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STUDY OF SERUM CALCIUM IN ESSENTIAL HYPERTENSION

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ABSTRACT

Hypertension as a clinical entity is one of the most prevalent cardiovascular disorder with significant morbidity and mortality worldwide. The present study attempts to focus the serum calcium level among essential hypertensives and to correlate Serum calcium status with the blood pressure Sr. calcium was estimated in fifty hypertensives (M= 28, F=22) & fifty healthy controls (M=29; F=21). Efforts were also made to final out an association between body mass index and waist circumference with systolic & diastolic blood pressure. Body mass index was significantly more in those with stage II hypertension. Calcium level was significantly lower among hypertensive when compare to healthy controls. The blood pressure also correlated positively with body mass index and waist circumference whereas negatively correlated with Serum Calcium but no significant correlations found between Vitamin D and hypertension. In view of the significant changes Serum Calcium among Hypertensive population, community must be motivated to consume Calcium rich diet as a form of primary prevention for essential Hypertension.

KEYWORDS: Essential hypertension, serum calcium.

INTRODUCTION

Blood pressure elevated in the arterial circulation is termed as Hypertension (HTN) or high blood pressure. It is invariably a chronic condition of the body resulting in arterial hypertension.[1] The condition puts excessive strain on the heart, putting into strain the cardiac muscles. Hypertension remains the major risk factor for coronary cerebral and peripheral vascular disease. According to WHO, hypertension is the most common cause of preventable deaths in developed countries and increasingly significant in developing countries. It is often associated with additional cardiovascular disease risk factors, and the risk of cardiovascular disease increases with the total burden of risk factors. Essential hypertension comprises more than 90% of hypertension and it is an important risk factor for cardiovascular diseases in elderly.[2]

The overall prevalence of hypertension in the population has been reported between 6% and 32%. Disturbed calcium metabolism may play an important role in the patho-physiology of essential hypertension. Ionized calcium (Ca^{2+}) acts as an intracellular second messenger in excitation-contraction coupling in vascular smooth muscle (VSM) cells. The free intracellular calcium concentration determines the tension in VSM cells, thereby contributing to peripheral vascular resistance (PVR).[3]

Many studies have shown that a correlation exists between serum calcium and blood pressure.

The aim of this study was to assess the levels of serum calcium in patients with primary hypertension and to correlate the serum calcium levels with blood pressure.

MATERIALS AND METHOD

Patients visiting Medicine outpatient and patients admitted in the Medicine wards of, Karnataka Institute of Medical Sciences, Hubli were taken for study after taking written informed consent and approval from institutional ethics committee. Information was collected through a pretested and structured Performa for each patient. Among 100 subjects, 50 were cases (Hypertensive) and 50 were controls (Normotensives). Considering the inclusion and exclusion criteria. Patients with primary hypertension. Patients whose age is above 18 years were included. Patients with renal failure, Pregnancy and Patients with acute diarrhoeal diseases were excluded. All the patients were subjected careful physical examination and biochemical analysis to exclude secondary hypertension. Patient's height and weight were measured. The body mass index was calculated using the formula weight / height ^{2}. Patient's hip and waist circumferences were measured. All the peripheral pulses were checked with special attention to carotid and the femoral to detect evidence for early atherosclerosis. An ocular fundus examination was done to detect hypertensive retinopathy. Patients were

informed to refrain from smoking or drinking tea or coffee for at least thirty minutes before measuring blood pressure. Blood pressure was recorded in sitting position after resting for 10 minutes and 2 readings were recorded and mean of these readings was noted as a final blood pressure. The JNC 7 criteria for establishing hypertension was followed.

Statistical Analysis

The collected data was analyzed statistically using epidemiological Information package – 2002 developed by centers for disease control and prevention, Atlanta. Significance was considered if the 'p' value was below 0.05. 't' test is used to find out whether or not there exist a mean difference between the two groups.

RESULTS AND OBSERVATIONS

Total number of subjects included in this study was 100. Among these 50 were cases (Hypertensive) and 50 were controls (Normotensives).

