

A STUDY OF SERUM CALCIUM AND MAGNESIUM LEVELS IN ESSENTIAL HYPERTENSION

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ABSTRACT

Aim: To study the serum levels of calcium and magnesium in patients of essential hypertension and their correlation with essential hypertension.

Material and Method: The present study was a cross sectional study which was carried out at L. N. Medical College & Associated J. K. Hospital Bhopal in a span of 1 year. 50 hypertensives and 50 normotensive subjects were selected from medicine O.P.D, and their serum calcium and magnesium levels were estimated.

Statistical Analysis- by Z- test.

Observation- Serum magnesium level was significantly higher in elderly hypertensive's than younger hypertensives. Serum magnesium levels was low in female hypertensives as compared to female control group.($p < 0.02$) Significantly lower mean serum calcium was found in hypertensive than normotensive controls in age group < 59 , while in age group ≥ 60 years mean serum calcium was found to be higher in hypertensive than normotensive controls. Low serum calcium level was found in male hypertensive than female hypertensive patients.

Conclusion: Serum magnesium was significantly higher in elderly hypertensive then younger hypertensives. Serum calcium level of hypertensives and normotensives of different age groups was found to be variable. Mean serum calcium level in the age group ≥ 60 years was significantly higher in hypertensives that normotensives while in the age group ≤ 59 years mean, serum calcium was significantly lower in hypertensives compared to normotensives (P value < 0.02 that is significant).

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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. Prolonged cases of hypertension result in the remodeling of the cardiac architecture. Blood pressure always is measured in form of systolic or the upper side and the diastolic or the lower side of arterial pressure. Systolic pressure arises from the contraction of the cardiac muscle whereas the resting cardiac tissue originates the diastolic pressure.

Blood pressure always works as a two edged sword, too low or too high, the high blood pressure better known as hypertension can be forked into essential hypertension,

which does not have a relevant organic etiology or cause leading to the same. The other category is Secondary hypertension which invariably can be blamed due to certain obvious organic causes, like renal, endocrine, neural, cardiovascular. Epidemiologically, 90–95% of cases are categorized under "primary hypertension,^[2] the rest of the patients or cases fall under the secondary hypertension.

According to W.H.O expert community & 7th report of joint national committee on detection, evaluation & treatment of high blood pressure, hypertension is defined as a record of systolic blood pressure Blood more than 140mmHg & diastolic Blood Pressure more then 90mmHg ^[1].

Almost 20 in 100 people all across the globe suffer from hypertension. The severity of hypertension increases with

advanced age. Worldwide, approximately 1 billion people have hypertension, contributing to more than 7.1 million deaths per year.^[3] National health surveys in various countries have shown a high prevalence of poor control of hypertension.^[4]

Essential hypertension was so named by Otto Frank^[5], the increasing average blood pressure with age was erroneously believed by Frank to be essential for better perfusion through progressively sclerosing aging arteries but the actual data have shown that it increases morbidity & mortality so the term "Hypertonie essentielle" was replaced by idiopathic hypertension. Primary (essential) hypertension is the most common form of hypertension, accounting for 90–95% of all cases of hypertension. In almost all contemporary societies, blood pressure rises with aging and the risk of becoming hypertensive in later life is considerable. Hypertension results from a complex interaction of genes and environmental factors. Numerous common genetic variants with small effects on blood pressure have been identified as well as some rare genetic variants with large effects on blood pressure but the genetic basis of hypertension is still poorly understood. Several environmental factors influence blood pressure. Lifestyle factors that lower blood pressure include reduced dietary salt intake, increased consumption of fruits and low fat products (Dietary Approaches to Stop Hypertension (DASH diet)), exercise, weight loss and reduced alcohol intake. Stress appears to play a minor role with specific relaxation techniques not supported by the evidence. The possible role of other factors such as caffeine consumption, and vitamin D deficiency are less clear cut. Epidemiological data suggests a putative role for calcium and magnesium balance in blood pressure control, it may be important with regards to the more widely accepted although debated hypothesis relating sodium and potassium balance to hypertension. The role of calcium and magnesium in the pathogenesis of essential hypertension has recently received increasing attention.

