

## 2 Original article:

### **STUDY OF RELATIONSHIP BETWEEN SERUM CALCIUM & ARTERIAL BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION .**

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#### ABSTRACT :

Hypertension is the commonest cardiovascular disorder, affecting 20 % of the adult population in many countries .It is linked with coronary heart disease,stroke,congestive cardiac failure and renal dysfunction and is one of the major risk factor for cardiovascular mortality,which accounts for 20 to 50 % of all deaths.The use of calcium channel blocking agents in the treatment of hypertension shows the critical importance of calcium in the biochemical control of vascular smooth muscle tone,and thus of blood pressure homeostasis.Therefore, we designed a study to find correlation between serum calcium levels and blood pressure .50 normotensive and 50 hypertensive were studied and compared.

#### AIMS & OBJECTIVE :

To estimate serum calcium in a group of hypertensive patients and matched controls .

To compare the level of serum calcium in hypertensive and normotensive control group .

To study correlation between serum calcium and arterial blood pressure in hypertensive individuals .

**RESULT :**In our study,a significant high levels of serum calcium were found in hypertensive group as compared to normotensive group( $P < 0.01$ ). A statistically significant linear correlation was found between serum calcium and both systolic and diastolic blood pressure in hypertensive males ( $P < 0.01$ ).

**CONCLUSION :**Our study shows a significant correlation between high serum calcium levels and high blood pressure.According to the present study,increased serum calcium leads to hypertension .Hence, serum calcium levels should be estimated in hypertensive patients .

#### INTRODUCTION :

The importance of calcium in cardiac muscle contraction,has been increasingly recognised(1).The use of calcium channel blocking agents in the treatment of hypertension shows the critical importance of calcium in the biochemical control of vascular smooth muscle tone,and thus of blood pressure homeostasis(2).

Despite the advances,the relation of clinical aspects of calcium metabolism such as dietary calcium intake ,renal disposition of calcium and circulating levels of calcium regulating hormones ,as well as calcium itself ,to disorders of blood pressure regulation such as hypertension remains an ambiguous one.A rapidly expanding literature suggests that alterations of these clinical metabolic variables are indeed found in human hypertensive disease and they may contribute to the pathophysiology of hypertension(3,4,5,6).However,these alterations seem to suggest that calcium may either exacerbate or alleviate hypertension.

The report by McCarron and Morris (7) and other recent preliminary reports (8,9) show the ability of oral calcium supplements to lower blood pressure in some subjects with essential hypertension. Population survey show a positive relation between blood pressure and serum calcium levels (10), and increased intracellular free cytosolic calcium levels have been reported in hypertensive persons (11). Acute elevation or suppression of circulating calcium levels result in concomitant elevation or suppression of blood pressure (12,13) and the chronic hypercalcemia of hyperparathyroidism and vitamin D intoxication is also associated with an increased incidence of chronic hypertension (14,20). These all studies tend to portray calcium as a pathogenic or exacerbating factor in hypertensive disease .

Material and Method :

The subjects included in this study were 50 fresh hypertensive patients ,who attended general OPD of JJ Hospital for minor ailments other than hypertension. Healthy age, sex and diet matched 50 normotensive individuals served as controls. All the individuals selected were apparently in good general health. A full medical history of these subjects was first obtained which provided the basis for selection . Informed written consent was taken before the studies from study group and control group .

Inclusion Criteria : All the male subjects belonged to the age group 22 – 75 years. All the subjects had their weight between 52 -92 kgs . Only subjects with mixed diet were included in the study. Subjects who did not give history of consuming alcohol and smoking were taken. All subjects chosen were employees having a similar level of physical activity . Subjects belonged to the middle socio economic strata .

Exclusion Criteria :Subjects with clinical history of ischemic heart disease ,thyroid,hepatic,renal or pancreatic disorders .Subjects who were on any drugs for systemic disease.

The protocol of the study was approved by the ethical committee and departmental research committee, Grant govt medical college, Mumbai .

Method :

Measurement of arterial blood pressure :It was based on actual blood pressure recorded with standard mercury sphygmomanometer. Blood pressure was recorded from the right arm for three times at three minute intervals with the subject in supine position .

Estimation of serum calcium level:Serum calcium estimation was done by Trinder’s method. With the help of photometric technique(15,16) .

Statistical Analysis :

To test whether there was any significant difference in the study variables between the study groups ( normotensives and hypertensives ), Z test was applied. The Z test is a test of significance between mean values of any two groups whose number is more than 30. A Z value of more than 2 is significant at 95% level of significance(23). Correlation coefficient (r)/ Pearson product –moment correlation coefficient test was used for linear relationship between two variables .

Observation:

Table No.1: Age Distribution in study group

Study Group	Age Range (yrs)	Mean (yrs)	Standard Deviation
Normotensives (n=50)	22-75	44.14	13.3057

Hypertensives (n=50)	25-73	42.54	10.2649
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Table 1 indicates that out of 50 normotensive patients studied their age were between 22-75 yrs, while the hypertensive patients had their age between 25-73 years. The mean age of normotensive patients was 44.14 years and the standard deviation worked out to be 13.3057 years. The mean age of hypertensives was 42.54 years with a standard deviation of 10.2649

Table No 2 :Mean Serum Calcium levels in study groups

Study Groups	Mean Serum Calcium mgm%	Standard Deviation (S.D)	Standard Error (S.E)	Mean $\pm$ 2 S.E. 95% Confidence interval (C.I)
Normotensives (n=50)	9.268	0.646	0.0913	9.0854-9.4506
Hypertensives (n=50)	11.232	1.1875	0.1679	10.8962-11.5678

