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Corresponding Author:
Dr. Devendra Pratap Singh Rajput,
LN Medical College,
Bhopal, M.P. India

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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).

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 “Hypertonic 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. [6] 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 LN 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
Principle of Cresolphthalein method and magnesium was based on Beer & combert's law. Calcium was measured by calmagite method. The working of photometer is estimated by the method of semi automated photometric analysis by using model RA-50. The sample was immediately centrifuged at 3000 rpm for 20 minutes & clear supernatant serum pipetted out.

Methods of estimation of serum calcium & magnesium

Serum magnesium and serum calcium was estimated in all 50 hypertensive and 50 normotensive groups. In the hypertensive group it was between 8.50-9.59 mg/dl, while in the control group it was between 8.20-10.51 mg/dl.

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

Table 2 - Showing serum magnesium level in cases and control

<table>
<thead>
<tr>
<th>ITEM</th>
<th>SERUM MAGNESIUM IN CASES AND CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Percentage</td>
</tr>
<tr>
<td>1.20-2.19</td>
<td>36</td>
</tr>
<tr>
<td>2.20-2.64</td>
<td>13</td>
</tr>
<tr>
<td>&gt;2.65</td>
<td>1</td>
</tr>
</tbody>
</table>

In the hypertensive group the range of serum calcium was 8.50-9.59 mg/dl and 11 hypertensive (22%) showed level between 9.60-10.49 mg/dl. 9 hypertensive (18%) had serum calcium > 10.50 mg/dl and 12 hypertensive (24%) showed level < 8.49 mg/dl. (Table 1)

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

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Table : 1- Showing serum calcium in hypertensives and normotensives.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>HYPERTENSIVE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Mg (mg/dl)</td>
<td>1.836</td>
<td>0.471</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>HYPERTENSIVE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Mean</td>
<td>58.50</td>
<td>58.50</td>
</tr>
<tr>
<td>S.D.</td>
<td>9.57</td>
<td>9.57</td>
</tr>
</tbody>
</table>
Serum magnesium was higher in elderly hypertensive than younger patients \( (P < 0.02) \).

Mean difference is 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.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>MILD HYPERTENSION</th>
<th>MODERATE TO SEVERE HYPERTENSION</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean serum Magnesium</td>
<td>1.7880</td>
<td>1.8879</td>
<td>1.8460</td>
</tr>
<tr>
<td>In mg%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>HYPERTENSION MEAN</th>
<th>HYPERTENSION S.D</th>
<th>CONTROL MEAN</th>
<th>CONTROL S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Calcium in mg%</td>
<td>9.2792</td>
<td>0.194</td>
<td>9.5743</td>
<td>0.6834</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>HYPERTENSIVES</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Ca++ level(mg%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 59 Years</td>
<td>9.03</td>
<td>9.3565</td>
</tr>
<tr>
<td>S.D.</td>
<td>48</td>
<td>9.1037</td>
</tr>
<tr>
<td>&gt; 60 Years</td>
<td>1.16</td>
<td>9.5862</td>
</tr>
<tr>
<td>S.D.</td>
<td>81</td>
<td></td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>HYPERTENSIVE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Ca++ (mg %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9.019</td>
<td>9.539</td>
</tr>
<tr>
<td>S.D.</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1.06</td>
<td>0.79</td>
</tr>
<tr>
<td>S.D.</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
DISCUSSION

In the present study serum calcium concentration level in 50 hypertensive subjects was found within normal limits in both control (9.5743±0.6834mg/dl) and hypertensive groups (9.2792±0.194mg/dl).

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

G. Paolissi 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[11].

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]

Resmick LM et al. found serum magnesium in hypertensive and controls with in 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 homogeneous 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 at al we studied altogether 50 hypertensive 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±0.43mg/dl) and younger
Hypertension. 2003

Calcium levels found no association between blood pressure and serum al.
were more among elderly patients as seen by Resmck LM et
range (that in control value). Such outcome of our study may
age matched control and also among them, though most of the
serum magnesium level is higher when compared to that of
In our study we found that in elderly hypertensive
<0.02 that is significant).

No significant difference in serum
significant (P>0.02). No significant difference in serum
calcium was significantly lower in hypertensives
4. There was significant difference in serum calcium level of
hypertensives and normotensives in 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,
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compared to normotensives (P value <0.02 that is

CONCLUSION
The present study concludes:
1. The mean serum magnesium was found to be
1.846±0.2954mg/dl and mean serum calcium was
9.574±0.6834 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±0.471mg/dl and level of serum calcium was
9.2792±1.0948mg/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
hypertensives and normotensives of different age group
was found. Mean serum calcium level in the age group ≥ 60
years was significantly higher in hypertensives than normotensives

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7.
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compared to normotensives (P value <0.02 that is