Magnesium is a biologically essential cation, which has recently received considerable attention in clinical medicine, especially with regard to the role of its depletion in cardiovascular pathophysiology^[2]. Magnesium is the fourth most abundant cation in the body and the second most abundant intra cellular cation next to potassium.^[6] Some authors have shown recently an increasing interest in the effects of calcium and magnesium on blood pressure.^[7] Many reports have appeared in recent year discussing association between serum magnesium levels and hypertension. Accumulating evidence implicates a role of serum calcium and magnesium and pathophysiology of essential hypertension.^[8,9] High blood pressure has been linked to hypomagnesaemia. An inverse relationship between magnesium and blood pressure is apparent according to various study results^[10]. Some data even support a role for magnesium in the pathophysiology of essential hypertension ^[11].

Calcium plays an important role in the pathophysiology of essential hypertension. Alterations in the intracellular free Calcium regulation as well as disturbances of extracellular calcium homeostasis have been observed in patients with essential hypertension. Abnormalities of calcium metabolism

in cases of essential hypertension have been described by many researchers in recent past^[12,13]. Although some other researchers^[14] disagree with the above presumption. The calcium ion plays a major role as an intracellular second messenger in excitation contraction coupling in cardiac and smooth muscle cells. The free intracellular calcium concentration thus, determines the tension in vascular smooth muscle cells thereby resulting in peripheral vascular resistance. Abnormal Calcium metabolism has been projected as one of the important causative factor for essential hypertension by many workers. It has been hypothesized that a generalized defect of calcium regulation might be of importance in the pathogenesis of essential hypertension.

Increased levels of extracellular magnesium inhibit calcium influx. Conversely, reduced extracellular magnesium activates calcium influx via calcium channels. Low intracellular magnesium concentrations stimulate inositol-trisphosphate-(IP₃-) mediated mobilization of intracellular calcium and reduce Ca²⁺-ATPase activity. Thus, calcium efflux and sarcoplasmic reticular calcium reuptake are reduced, leading to cytosolic accumulation of calcium and increased intracellular calcium concentration, which is a crucial factor for vasoconstriction. Increased intracellular levels of magnesium result in decreased intracellular free calcium concentration promoting vasodilation. The action of magnesium as a calcium channel blocker may also help to reduce the release of calcium and thus reducing vascular resistance. In addition, magnesium also activates the Na-K ATPase pump that controls the balance of these minerals contributing to the homeostasis of electrolytes in cells ^[15].

Due to conflicting reports on the role of serum calcium and magnesium in essential hypertension, the present study is planned to estimate the serum calcium and magnesium levels in patients with essential hypertension and compare it with normal individuals.

AIMS AND OBJECTIVES

1. To study the level of serum calcium and magnesium in essential hypertension.
2. To study whether any correlation exists between levels of serum calcium and magnesium with essential hypertension.

MATERIAL & METHODS

The present study was carried out in the medicine department and central laboratory of L.N Medical College & associated J. K. Hospital, Bhopal from March 2011 to february 2012 in a span of 1 year. An ethical clearance from the institution and an informed consent from the study subjects were duly obtained.

Total 50 newly diagnosed hypertensive cases were studied of which 28 were males and 22 were females. 50, age and sex matched controls were also selected for this study.

Exclusion criteria:

1. Known hypertensive patients who were taking antihypertensive drugs.
2. Patients with Secondary hypertension.
3. Hypertensive subjects with obvious cardiovascular (IHD, LVH, Cardiomyopathy), neurological(Stroke) , renal complications

(Proteinuria, elevated serum creatinine > 1.5 mg%), and hypertensive retinopathy..

The normotensive control group was selected amongst normal healthy subjects of both sexes.

MEASUREMENT OF 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^[1].

After selection, subject's detailed history & examination was done. Study subject's blood & urine samples were collected and following laboratory tests were done-

1. Hematocrit
2. Urine for albumin and microscopic examination
3. Blood urea,serum creatinine
4. Serum sodium,potassium,calcium and magnesium
5. Fasting blood sugar

All pt's ECG were done to rule out left ventricular hypertrophy.