Z=4.2786 , P<0.01 (Highly Significant)

Mean serum calcium of the normotensive group was 9.268mgm% with a standard deviation of 0.6460 and standard error of 0.0913. Mean serum calcium of the hypertensive group was 11.232 with a standard deviation of 1.1875 and standard error of 0.1679. There is an apparent difference in the two observed means. Z test was applied to test this difference. The Z value worked out to be 4.2786, which was statistically significant i.e P<0.01. Thus it is highly unlikely that this difference has occurred by chance. Thus, findings were confirmed by the 95% confidence intervals values in the two groups. In the normotensive group the 95% confidence interval limits were 9.0854-9.4506. 95% confidence intervals limits in the hypertension group were 10.8962-11.5678. As the above limits in the two groups do not overlap, there is a significant difference between mean serum calcium values in the normotensive group viz hypertensive group.

Table .No 3 :Correlation coefficients

	Correlation Coefficient 'r'	P Value
Systolic blood pressure Vs serum calcium	0.55	<0.01
Serum calcium Vs systolic blood pressure	0.53	<0.01
Diastolic blood pressure Vs serum calcium	0.55	<0.01
Serum calcium Vs diastolic blood pressure	0.52	<0.01

In all the four situations, the correlation coefficient were highly significant at degrees of freedom, 48(n-2) (P<0.01). Thus, correlation between the above variables is highly unlikely to have occurred by chance and is highly significant.

Discussion :Cardiac muscle relaxes completely between beats. Under these circumstances, calcium is well below  $10^{-7}$  M, the threshold concentration for contraction. A very different situation is encountered in vascular smooth muscle. Some resting tension (tone) is normally maintained in most resistance vessels. This implies that intracellular calcium, must be constantly maintained above  $10^{-7}$  M because there is no reason to suspect that other factors such as the intracellular magnesium or adenosine 5 triphosphate concentrations are limiting (17). It is generally recognised that most forms of hypertension are associated with an increased peripheral resistance due to maintained abnormal constriction of the small "resistance vessels". Thickening of

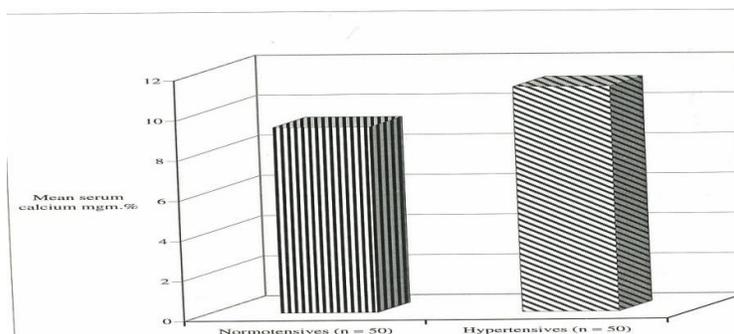
the vessel walls and consequent narrowing of lumina may contribute to the maintenance of chronic hypertensive state.

In our study, a significant high levels of serum calcium were found in hypertensive group as compared to normotensive group ( $P < 0.01$ ). Tobin L.J (18) has stressed the fact that increased vascular smooth muscle tone must play an important role. Hypertension is usually present before the vessel wall changes occur and the blood pressure can return to normal after treatment, even though the vessel walls throughout the body remained thickened. Thus, changes in tone reflect changes in intracellular calcium and that a rise in the mean intracellular calcium may be final common path by which most, if not all, hypertension is produced.

Several lines of evidence support that the level of serum calcium may play a role in the regulation of blood pressure. Theoretically, such an effect may be mediated through a primary change in cardiac output or peripheral vascular resistance or both, or through altered release or action, or both, of pressor substances such as renin and catecholamines.

Shiner P.T et al (19) reported, increased myocardial contractility and bradycardia without significant change in blood pressure during a short infusion in unanaesthetized humans, which elevated serum calcium by 1.5 mg/dl. Studies using local perfusion of the forelimb, kidney or heart in the dog showed that a slight elevation of calcium in the perfusate caused both arteriolar constriction and increased myocardial contractility. But no consistent change in cardiac output has been found during calcium infusions. It seems likely therefore, that an increase in peripheral resistance is the major factor underlying the hypertension induced by hypercalcemia. Many workers have implicated calcium in the pathogenesis of some forms of hypertension. Increase in platelet cytosolic calcium level has been reported in some hypertensives (2). Hypertension has also been found in patients with hyperparathyroidism as well as in hypercalcemic states (18). The mechanism by which hypercalcemia elevates blood pressure, probably involves a direct increase in the contractility of vascular smooth muscle and activation of sympathetic nervous system.

In the present study, the total serum calcium level is studied. The ionized serum calcium level is not studied. It can be assumed, however, that in a population with a normal total serum protein content and a normal serum pH both factors known to influence the relation between total and ionised calcium – ionised calcium will be a constant function of total serum calcium. Our findings might also help to explain the beneficial role of calcium antagonists in the treatment of hypertension (20). It is quite clear from this study that increased serum calcium level is significantly associated with hypertension and so by giving calcium supplement it might worsen the situation (21). Hence, its use in the treatment in hypertensive patients is questionable and needed to be studied in great detail. Though some studies contradict this statement (22).



#### CONCLUSION :

Our study shows a significant correlation between high serum calcium levels and high blood pressure. According to the present study, increased serum calcium leads to hypertension. Hence, serum calcium levels should be estimated in hypertensive patients.

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