"STUDY OF SERUM CALCIUM IN ESSENTIAL HYPERTENSION AND ITS CO-RELATION WITH SEVERITY OF THE DISEASE"

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Dissertation submitted to BLDE Deemed to be University, Vijayapura

In partial fulfillment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

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Dr. JAYDEEPKUMAR D. DHAMELIYA

LIST OF ABBREVIATIONS USED

Ca -	Calcium
BP -	Blood Pressure
HTN -	Hypertension
N -	Number
SD -	Standard Deviation
WHO -	World Health Organization
$1,25(OH)_2D$ -	1,25 Dihydroxy Vitamin D
CT -	Computed Tomography
JNC -	Joint national Committee
BMI -	Body MASs Index
GRF -	Glomerular Filtration Rate
ADH -	Anti Diuretic Hormone
NO -	Nitric oxide
ISH -	Isolated Systolic Hypertension
AMP -	Adenosine monophosphate
Mg+ -	Magnesium ion
Dl -	Decilitre

ABSTRACT

BACKGROUND:

Hypertension is one of the leading causes of death and disability among adults all over the world and emerging health problem in India. Over 90% of patients with high blood pressure have 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

AIM:

To study the levels of serum Calcium in patients with primary hypertension and to correlate the serum Calcium levels with severity of disease

MATERIALS AND METHODS:

Information for the study was collected from patients admitted to BLDEDU'S Shri B.M Patil Medical college Hospital and Research center, Vijayapura from November 2016 to August 2018. Patients were screened and who met inclusion criteria where studied. A Comparative Study was done. serum calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and results were obtained compared.

RESULTS:

In our study mean age in hypertensive patients was 50.80 ± 19.38 and in controls it was 43.19 ± 19.171. There was no significant difference of serum calcium was obtained in relation to age in both the Stage of Hypertension. There was no significant difference in relation to gender. In total Hypertensives cases mean ± SD of S. Calcium was 8.408 ± 1.07 mg/dl while in normotensives cases it was 9.190 ± 0.7827 mg/dl.In all Stage I Hypertensive case mean ± SD of S. Calcium was 8.626 ±

0.6012 mg/dl (p = 0.032) while in Stage II Hypertensive it was 8.190 ± 1.3668 mg/dl (p = 0.0001). This results were significantly low than normotensives. But comparing both Stage of Hypertension mean was lower in stage II but it is not significantly low. So level of S. Calcium has inverse relation with Hypertension severity.

CONCLUSION:

In patients of Essential hypertension mean serum Calcium levels were found to be low in comparison to Normotensives. Further, Stage II Hypertensive patient has more reduced levels of serum calcium than Stage I, hence low Serum Calcium levels were associated as the severity of the disease increases.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Hypertension is one of the leading causes of the global burden of disease. Approximately 7.6 million deaths (13-15% of the total) and 92 million disability-adjusted life years worldwide were attributable to high blood pressure in 2001.[1][2] The WHO rates Hypertension as one of the most important causes of premature death worldwide.[3][2] There is strong positive and continuous correlation between BP and the risk of cardiovascular disease (myocardial infarction, heart failure), renal disease, stroke and mortality. This correlation is more robust with systolic than with diastolic Blood Pressure.([4]

Hypertension is due to specific causes in a small fraction of cases, but in the vast majority of individuals (≈90-95%), its etiology cannot be determined; therefore, the essential hypertension term is employed.[5–7] Essential hypertension is currently understood as a multifactorial disease arising from the combined action of many genetic, environmental, and behavioral factors.[8–10]

. Alterations in the intracellular free Calcium regulation as well as disturbances of extracellular calcium homeostasis have been observed in patients with essential hypertension.[11]

Many researchers even recommend a regular consumption of the recommended daily levels of dietary calcium to combat with hypertensive disorders.[12][13] In a country like India, people tend to have a diet rich in Sodium and poor in Potassium and Calcium, this change in diet can change hypertension course and progress.[11]

AIM OF THE STUDY

1. To study the levels of serum Calcium in patients with Essential Hypertension.
2. To correlate the serum Calcium levels with severity of disease.