Analysis of cases and controls with respect to age: The age of the subjects in the study group ranged from forty to sixty years. The mean and standard deviation for the age of the cases and controls were 52.48± 11.89years and 40.38± 6.90 years respectively. The study group and the control group did not differ from each other statistically with reference to age.

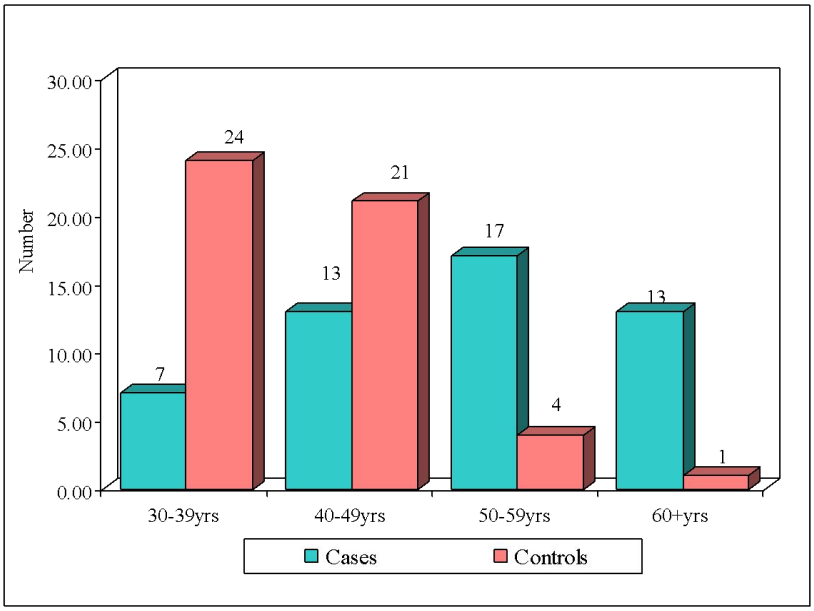
Table 1: Distribution of cases and control in relation to age groups

Age groups	Cases	%	Controls	%	Total	%
30-39yrs	7	14.0	24	48.0	31	31.0
40-49yrs	13	26.0	21	42.0	34	34.0.0
50-59yrs	17	34.0	4	8.0	21	21.0
60+yrs	13	26.0	1	2.0	14	14.0
Total	50	100.0	50	100.0	100	100.0
Mean age	52.48	40.38	49.43			
SD age	11.89	6.90	11.42			

Gender: Among the 50 cases studied, there were 28 males and 22 females. Among the 50 controls, there were 29 males and 21 females.

Table 2: Distribution of cases and control in relation to sex.

Sex	Cases	%	Controls	%	Total	%
Male	28	56.0	29	58.0	57	57.0
Female	22	44.0	21	42.0	43	43.0
Total	50	100.0	50	100.0	100	100.0

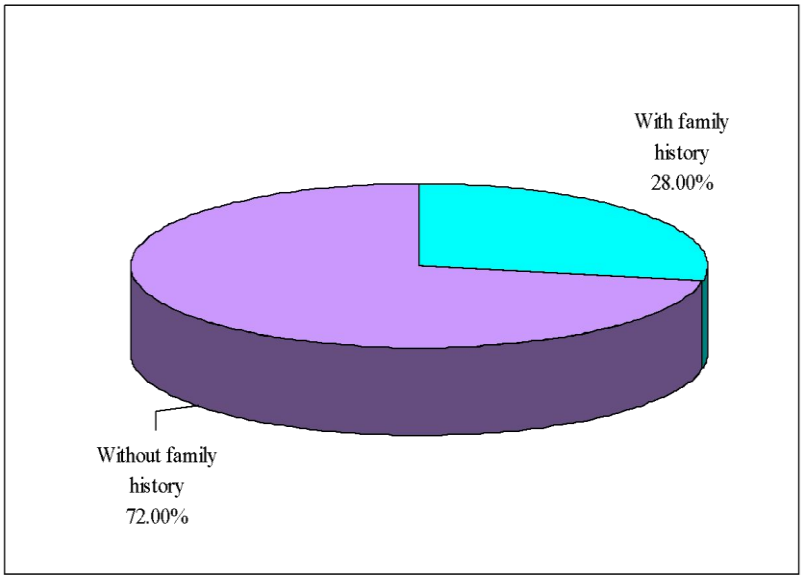


Graph 1: Distribution of respondents by age group and sex

Among 50 cases there were 14 patients (28%) with positive family history.