Methods of estimation of serum calcium & magnesium

5 cc of blood was obtained by venepuncture of the antecubital vein without stasis in a dry sterile glass bottle. The sample was immediately centrifuged at 3000 rpm for 20 minutes & clear supernatant serum pipetted out.

The serum calcium & magnesium ions were estimated by the method of semi automated photometric analysis by using model RA-50. The working of photometer is based on Beer & combert's law. calcium was measured by cresolphthalein complexone method and magnesium was measured by calmagite method.

Principle of Cresolphthalein method

Calcium, in an alkaline medium reacts with cresolphthalein complexone to form an intense chromospheres which absorbs light at 575mm (570-580) magnesium and iron are excluded from the reaction by complexing with 8 hydroxy quinoline.

Principle of Calmagite method

Magnesium ion reacts in an alkaline medium with the metalochrome dye calmagite to form a chromosphere which absorbs light at 520mm. calcium is excluded by complexing with EDTA.

Normal value of serum calcium – 8.50-10.5 mg/dl

Normal value of serum magnesium- 1.70-2.70mg/dl

STATISTICAL ANALYSIS:

Z- test was used as the statistical tool in the present study.

OBSERVATIONS

The study comprised of 50 cases and 50 controls . 50 cases consists of 28 (56%) male and 22 (44%) females. 29 persons were of 59 or less age group and 21 persons were of 60 years or more.

50, age and sex matched controls were also selected for this study.

Blood pressure- Blood was measured in both controls and patients. Mean systolic blood pressure of hypertensive subjects was 156.32±15.37mmHg and that of control was 118.53±10.56 ,Mean diastolic blood pressure in hypertensive subjects was 99.44±7.63mmHg and that of control was 79.93±4.45 mmHg .

Serum magnesium and serum calcium was estimated in all 50 hypertensive and 50 normotensive control.

Mean serum calcium was 9.2792±1.094mg/dl in hypertensives and 9.5743±0.6834 mg/dl in control group.

Table 1- Showing serum calcium in hypertensives and normotensives.

SERUM CALCIUM IN HYPERTENSIVE AND NORMOTENSIVE PATIENTS	HYPERTENSIVES		CONTROL	
	No.	Percentage	No	Percentage
8.5-9.59	19	38%	22	44%
9.60-10.49	11	22%	15	30%
>10.50	8	16%	9	18%
<8.49	12	24%	4	8%

19 hypertensive (38%) showed level between 8.50-9.59mg/dl and 11 hypertensive (22%) showed level between 9.60-10.49mg/dl. 8 hypertensive (16%) had serum calcium > 10.50mg/dl and 12 hypertensive (24%) showed level < 8.49mg/dl. (Table 1)

22 controls (44%) showed serum calcium level between 8.50-9.59mg/dl. 15 (30%) control showed level between 9.60-10.49mg/dl, 9(18%) control had serum calcium > 10.50mg/dl and 4(8%) had serum calcium < 8.49 mg/dl (table 1)

In the hypertensive group the range of serum calcium was 6.76-11.60 mg/dl, while in the control group it was between 8.20-10.51mg/dl.

Table 2- Showing serum magnesium level in cases and control

SERUM MAGENESIUM IN CASES AND CONTROL	HYPERTENSIVES		CONTROL	
	No.	Percentage	No	Percentage
1.20-2.19	36	72%	43	86%
2.20-2.64	13	26%	7	14%
>2.65	1	2%	-	-

Serum magnesium was estimated in both the hypertensive and control group. In the control group the range of serum magnesium was between 1.20-2.50mg/dl, while in hypertensive group it was between group 1.20-2.65mg/dl. Mean serum magnesium was 1.836±0.471 mg/dl in hypertensive groups and 1.846±0.2954mg/dl in control group. 36 hypertensive patient (72%) showed level between 1.20-2.19mg/dl and 13 (26%) hypertensive showed level between 2.20-2.64mg/dl and 1 hypertensive (2%) showed level >2.65mg/dl. 43 (86%) normotensive (control) showed serum magnesium between 1.20-2.19 mg/dl, 7 control (14%) showed level between 2.20-2.64 mg/dl. (Table 2).