REVIEW OF LITERATURE

CALCIUM

INTRODUCTION:

FIGURE 1 – CALCIUM ELEMENT

It is the fifth most abundant element in Earth's crust and the third most abundant metal, after iron and aluminium.Calcium is also the most abandant metal and fifth-most abundant element in the human body.

Calcium plays crucial role in various cellular function and physiologic Thus, extracellular calcium concentrations are maintained within an exquisitely narrow range through a series of feedback mechanisms.[14]

STRUCTURE:

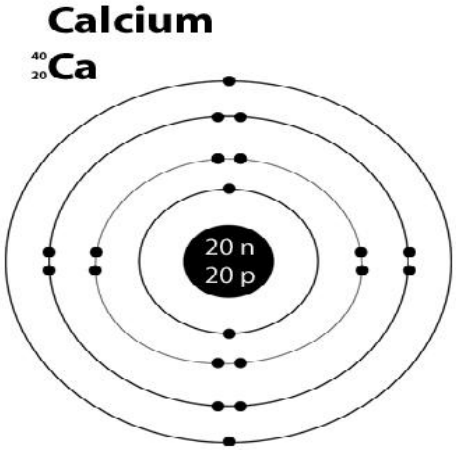


FIGURE 2 – CHEMICAL STRUCTURE OF CALCIUM

HISTORY:

The name calcium is derived from latin word calas meaning lime was known as early as the first centuries when the ancient Romans prepared lime as CaO.[15]

It was not actually isolated until 1808 in England when Sir Humphrey Davy electrolyzed a mixture of lime and mercuric oxide.[15]

METABOLISM[16]**:**

Feedback mechanisms maintaining extracellular calcium concentrations within a narrow, physiologic range (8.9–10.1 mg/dL). Fall in serum Calcium leads to secretion of Parathyroid hormone (PTH) due to presence of receptors wich senses Calcium.

PTH causes increase in tubular reabsorption of calcium by thekidney and resorption of calcium from bone and also stimulates production of 1,25(OH)2D

1,25(OH)2D acts principally on the intestine to increase calcium absorption..

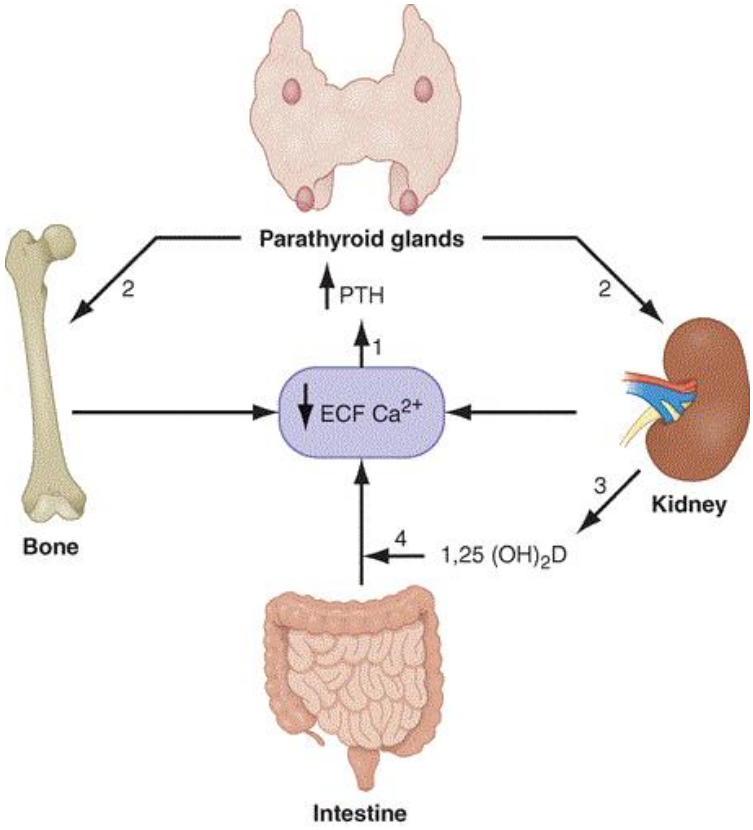


FIGURE 3 – CALCIUM REGULATON

FUNCTIONS[15]:

i. Ca has effect on nerve excitability, mainly on the peripheral neuromuscular mechanism.