Table 3: Distribution of cases by family history

Family history	No of cases	% of cases
With family history	14	28.0
Without family history	36	72.0
Total	50	100.0

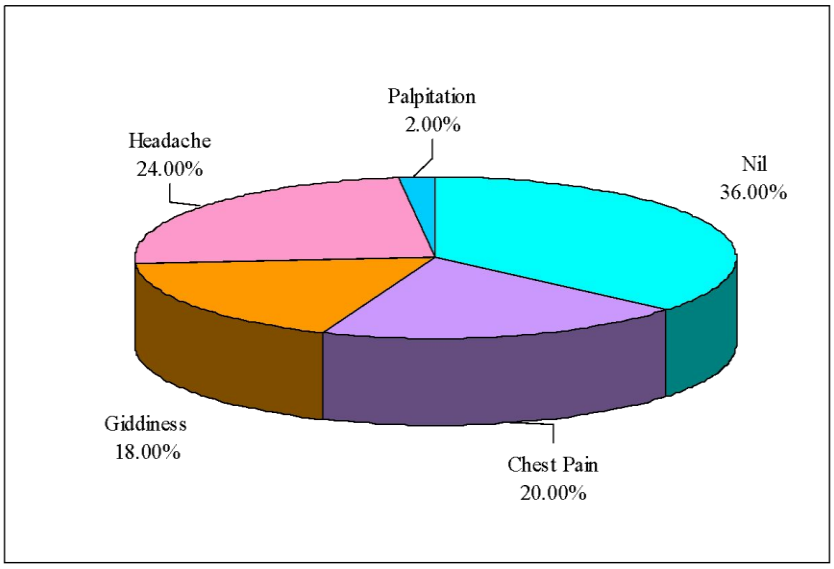


Graph 3: Distribution of cases by family history

Among cases, there were 18 patients who did not have any symptoms, 10 patients with chest pain, 9 with giddiness, 12 with palpitation and 1 patient with palpitation were taken up for study.

Table 4: Distribution of cases by symptoms

Symptoms	No of cases	% of cases
Nil	18	36.0
Chest Pain	10	20.0
Giddiness	9	18.0
Headache	12	24.0
Palpitation	1	2.0
Total	50	100.0



Graph 4: Distribution of cases by symptoms

As we can see from the table below that headache was the most common presenting symptom among cases. (12 cases).

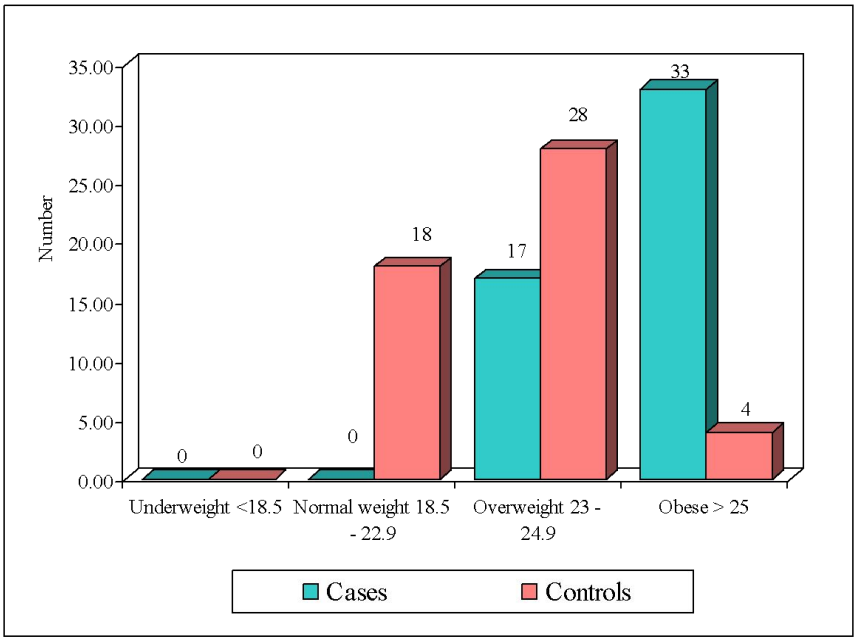
Table 5: Analysis of presenting symptoms in male and females (cases)

