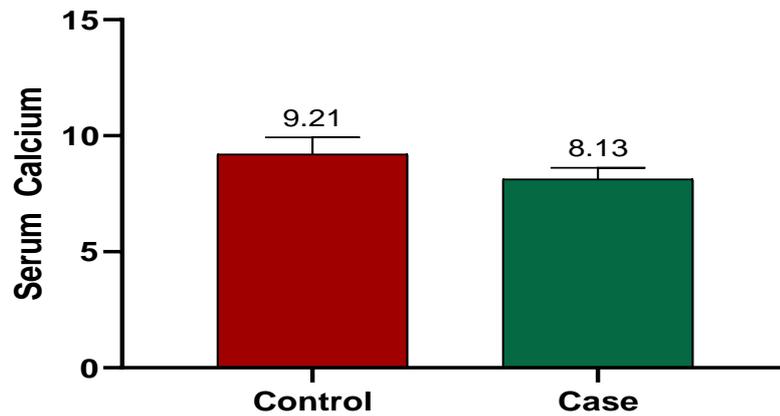


Fig 3: Serum calcium among controls and cases

Group	Correlation variables	Pearson correlation (r)	P value
Control	SBP Vs. Calcium	0.2978	0.1100
	DBP Vs. Calcium	0.2726	0.1449
Case	SBP Vs. Calcium	-0.09047	0.6345
	DBP Vs. Calcium	-0.06065	0.7502

Table 1: Correlation analysis of blood pressure with Serum calcium

Discussion :

In present study, serum calcium in control group was 9.207 ± 0.7249 and in cases was 8.130 ± 0.4843 which was a significant difference. Prasad *et al.* found that the mean total blood calcium and ionised calcium levels in group A were 9.207 ± 0.7249 mg/dl and 1.0303 ± 0.0957 mmol/l, respectively, whereas the mean total serum calcium and ionised calcium levels in group B (controls) were 9.0765 ± 0.6143 mg/dl and 1.296 ± 0.0873 mmol/l. Total calcium levels were not considerably higher in essential hypertensives, but they were significantly higher when compared to ionised calcium levels, according to statistical analysis [12]. The mean amount of total serum calcium was not significantly different between hypertensive and normotensive groups, according to Pawade *et al.* [13]. In recent research by Kar *et al.*, the mean blood total calcium level in hypertension patients was lower than in controls, although the difference was not significant [14].

In the present study, the systolic blood pressure in control group was 111.1 ± 7.570 and in cases was 158.1 ± 9.066 . There was significant difference between the two groups. A correlation between Ca^{2+} levels and SBP was attempted in a study by Subhash and Ramanathan. Calcium levels was found to have negative correlation with SBP to a significant level, which was not supported by the results of the current study [15]. In his research, Ottar Hals [16] discovered that systolic blood pressure before therapy was inversely associated to serum ionised calcium. According to Morris *et al.* [17] and Martinez *et al.* [18], there was an inverse relation between calcium and hypertension.

In the present study, the diastolic blood pressure in control group was 72.80 ± 6.183 and in cases was 92.33 ± 6.456 . There was a significant difference between the two groups. In addition, Subhash and Ramanathan looked for a link between calcium levels and DBP. They discovered an inverse connection between calcium and DBP, which matches the current study findings [15]. Folsom *et al.* looked examined blood calcium levels in essential hypertensive and normotensive people [19].

In case group, the correlation analysis of systolic blood pressure vs. calcium revealed a negative correlation of $r=-0.09047$ which was significant. The correlation analysis of diastolic blood pressure vs. calcium revealed a negative correlation of $r=-0.06065$ which was significant.

The hypertensive group consisted of 28 patients with a diastolic blood pressure more than 90 mm Hg who were not receiving antihypertensive medication at the time of the trial. Each hypertension individual was paired with a normotensive control. The controls had to have the same race, age, and gender as the hypertensive individual. The mean blood levels of ultra-filterable calcium and ionised calcium were lower in hypertensive patients. In hypertensive participants, calculated serum complexed calcium concentrations were substantially lower, but protein bound calcium concentrations were significantly greater. There were no differences in blood phosphorus, serum albumin, or dietary calcium consumption between the two groups [19].