ii. Skeletal muscle integrity is affected by Ca levels. Contractility of muscle increases with rise in ionized calcium and vice versa.

iii. It has crucial role in maintaining the tone and contractility of heart

iv. one of the clotting factor

v. Calcium is essential in formation of Bone and certain tissues.

DISTRIBUTION IN BODY[15]:

The body contains about 2% of Ca and 98% of this is in the bones. The cell and body fluid contains from 10 – 15 mg per 100 gm. Out of the blood, the cerebrospinal fluid contains only 6 mg per 100 gm.

The blood Ca is in two distinct forms,

1. Protein bound part mainly with albumin
2. Ionic calcium, involved in the various physiological activities.

NORMAL VALUES:

Ionized calcium is 1.12-1.45 mmol/L (4.54-5.61 mg/dL).

Total calcium is 2.2-2.6 mmol/L(9-10.5 mg/dl).

SOURCES OF CALCIUM:

Calcium is present in both animal and plant foods.

1. Dairy foods (milk, yoghurt and cheese)
2. Green leafy vegetables like fenugreek leaves and broccoli.
3. Cereals like Ragi, nuts
4. seeds like almonds, pistachios and sesame seeds,
5. fishes like salmon, sardines etc.

RECOMMANDED DIETERY ALLOWANCE:

Indian Council of Medical Research (ICMR) recommends calcium per day

- 1 to 9 yr - 600 mg/day
- 10 to 17yr - 800 mg/day
- normal adult male and female - 600 mg/day
- pregnant and lactating mothers - 1200 mg/day

HYPERTENSION

HISTORY:

Stephen Hales (1733),an eighth century clergyman and pioneer of experimental physiology measured BP for the first time in horses. The height of column of blood in a vertical tube inserted into an artery denoted the BP.In 1886 Riva Rocci invented the pneumatic compression cuff to measure the BP.Sir Clifford Allbutt in 1896 made a fundamental observation when he recognized the distinction between hypertension due to renal disease and hypertension in which no evidence of renal disease could be discovered (essential hypertension).Tigerstedt and Bergman (1898) isolated a pressor substance from the renal cortex and named it renin.

In 1905, NS Korotkoff, a Russian Physician described Korotkoff sounds and laterErlanger (1921) put forward the concept that muffling of sounds denotes Diastolic Blood Pressure.Prior to Australian cardiovascular physiologist Paul Korner, in the 1940s, little was known about essential hypertension.[16]

In 1968 Sir George Pickering advocated the concept that hypertension was only a quantitative deviation from the normal so that people were arbitrarily called hypertensives if they were on the higher position of the unimodal distribution curve.

De Wardener and Mc. Gregor in the 1980's postulated a causal role for the sodium.. Thus hypertension may not be a distinct disease caused by specific abnormalities. Single or specific cause for hypertension is not found even today.

With the development of potent drug treatment, beginning with ganglion blocking agents, which came into clinical usage in 1950s another revolution in understanding of hypertension, was achieved.

With the advent of newer investigational modalities like CT scan in 1979 and radionuclide studies of late, the diagnosis of various causes of secondary hypertension

has been made easy. Zeitler (1971) and Gruwentzig (1978) performed balloonangioplasty of the renal artery successfully and gave an impetus to this new therapeutic technique to treat renovascular hypertension.

BLOOD PRESSURE:

DEFINITION:[17]

Blood pressure is defined as the lateral pressure exerted by the column of blood against any unit area of the vessel wall. It is almost always measured in millimetres of mercury (mmHg).

MEASUREMENT OF BLOOD PRESSURE[18]:

Preparation:

1. The patient should sit quietly for 5 min with the arm bared and supported at the level of the heart and the back resting against a chair.
2. No caffeine, smoking, Alcohol, full bladder within 30 min.
3. A quiet, warm setting.