Symptoms	Male	%	Female	%	Total
Chest Pain	5	50.0	5	50.0	10
Giddiness	5	55.6	4	44.4	9
Headache	7	58.3	5	41.7	12
Palpitation	1	100.0	0	0.0	1

Among cases 33 (66%) were found out to be in obese group compared to 4 (8%) in controls.

Table 6: Distribution of cases and controls with respect to Body Mass Index (BMI)

BMI	Cases	%	Controls	%	Total
Underweight <18.5	0	0.0	0	0.0	0
Normal weight 18.5 – 22.9	0	0.0	18	36.0	18
Overweight 23 – 24.9	17	34.0	28	56.0	45
Obese > 25	33	66.0	4	8.0	37
Total	50	100.0	50	100.0	100



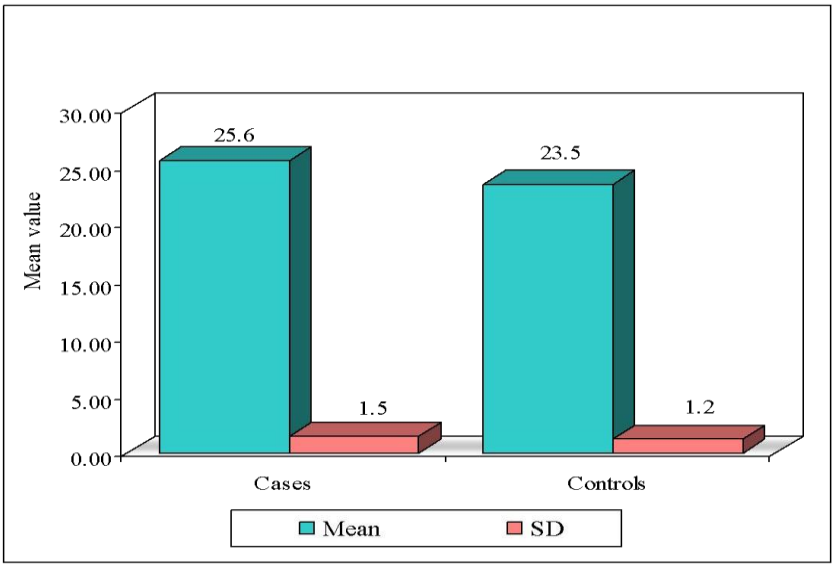
Graph 6: Distribution of cases and controls with respect to Body Mass Index (BMI)

Significant difference was found in mean BMI of cases (25.5 with S.D of 1.5) compared to mean BMI of controls (23.5 with S.D of 1.20). Details given below shows that BMI of cases is significantly higher in cases than in controls.

Table 7: Comparison of cases and controls with BMI scores by 't' test

Group	N	Mean	SD	t-value	p-value
Cases	50	25.6060	1.4613	7.6561	0.0000*
Controls	50	23.5400	1.2271		

*p<0.05



Graph 7: Comparison of cases and controls with respect to Body Mass Index(BMI)

Among cases males had the mean BMI of 25.87±1.6 and in females BMI was 25.27±1.21 which was significantly higher than controls where in males, mean BMI was 23.54±1.2 and in females it was 23.54±1.29.

Table 8: Mean BMI of cases and controls with respect to gender

Gender	Cases		Controls		Total	
	Mean	SD	Mean	SD	Mean	SD
Male	25.87	1.61	23.54	1.20	24.68	1.83
Female	25.27	1.21	23.54	1.29	24.43	1.51
Total	25.61	1.46	23.54	1.23	24.57	1.70

Among 24 grade 1 hypertensives 13 were obese and among grade 2 hypertensives 20 were obese and cases with normal BMI were not found to be having hypertension. This shows that hypertension was more seen in obese cases than in normal cases.