Table 3- Showing mean serum magnesium value in case and control group

ITEM	HYPERTENSIVE		CONTROL	
	Mean	S.D.	Mean	S.D.
Serum Mg (mg/dl)	1.836	0.471	1.846	0.2954

Mean age in years in hypertensive group irrespective of sex was 57.42 years with standard deviation of 11.89 and in control it was 58.50 years with standard deviation of 10.32. Thus mean age in both groups was more or less equal.

Mean serum magnesium level in patients is 1.836 mg/dl with standard deviation of 0.471mg/dl, while in control group it was 1.846mg/dl with standard deviation of 0.2954mg/dl thus difference is not significant, P value = 0.91 (table 3)

Table 4- Showing mean serum Mg⁺⁺ levels in males and female of case and control group.

ITEM	HYPERTENSIVE				CONTROL			
	Male		Female		Male		Female	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Serum								

Mg ⁺⁺ level In Mg%	1.74	0.47	1.93	0.44	1.91	0.28	1.70	0.24
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Serum magnesium was higher in elderly hypertensive than younger patients (P < 0.02).

Mean difference in serum magnesium level between male and female patient, male hypertensive and male control subjects was insignificant, P value is >0.02

Mean difference in serum magnesium between female hypertensive and female control subjects was significant P value <0.02 (table 4)

Table 5- Showing mean serum magnesium level in mild and moderate to severe hypertension and control.

ITEM	MILD HYPERTENSION	MODERATE TO SEVERE HYPERTENSION	CONTROL
Mean serum Magnesium In mg%	1.7880	1.8879	1.8460

Mean difference in serum magnesium in between mild and moderate to severe hypertension was not significant, P value is >0.02.

TABLE 6: Showing mean serum calcium levels with standard deviation in hypertensive and control groups.

ITEM	HYPERTENSION MEAN	HYPERTENSION S.D	CONTROL MEAN	CONTROL S.D
Serum Calcium in mg%	9.2792	0.194	9.5743	0.6834

Mean serum calcium level in patients is 9.2792±0.194mg/dl while in control group it was 9.5743±0.683mg/dl thus difference is not significant with P value is >0.02 .

There was difference between the means of serum calcium of two age groups, serum calcium being higher in elderly hypertensive than younger patients, P value is <0.02 that was significant. Difference between the mean of serum calcium of patients and control subjects of age group <59 years was also significant (P value <0.02). Difference between the means of serum calcium of patients and control group of age >60 years is significant with P value <0.02, that is significant higher values of serum calcium found in cases than control group (Table 7)

Table 7- showing Ca⁺⁺ levels in case and controls according to age group.

ITEM	HYPERTENSIVES				CONTROLS			
	≤59 Years		≥60 Years		≤59 Years		≥60 Years	
Serum Ca ⁺⁺ level(mg%)	Mea n	S.D.	Me an	S.D.	Mea n	S.D.	Mea n	S.D.
		9.0348	1.1681	9.641	0.7409	9.6890	0.6693	9.4191

Mean difference in serum calcium level between male and female patients were significant. Serum calcium was lower in male hypertensive subjects than female hypertensives. (P value is <0.02)

Table 8- Showing mean serum Calcium level in male and female case and control group.

ITEM	HYPERTENSIVE				CONTROL			
	Male		Female		Male		Female	
Serum Ca ⁺⁺ (mg %)	Mean	S.D.	Mea n	S.D.	Mean	S.D.	Mean	S.D.
		9.0196	1.061	9.610	1.097	9.6027	0.6020	9.5391

Mean difference of serum calcium between male hypertensive and male controls were significant with lower value in male hypertensives but was not true for females.(Table 8)

Table 9- Showing mean serum calcium level in mild and moderate to severe hypertension and control subjects.

ITEM	HYPERTENSIVES		CONTROL S
	Mild Hypertension	Moderate to severe H.T.	
Mean serum Calcium (mg%)	9.3565	9.1037	9.5862

Mean difference in serum calcium between mild and moderate to severe hypertensive was not significant, but the difference between moderate to severe hypertensive and control group was significant, lower value was found in moderate to severe hypertensive group(P value is <0.02)(Table 9) .