Technique:

Number of readings:

On each occasion, take atleast two readings, separated by as much time as is practical; if readings vary >5 mmHg, take additional reading

Method:

1. Inflate the bladder quickly to a pressure 20 mmHg above the systolic pressure, recognized by disappearance of radial pulse, to avoid an auscultatory gap.
2. Deflate the bladder 2 to 3 mmHg/second.
3. Record the Korotkoff phase I (appearance) and phase V (disappearance). Phase I corresponds to systolic pressure and phase Vprovides a better measure of diastolic blood pressure. Nevertheless, inthose conditions where Korotkoff sounds remain audible despite complete deflation of the cuff (aortic regurgitation, arteriovenous fistula, pregnancy) phase IV (muffling) must be used for the diastolic measurement.

4 If the Korotkoff sounds are weak, have the patient raise the arm and open and close the hand 5-10 times, then inflate the bladder quickly

CLASSIFICATION OF BLOOD PRESSURE JNC8 GUIDELINES[3][19]:

TABLE –

Pressure category	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal	< 120	< 80
Prehypertension	120 – 139	80 – 89
Hypertension		
Stage I	140-159	90 – 99
Stage II	>160	>100

HYPERTENSION

DEFINITION:

Systolic BP measurement of 130 mm Hg or higher or any diastolic BP measurement of 80 mm Hg or higher.13 Clinically, hypertension might be defined as that level of blood pressure at which the institution of therapy reduces blood pressure related morbidity and mortality.[20]

INCIDENCE AND PREVALENCE:

The overall prevalence of hypertension varies from 6 – 32 %. thus affecting 1 billion population worldwide. In India the prevalence of hypertension is 59.9 and 69.9 per 1000 in males and females in urban population while it is 35.5 and 35.9 per 1000 in males and females in rural population respectively.Overall prevalence for hypertension in India was 29.8%.[21]

Gender Differences:

Hypertension is an important risk factor for cardiovascular disease in women. After 65 year of the prevalence of hypertension is higher in women than men. In middle aged and older women Obesity is significantly more common hence cross over of prevalence may be present. Women using Oral contraceptive pills has increase the risk of development of hypertension in younger women. Hormone replacement therapy does not raise the blood pressure in women who are normotensive at the start of treatment.

Etiologically Hypertension can be divided into two types.

1. Primary or essential hypertension.
2. Secondary hypertension

PRIMARY HYPERTENSION

DEFINITION:

A type of hypertension when there is no identifiable cause. Primary hypertension is also called Essential hypertension or Idiopathic hypertension. Affecting around 90-95% of hypertensive patients, it is the most common type of hypertension.[20]

It tends to be familial and is likely to be the consequence of an interaction between genetic and environmental factors. As the age increases chance of development of essential hypertension also increases, and if there is relatively high blood pressure at young age the risk of development of hypertension increases.[5]

RISK FACTORS

Although, essential hypertension has no identifiable cause as per definition several risk factors have been identified.

Genetic

Family history of hypertension increases the chance of development of Hypertension.In blacks prevalence of Primary hypertension is four times more than white and in Black people it progress more rapidly, with more severity and associated with high mortality.

> 50 genes have been studied in association with hypertension. Studies also shows that single gene mutation can also cause hypertension.Unbiased genome-wide analyses of BP genomics have identified 43 genetic variants associated with systolic, diastolic BP, and HTN.[22]Kim et al study has linked Angiotensinogen gene with

hypertension. They have concluded that blood pressure increases as number of this gene are more.[23]

Many studies has showed the relation of genetic variation and chances of development of hypertension but still effect of genetic variance on blood pressure is not fully understood

Age

Increase in the age is associated with development of hypertension but in such scenario other factors are also associated. Pathogenesis can be age related stiffness of arteries which makes arteries less compliant. Decrease in the sodium excretion due to reduction in GFR and renal microvascular disease with increasing age is other possible pathogenesis.[24]

Obesity

In compare to normal weight individuals, Obese individuals have five times more risk of development of hypertension and excess weight attributes two third of total cases. When BMI is >25 kg/m2 85% individuals with develop disease. Probable pathogenesis is sympathetic nervous system activation and RAAS system as well.[25]

Salt

Sodium sensitivity is associated with one third cases of primary hypertension.[26]When sodium intake is more than excretion capacity of kidney, intravascular shift of fluids occurs, cardiac output increases and hence blood pressure. Rise in blood pressure is also to increase sodium excretion to kidney.