Based on the current evidence and experience, calcium supplementation along with increased dietary consumption of calcium-rich foods would be advised for non-specific hypertension

therapy and prevention. Although some other studies do not support calcium therapy for the treatment and prevention of hypertension, calcium can still be utilised for other reasons, such as osteoporosis prevention. As a result, for both adolescents and adults, it is recommended that calcium intake be maintained at 1.0 to 1.5 grammes per day by food consumption and supplementation. In individuals who are receptive, this dosage should be adequate to induce a blood pressure lowering response ^[20].

Conclusion :

Serum calcium in control group was 9.207 ± 0.7249 and in cases 8.130 ± 0.4843 . There was a significant difference between the two groups. Systolic Blood Pressure in control group was 111.1 ± 7.570 and in cases was 158.1 ± 9.066 . There was significant difference between the two groups. Diastolic Blood Pressure in control group was 72.80 ± 6.183 and in cases was 92.33 ± 6.456 . Correlation analysis in both systolic and diastolic blood pressure shows negative correlation. There was a significant difference between the two groups. Patients with lower calcium level tends to have raised blood pressure. Thus, routine dietary restriction salt in hypertensive individuals can help in better management of hypertension.

References :

1. Organization WH. The world health report: reducing risks, promoting healthy life: World Health Organization, 2002.
2. Victor RG, Kaplan N. Systemic Hypertension: Mechanism and Diagnosis; BRAUNWALD'S Heart Disease. Libby P, Bonow RO, Mann DL, Zipes DP, editors, 2012, 8.
3. Iqbal AM, Jamal SF. Essential hypertension. Stat Pearls, 2020.
4. Whelton PK, Carey RM, Aronow WS, Casey Jr DE, Collins KJ, Dennison Himmelfarb C, *et al.* Guideline for the prevention, detection, evaluation and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2017;71(19): e127-e248.
5. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, *et al.* ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). European heart journal. 2018;39(33):3021-104.
6. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, *et al.* evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). Jama. 2014;311(5):507-20.
7. McCarron DA. Is calcium more important than sodium in the pathogenesis of essential hypertension? Hypertension. 1985;7(4):607-27.
8. Jones D, Jones J, Lloyd H, Lucas P, Wilkins W, Walker D. Changes in blood pressure and renal function after parathyroidectomy in primary hyperparathyroidism. Postgraduate

- medical journal. 1983;59(692):350-3.
9. Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, *et al.* Effects of dietary calcium supplementation on blood pressure: a meta-analysis of randomized controlled trials. *Jama*. 1996;275(13):1016-22.
 10. Cappuccio FP, Siani A, Strazzullo P. Oral calcium supplementation and blood pressure: an overview of randomized controlled trials. *Journal of hypertension*. 1989;7(12):941-6.
 11. Van Mierlo LA, Arends LR, Streppel MT, Zeegers M, Kok FJ, Grobbee DE, *et al.* Blood pressure response to calcium supplementation: a meta-analysis of randomized controlled trials. *Journal of human hypertension*. 2006;20(8):571-80.
 12. Prasad RV, Kumar A, Agarwal P. Estimation of Serum Calcium Level in Essential Hypertension and Its Prognostic Significance. *Int. J Sci. Res.* 2019;8(7):2277-8179.
 13. Pawade YR, Ghangale SS, Apte IC, Nagdeote A, Warade JP. Serum calcium: Can it be a diagnostic and prognostic marker in essential hypertension. *J Clin. Diagn Res.* 2011;5(1):58-62.
 14. Kar K, Sinha S, Dasgupta A, Sen S. Significance of Ionized calcium in hypertension. *Int. J Pharma Res Health Sci.* 2014;2(4):273-80.
 15. Vidya S, Ramanathan K. Study of Serum Calcium Levels in Newly Detected Patients with Essential Hypertension. *Int. J Contemp. Med Res.* 2019;6(10):21-6.
 16. Midtbø K, Hals O. Serum Ionized Calcium A Predictor of Therapeutic Response To Slow Calcium Channel Blockade in Essential Hypertension. *Angiology*. 1987;38(11):841-6.
 17. Morris CD, Reusser ME. Editors. Calcium intake and blood pressure: epidemiology revisited. *Seminars in nephrology*, 1995.
 18. Martinez C. Calcium and hypertension. *Nutrition bytes*, 1998, 4(2).
 19. Folsom AR, Smith CL, Prineas RJ, Grimm Jr RH. Serum calcium fractions in essential hypertensive and matched normotensive subjects. *Hypertension*. 1986;8(1):11-5.
 20. Gupta R, Guptha S. Strategies for initial management of hypertension. *The Indian journal of medical research*. 2010;132(5):531.