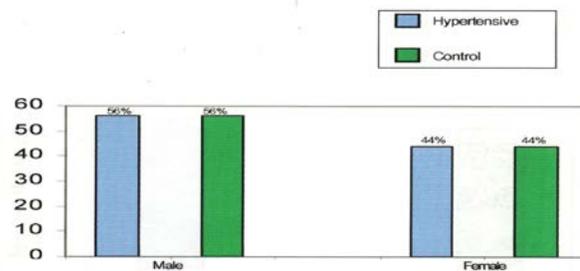


Fig. 1 : Showing Sex incidence in study group.

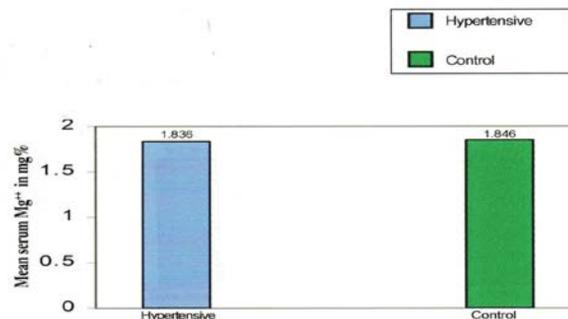


Fig. 2 : Showing mean serum Mg⁺⁺ level.

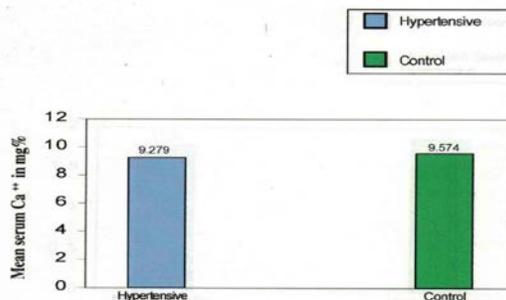


Fig. 3 : Showing mean serum Ca⁺⁺ level.

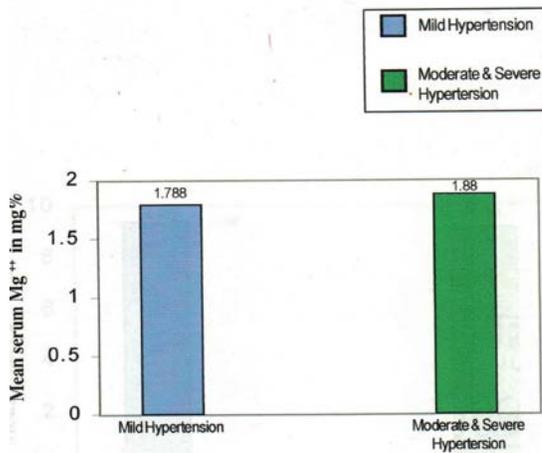


Fig. 4 : Showing mean serum Mg⁺⁺ level in mild & moderate to severe hypertensives.

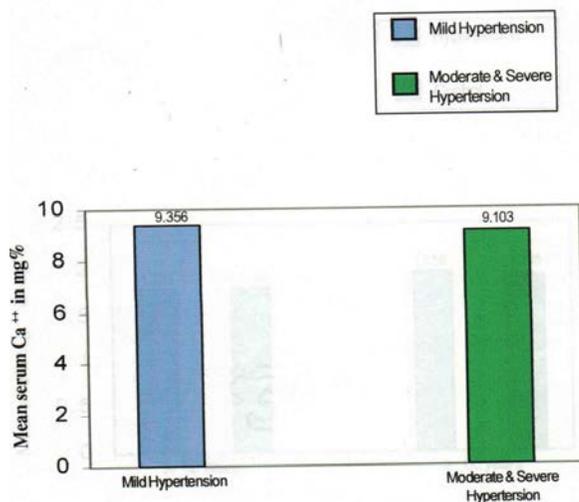


Fig. 5 : Showing mean serum Ca⁺⁺ level in mild & moderate to severe hypertensives.