Table 9: BMI with respect to grades in cases

BMI	Grade 1	%	Grade 2	%	Total
Underweight <18.5	0	0.00	0	0.00	0
Normal weight 18.5 – 22.9	0	0.00	0	0.00	0
Overweight 23 – 24.9	11	64.7	6	35.3	17
Obese > 25	13	39.4	20	60.6	33
Total	24	48.0	26	52.0	50

The following table clearly shows that SBP in cases (156.7±7.7 mm Hg) was significantly higher than in controls (112.9±2.03 mm Hg). And DBP was also high in cases (89.8±6.3 mmHg) than in controls (75.3± 4.9 mm Hg).

Table 10: Comparison of cases and controls with SBP and DBP scores by t test

Variable	Group	n	Mean	SD	t-value	p-value
SBP	Cases	50	156.7200	7.7382	38.6787	0.0000*
	Controls	50	112.9600	2.0300		
DBP	Cases	50	89.8800	6.3298	12.8038	0.0000*
	Controls	50	75.3600	4.9229		

*p<0.05

Table 11: Distribution of cases with respect to grading of hypertension

Grades	No of cases	% of cases
Grade 1	24	48.0
Grade 2	26	52.0
Total	50	100.00

Calcium was significantly lower in Hypertensives than in normotensives with p value of 0.0000 which is depicted in following table.

Table 12: Comparison of cases and control with respect to Serum calcium

Group	n	Mean	SD	t-value	p-value
Cases	50	8.0020	0.6520	-8.7814	0.0000*
Controls	50	9.0282	0.5077		

Table 13: Comparison of cases and control with respect to albumin, Albumin D and Creatinine (mg/dl) by t test

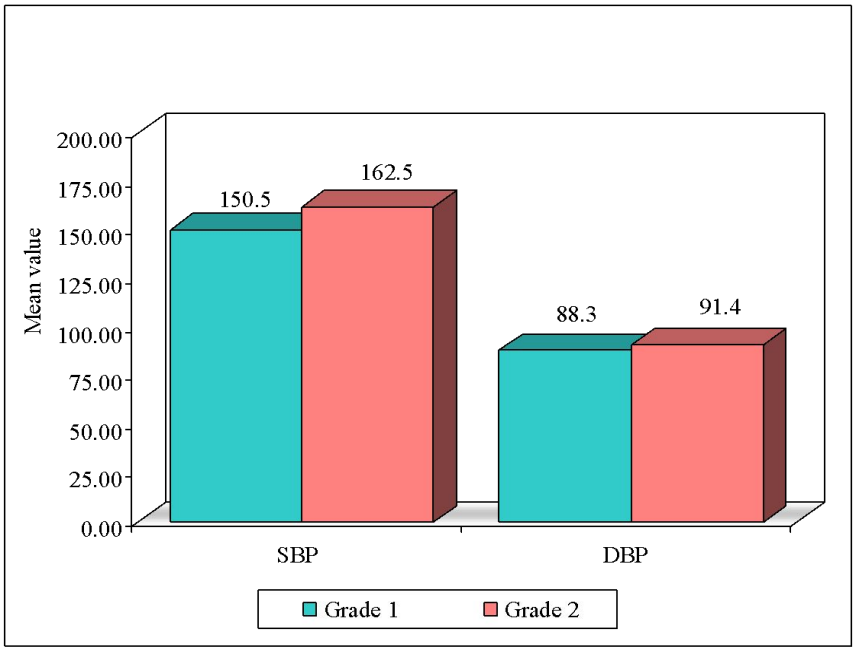
Variable	Group	N	Mean	SD	t-value **-0.6435**	p-value **0.5214**
Albumin (g/dl)	Cases	50	3.8680	0.4582		
	Controls	50	3.9158	0.2567		
Vitamin D (ng/ml)	Cases	50	17.5992	6.5543	-1.4890	0.1397
	ContrOLol s	50	25.1900	3.7565		
Creatinine (mg/dl)	Cases	50	3.2040	13.9721	1.1828	0.2398
	Controls	50	0.8660	0.3852		

Among grade 1 hypertensives, mean SBP was 150.5±3.6 mm Hg and in grade 2 it was 162.4±5.8 mmHg. And DBP among grade 1 hypertensives was 88.2±5.4 mm Hg and in grade 2 it was 91.3± 6.7 mm Hg.