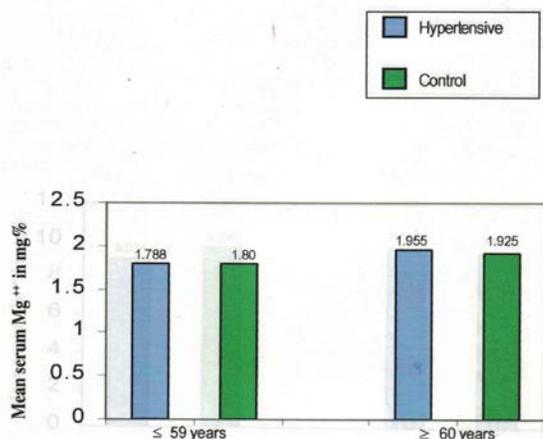


Fig. 6 : Showing mean serum Mg⁺⁺ level in hypertensives & control in younger and elderly age groups.

limits in both control ($9.5743 \pm 0.6834 \text{mg/dl}$) and hypertensive groups ($9.2792 \pm 0.194 \text{mg/dl}$).

The mean serum magnesium level in 50 hypertensive subjects was 1.836 ± 0.471 (mean \pm SD) and that of 50 normotensive subjects was $1.846 \pm 0.2954 \text{mg/dl}$. No significant difference between 2 groups was found.

G. paolisso et al found lowering of serum magnesium in hypertensive subjects compared to normotensive control, the study indicated lowered level of Plasma and erythrocytic magnesium in hypertensive than in normotensive subjects^[16].

However the finding of normal serum magnesium level in our study may be explained by the fact that alteration of serum magnesium in hypertensive may not be uniform phenomenon. clinical trials of magnesium supplementation in hypertensive patients show divergent results. Some studies demonstrate low serum magnesium levels in hypertensive patients when compared with normotensive subjects, and blood pressure levels reduction after magnesium supplementation, although other studies have not confirmed this finding. For this reason, while adequate intake of magnesium through diet is recommended, supplementation of this mineral is not indicated as part of antihypertensive treatment^[14].

Garcia Zozaya JL et al studied 60 hypertensive patients (35 men and 25 women with an average age of 40 years) for signs of metabolic changes, with special emphasis on the relationship between the calcium and magnesium levels. The control group comprised 37 normotensive subjects (19 men and 18 women with an average age of 39 years). As far as magnesium is concerned their only positive finding was decreased urinary excretion of magnesium in hypertensive than control. They also found an inverse correlation between magnesium excretion and blood pressure.^[17]

Resmck LM et al found serum magnesium in hypertensive and controls within normal limits they studied the relation of plasma renin activity to serum level of magnesium and ionized calcium in 102 normotensive and 92 patients with essential hypertension who were divided into low renin, normal renin and high renin groups. serum magnesium levels were higher in patients with low renin hypertension and lower in patients with high renin hypertension than in those with normal renin hypertension, P value <0.02, if renin sodium profiling were not used, and instead all the patients were considered together as if they were single homogenous group, the hypertensive subject as a whole would then appear to have no deviation in magnesium metabolism and would be apparently indistinguishable from normal control^[18].

Our study comply with the findings of Resnick et al we studied altogether 50 hypertension patients and 50 control subjects in the control group serum magnesium ranged from 1.20-2.50 mg/dl, out of 50 hypertensive only 6 patient showed hypermagnesemia and none showed hypomagnesemia when compared with control subjects. But as a whole P value was >0.02 and thus difference between two groups was insignificant. But when we divided the patients into two groups according to age then it was seen that older age group (60 years and above) had serum magnesium level higher ($1.955 \pm 0.43 \text{mg/dl}$) and younger

DISCUSSION

In the present study serum calcium concentration level in 50 hypertensive subjects was found within normal

group (59 years and below) had serum magnesium level lower ($1.788 \pm 0.49 \text{ mg/dl}$) P value < 0.02 .)

There was no significant difference between serum magnesium level of elderly hypertensive and elderly normotensive subjects ($1.925 \pm 0.178 \text{ mg/dl}$) and serum magnesium level of younger hypertensive also was not significantly different from young normotensive subjects ($1.788 \pm 0.49 \text{ mg/dl}$ and $1.80 \pm 0.34 \text{ mg/dl}$).