Table 14: Comparison of grade 1 and grade 2 with SBP and DBP scores by t test

Variable	Grade	n	Mean	SD	t-value	p-value
SBP	Grade 1	24	150.5000	3.6475	-8.6389	0.0000*
	Grade 2	26	162.4615	5.8050		
DBP	Grade 1	24	88.2500	5.4792	-1.7882	0.0800
	Grade 2	26	91.3846	6.7828		

*p<0.05



Graph 14: Comparison of grade 1 and grade 2 with SBP and DBP scores by t test

Table 15: Comparison of male and females with respect to Serum calcium, albumin, vitamin D and Creatinine (mg/dl) –overall samples

Variable	Sex	n	Mean	SD	t-value	p-value
Serum calcium (mg/dl)	Male	57	8.5861	0.7635	1.0531	0.2949
	Female	43	8.4209	0.7939		
Albumin (g/dl)	Male	57	3.9332	0.3513	1.2870	0.2011
	Female	43	3.8372	0.3916		
Vitamin D (ng/ml)	Male	57	18.1382	5.3541	-0.5472	0.5855
	Female	43	18.7344	5.4460		
Creatinine (mg/dl)	Male	57	2.7211	13.1223	0.7961	0.4279
	Female	43	1.1256	0.3274		

From following it is evident that serum calcium and vitamin D is slightly lower in females.

Table 16: Comparison of male and females with respect to Serum calcium, albumin, vitamin D and Creatinine (mg/dl) –cases samples

Variable	Sex	n	Mean	SD	t-value	p-value
Serum calcium (mg/dl)	Male	28	8.0500	0.6642	0.5833	0.5624
	Female	22	7.9409	0.6464		
Albumin (g/dl)	Male	28	3.9250	0.4195	0.9921	0.3261
	Female	22	3.7955	0.5038		
Vitamin D (ng/ml)	Male	28	18.2064	6.7539	0.7356	0.4656
	Female	22	16.8264	6.3618		
Creatinine (mg/dl)	Male	28	4.7500	18.6704	0.8806	0.3829
	Female	22	1.2364	0.3048		

Table 17: Comparison of male and females with respect to Serum calcium, albumin, vitamin D and Creatinine (mg/dl) in controls

Variable	Sex	n	Mean	SD	t-value	p-value
Serum calcium (mg/dl)	Male	29	9.1038	0.4190	1.2442	0.2195
	Female	21	8.9238	0.6049		
Albumin (g/dl)	Male	29	3.9410	0.2773	0.8139	0.4197
	Female	21	3.8810	0.2272		
Vitamin D (ng/ml)	Male	29	18.0724	3.6522	-2.6153	0.0119*
	Female	21	20.7333	3.4039		
Creatinine (mg/dl)	Male	29	0.7621	0.4021	-2.3421	0.0234*

Table 18: Distribution of cases with respect to systemic examination

Systemic examination	No of cases	% of cases
B/L creps	8	16.0
Nil	42	84.0
Total	50	100.0

Table 19: Distribution of cases with respect to fundus

Fundus	No of cases	% of cases
Grade 1	7	14.0
Grade 2	4	8.0
Nil	39	78.00
Total	50	100.0

Table 20-: Distribution of cases with respect to ECG

ECG	No of cases	% of cases
LVH	21	42.0
No LVH	29	58.0
Total	50	100.0

Distribution of cases and controls with respect to cardio vascular risk factors:

Table 21: Risk factors among cases and controls

	Smoking	Alcohol	Both	Nil
Cases	13	5	5	27
Controls	6	4	3	37

From the above table it is clear that smokers and alcoholics have more chances of developing hypertension. But since alcoholism and smoking were noticed mostly among men only in this part of the country, statistical analysis was not attempted for these risk factors.