In our study mean serum magnesium in male hypertensive was $1.74 \pm 0.47 \text{ mg/dl}$ and female hypertensive was $1.93 \pm 0.44 \text{ mg/dl}$. Difference between two mean was not significant ($P > 0.02$). No significant difference in serum magnesium seen between male hypertensive and male normotensives. But there was significant difference between female hypertensive and female normotensives (P value < 0.02 that is significant).

In our study we found that in elderly hypertensive serum magnesium level is higher when compared to that of age matched control and also among them, though most of the patients and serum magnesium level with in the normal range (that in control value). Such outcome of our study may be due to the fact that high renin hypertensive population were more in younger patient and low renin hypertensive were more among elderly patients as seen by Resmck LM et al. [18]

In the present study the mean serum calcium level in 50 hypertensive subjects was $9.2792 \pm 0.1940 \text{ mg/dl}$ (mean \pm S.D) and that of 50 normotensvie subjects was $9.5743 \pm 0.6834 \text{ mg/dl}$ (mean \pm SD). No significant difference was found between the two group ($P > 0.02$). In previous studies some worker have found lowering of serum calcium in hypertensive subjects compared to normotensive subjects. Studies on serum calcium, reported that calcium was significantly higher in patients with hypertension then in normontensive [19,20]

In one study it was found that Blood pressure and calcium intake is inversely related, high blood pressure is related with low calcium and low blood pressure with high calcium intake (mccarron et al) [21]

In contrast to all these studies some other studied showed positive correlation between serum calcium and both systolic and diastolic blood pressure, other researchers found no association between blood pressure and serum calcium levels [22]

In our study we studied altogether 50 hypertensive patients and 50 control subjects. In the control group serum calcium ranged from 8.20-10.51mg/dl. Out of 50 hypertensives 7 patients only showed hypercalcemia, 9 patients showed hypocalcemia, when compared with control subjects. But as a whole P value was > 0.02 and thus difference of this serum calcium level among two groups was insignificant. But when we divided the patient into 2 groups according to age then it was seen that older age group (60 years and above) had serum calcium level higher ($9.641 \pm 0.7409 \text{ mg/dl}$) than younger group of hypertensive ($9.0348 \pm 1.1681 \text{ mg/dl}$), serum calcium level of younger hypertensive group (≤ 59 years) was lower ($9.0348 \pm 1.1681 \text{ mg/dl}$) than younger group of control ($9.6890 \pm 0.6693 \text{ mg/dl}$) P < 0.02 that is significant. In older hypertensive ≥ 60 years ($9.641 \pm 0.7409 \text{ mg/dl}$) compared to

older normotensive control ($9.4141 \pm 0.6761 \text{ mg/dl}$), P value < 0.02 .

Mean difference between serum calcium level of male and female is not significant P value is > 0.02 , but male hypertensive showed lower level ($9.0196 \pm 1.061 \text{ mg/dl}$) than female hypertensive (9.610 ± 0.097), P value < 0.02 that is Significant. Male hypertensive showed significantly lower calcium than normotensive males (9.0196 ± 1.061 & $9.6027 \pm 0.6020 \text{ mg/dl}$ receptively), P value < 0.02 , but mean difference in serum calcium level between female hypertensive and control is not significant.

CONCLUSION

The present study concludes-

1. The mean serum magnesium was found to be $1.846 \pm 0.2954 \text{ mg/dl}$ and mean serum calcium was $9.5743 \pm 0.6834 \text{ mg/dl}$ in the control group. There is no relation of serum magnesium level with age and sex in control subjects.
2. The mean level of serum magnesium was $1.836 \pm 0.471 \text{ mg/dl}$ and level of serum calcium was $9.2792 \pm 1.0948 \text{ mg/dl}$ in hypertensive patients there was no significant change in serum calcium and magnesium in hypertensive patient when compared to that of control subjects.
3. serum magnesium level does not show any significant change either with sex of hypertensive patients or with the severity of hypertension. However serum magnesium was significantly higher in elderly hypertensive then younger hypertensives.
4. There was significant difference in serum calcium level of hypetensives and normotensives of different age group was found. Mean serum calcium level in the age group ≥ 60 years was significantly higher in hypertensives that normotensives while in the age group ≤ 59 years mean, serum calcium was significantly lower in hypertensives compared to normotensives (P value < 0.02 that is significant).

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