In the following table it is shown that, RBS was significantly high in cases (144.3±27.04 mg/dl) compared to controls (85.7± 11.6 m/dl).

Table 22: Comparison of cases and controls with respect to RBS (mg/dl) scores by t test

Group	Mean	SD	t-value	P-value
Cases	144.3600	27.0417	14.0841	0.0000*
Control	85.7200	11.6410		

In this table we can see that hypertensives (cases) have more Waist Circuference 93.2± 6.9 cms than controls, 77.72±9.9 cms. The difference is significant.

Table 23: Comparison of cases and controls with respect to WC (cms) scores by t test

Group	Mean	SD	t-value	P-value
Cases	93.2400	6.9622	9.0176	0.0000*
Control	77.7200	9.9817		

WHR was significantly high (1.004± 0.19) in cases than in controls who had WHR of 0.91±0.08.

Tabel 24: Comparison of cases and controls with respect to WHR scores by t test

Group	Mean	SD	t-value	P-value
Cases	1.0004	0.1098	4.3799	0.0000*
Control	0.9140	0.0860		

DISCUSSION

Hypertension is one of the leading causes of death and disability among all over the world. Hypertension is the most common form of cardiovascular disease and is present nearly 25% of adults and increases in prevalence with age. Approximately 54% of all strokes and 47% of all IHDs are attributed to hypertension.

In our study the mean serum calcium was estimated in the control and study groups. 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. In this study 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. 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 Touyz RH.[4] et al conducted study in Johannesburg, South Africa stated that the heterogeneous status of magnesium and calcium metabolism in hypertensive population may be related to the plasma renin activity (PRA). PRA and ionized calcium were significantly lower in black hypertensive as compared with the white hypertensive group (1.99±0.3 vs 5.6±1.02ng) ml/h for RA; 1.28±0.07 vs 1.42±0.01mmol/l for ionized calcium black hypertensives as compared with white hypertensives group (p<0.05). Ionized calcium was significantly increased (p<0.05) in white

hypertensive patient as compared with the normotensive control (1.42±0.01 vs1.29±0.04 mmol/l).

In a study conducted by Sudhakar et al in 2004[5] which is said to be the first study in Indian population, Serum calcium levels were measured in 117 subjects with essential hypertension and 77 first degree relatives. The results showed that serum calcium levels were significantly ($p<0.01$) decreased in both males and females with essential hypertension and their first-degree relatives when compared with the normotensive controls.

Another study conducted by Aaron Folsum et al (1986) where Concentrations of serum total calcium and serum calcium fractions were compared Between 28 hypertensive subjects and 28 race sex age matched Normotensive controls Hypertensive subjects had lower mean serum levels of ultrafilterable calcium (0.32 mg/dl; $p = 0.01$), ionized calcium (0.07mg/dl; $p = 0.09$) and complexed calcium (0.23mg/dl; $p = 0.04$) and higher levels of protein bound calcium (+ 0.36 mg/dl; $p = 0.07$). These findings add to the evidence that essential hypertension is associated with perturbations in calcium metabolism.

In Lind L study a pattern of negative calcium balanced with lowered levels of serum ionized calcium (Ca2+) increased urinary excretion of calcium has been reported in hypertensive men. It was found that salt sensitivity and was related to indexes of mineral metabolism. They conclusion, low levels and plasma ionized calcium and serum calcium where mainly support in hypertensive subjects with a low sensitivity to salt. The findings support the view that calcium metabolism is related to the regulation of BP.[6]

With the objective of effect of supplemental calcium on blood pressure, Heiner et al in 1996 conducted a study[7] in which investigators randomized people to calcium supplementation or placebo and measured blood pressure for at least 2 weeks. Fifty-six articles met the inclusion criteria and 33 were eligible for analysis, involving a total of 2412 patients. The study concluded that calcium supplementation may lead to a small reduction in systolic but not diastolic blood pressure With respect to blood pressure, the clinical trial findings when calcium intake is increased are conflicting, but there is a trend toward a positive effect with calcium supplements of 1.0 g to 1.55 g per day.

Based on the data and experience available, calcium supplementation on increased dietary intake of calcium rich foods would be recommended for treatment of hypertension nonspecifically for prevention of hypertension. Some other studies are not supporting calcium therapy for treatment and prevention of hypertension, still calcium can be used because of the other benefits like prevention of osteoporosis. Therefore, a recommendation that calcium intake be maintained at 1.0 to 1.5gm per day through dietary intake on supplements on both can be made for adolescents and adults. This level should be sufficient to achieve a blood pressure lowering response in those who are responsive.

A DASH study (Dietary Approaches to Stop Hypertension) was conducted b Frank M Sacks, et al in 1999 concluded that The DASH diet may offer an alternative drug therapy in hypertensive and as a population approach, may prevent hypertension Participants were 459 adults with untreated systolic blood pressure 160 mmHg and diastolic blood pressure 80 mmHg. After a 3week run in on a control diet typical of Americans, they were randomized to 8 weeks receiving either the control diet, or a diet rich in fruits and vegetables, o the DASH diet. The participants were given all of their food to eat, and body weight and sodium intake were held constant Blood pressure was measured at the clinic and by 24h ambulatory monitoring. The DASH diet lowered systolic blood pressure significantly in the total group by 533.0 mmHg, in African Americans by 6.9/3.7 mmHg, i n Caucasians by 3.3/2.4mmHg in h ypertensives by 11.6/5.3 mmHg and in nonhypertensives.[8]

In our study the mean BMI among the study group was 25.60± 1.46 and among the control group was 23.54 ± 1.22. The 'p' value was .00000. This shows that overweight and obesity also plays a role in the development of essential hypertension.

This was supported by a study conducted by Stamler.[9] They showed that the hypertension is about six times more common in obese than it is in lean subjects. The present study concurs with above observation. Overall, a 10kg difference in body weight was associated on average with a 3.0 mmHg difference in systolic and a 2.2 mmHg difference in diastolic pressure. In further analyses across centres, median body mass index was related significantly to median systolic blood pressure, median diastolic pressure and the prevalence of hypertension in both men and women. Body mass index was related to the slopes of systolic and diastolic blood pressure with age in women, but not in men.[10]

In our study, it was evident that, RBS was significantly high, in the range of Impaired Glucose Tolerance (IGT), in cases (144.3±27.04 mg/dl) compared to controls (85.7± 11.6 m/dl). Zhonghua Xin Xue Guan Bing Za Zhi et al in 2009,[11] studied the incidence of impaired glucose tolerance in hospitalized patients with essential hypertension without diabetes mellitus history and concluded that incidence of newly diagnosed disturbed glucometabolic status is common among patients with essential hypertension without DM history.

In our study we could see that hypertensives (cases) have more Waist Circuference 93.2± 6.9 cms than controls, 77.72±9.9 cms. And the difference was significant. And Also WHR was significantly high (1.004± 0.19) in cases than in controls who had WHR of 0.91±0.08. This clearly indicates that WC and WHR are markers for hypertension. In a study in 2007 by R. Gupta et al, it was concluded that there is a continuous positive relationship of all markers of obesity (bodymass index, waist size and waist hip ratio) with major coronary risk factorshypertension, diabetes and metabolic syndrome.[12]

In our study, Vitamin D in hypertensives was 17.59±6.55 ng/ml compared to Nonhypertensives where it was 25.19±3.75 ng/ml which was not significant ('p' was 0.1397). However Vitamin D might have been negatively related to hypertension. Observational studies suggest that low 25(OH)D levels are associated with a higher risk of hypertension. However, findings from randomized trials of vitamin D supplementation to lower blood pressure are inconsistent, possibly stemming from variability in study population, sample size, vitamin D dose and duration.[13]

The present study attempts to focus the serum calcium level among essential hypertensives who were free from any other illness (or) under any medication and to 104 correlate Sr. calcium status with the blood pressure.

CONCLUSION

The following conclusions were derived from our study,

1. Serum Calcium was significantly less among Hypertensives and correlated negatively with blood pressure.
2. In view of the significant changes Serum Calcium among Hypertensive population, community must be motivated to consume Calcium rich diet as a form of primary prevention for essential Hypertension.

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