Alcohol

high calories in alcohol leads to obesity,and eventually leads to hypertension after excessive alcohol consumption.[27]

Renin

High renin levels is risk factor for hypertension. The mechanism involved is high renin causes increased Angiotensin II, which leads to increased vasoconstriction, ADH and Aldosterone levels and causes increased sodium reabsorption in kidneys which leads to hypertension.

Diabetes

Insulin resistance and/or hyperinsulinemia can cause hypertension. Vasodilatory effect of insulin is present normally which without increase in mean arterial pressure exibit sympathetic activity. This mechanis, is over ride in metabolic syndrome where there is high sympathetic neural activity

Vitamin deficiency[28][29–31]

High rennin levels are observed with low Vitamin D levels. And Renin levels may contribute to hypertension. It is also observed that Potassium supplements can prevent rise in blood pressure and can also lower blood pressure in hypertension.

Sedentary lifestyle.

Regular moderate degree exercise helps in prevention of hypertension.

PATHOPHYSIOLOGY OF ESSENTIAL HYPERTENSION

INTRAVASCULAR VOLUME

The kidney is the culprit and victim in hypertension, producing a vicious cycle of progressive renal dysfunction and hypertension.[32] acquired or inherited defect in the kidney's ability to excrete the excessive sodium load imposed by a modern high salt diet.When sodium intake is more than excretion capacity of kidney, intravascular shift of fluids occurs, cardiac output increases and hence blood pressure.

Resetting of Pressure natriuresis:

In normotensive individuals, BP elevation invokes an immediate rise in renal sodium excretion to contract plasma volume .In almost all forms of hypertension, the pressure-natriuresis curve is shifted to the right and, in salt-sensitive hypertension, the slope is reduced. Resetting of the pressure-natriuresis curve leads to nocturia, one of the most common and bothersome symptoms in patients with uncontrolled hypertension. Hypertensive individuals excrete the same amount of a given dietary sodium load as normotensive individuals, but at a higher BP, and require many more hours to excrete the sodium load and achieve sodium balance

AUTONOMIC NERVOUS SYSTEM

Neural Mechanisms

In young adults, primary hypertension consistently is associated with increased heart rate and cardiac output, plasma and urinary norepinephrine levels, regional norepinephrine spillover, peripheral postganglionic sympathetic nerve firing (by microelectrode recordings) and alpha-adrenergic receptor–mediated vasoconstrictor tone in the peripheral circulation.[33]

Sympathetic overactivity has also been demonstrated in several other forms of established human hypertension like, hypertension associated with obesity, sleep apnoea, early type 2 diabetes mellitus and prediabetes, chronic kidney disease, heart failure and immunosuppressive therapy with calcineurin inhibitors such as cyclosporine.

In these conditions, central sympathetic outflow can be driven by deactivation of inhibitory neural inputs (e.g., baroreceptors), activation of excitatory neural inputs (e.g., carotid body chemoreceptors, renal afferents) or by circulating angiotensin II, which activates pools of excitatory brain stem neurons that are devoid of a blood-brain barrier

In hypertension, the baroreceptors are reset to defend a higher level of BP. Baroreflex control of sinus node function is impaired even in mild hypertension but baroreflex control of systemic vascular resistance and BP is well preserved.Partial baroreceptor dysfunction is common in elderly hypertensives and typically presents with a triad of orthostatic hypotension, supine hypertension and symptomatic postprandial hypotension, the latter initiated by splanchnic pooling after carbohydrate-rich meals.[34]

RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM

Activation of the renin-angiotensin-aldosterone system (RAAS) is one of the most important mechanisms contributing to endothelial cell dysfunction, vascular remodelling, and hypertension. Renin, a protease produced solely by the renal juxtaglomerular cells, cleaves angiotensinogen to Angiotensin I(A I), which is converted by angiotensin-converting enzyme to Angiotensin II(A II) .RAAS activation is a major homeostatic mechanism to counter hypovolemic hypotension (as with hemorrhage or salt and water deprivation). Suppression of serum aldosterone leads to increased renal sodium excretion, thereby shrinking plasma volume to protect against salt-sensitive hypertension.

Thus, in the setting of high dietary sodium and elevated BP, the RAAS should be completely suppressed and any degree of RAAS activity is inappropriate.

In African Caribbean hypertensives, serum aldosterone levels are higher than in white hypertensives despite lower plasma renin levels, implicating abnormal aldosterone production by renin-independent mechanisms, a formefruste of primary aldosteronism

Receptor mediated actions of angiotensin II:

Two main types of angiotensin receptors are known. AT1 receptors are widely expressed in the vasculature, kidney, adrenals, heart, liver and brain.

AT 1 receptor activation explains most of the hypertensive actions of A II. Furthermore, constitutes a major therapeutic target for interrupting every step in cardiovascular disease progression, from vascular remodelling and formation of atherosclerotic plaque to stroke, myocardial infarction (MI) and death.

In contrast, AT_2 receptors are widely distributed in the fetus but in adults, are found only in the adrenal medulla, uterus, ovary, vascular endothelium and distinct

brain regions.Inrodents, AT_2 receptor activation opposes some of the deleterious effects of AT_1 receptors by promoting endothelium-dependent vasodilation by bradykinin and nitric oxide pathways. However, recent animal studies have suggested that AT_2 receptors can be profibrotic but their role in human hypertension remains speculative

VASCULAR PATHOPHYSIOLOGY

Alterations in small and large arteries integrity and function play a pivotal role.

Endothelial dysfunction:

The endothelial lining of blood vessels is critical to vascular health and constitutes a major defence against hypertension. Defective release of endothelial-derived relaxing factors like NO, endothelium-derived hyperpolarizing factor and increased release of endothelium-derived constricting, proinflammatory, prothrombotic and growth factors. The latter include endothelin, thromboxane and TGF-β.[35]

The endothelium of all blood vessels expresses the enzyme nitric oxide synthase (NOS), which can be activated by bradykinin or acetylcholine or by the cyclic laminar shear stress that accompanies hypertension, particularly with the widened pulse pressure in ISH. Once activated, NOS converts l-arginine to citrulline, an inert substance and nitric oxide (NO), a volatile gas that diffuses to the adjacent vascular smooth muscle and activates a series of G kinases that culminate in vasodilation.(36)

In humans, endothelium-dependent vasodilation can be assessed by measuring increases in the large artery (forearm or coronary) diameter following intraarterial infusion of acetylcholine or release of ischemia (e.g., arrested forearm circulation) or a sudden elevation in BP (cold pressor test).

Competitive inhibitors of NOS specifically block endothelium-dependent dilation but do not block the dilation of these arteries produced by exogenous nitrovasodilators (e.g., nitroglycerin, nitroprusside). These measurements most often are obtained with brachial artery ultrasound. More accurate measurements require invasive techniques

Vascular remodelling:

Remodelling of arteries occurs by endothelial cell dysfunction, neurohormonal activation and elevated BP, which further perpetuates the hypertension.[37][38]

"An increase in the medial thickness relative to lumen diameter (increased media-to-lumen ratio) is the hallmark of hypertensive remodelling in small and large arteries.The media-to-lumen ratio increases but the medial cross-sectional area remains unchanged. By decreasing lumen diameter in the peripheral circulation, inward eutrophic remodelling increases systemic vascular resistance, the hemodynamic hallmark of diastolic hypertension."[39]

COMPLICATIONS

The pathological hallmark of untreated hypertension is acceleration of atherosclerosis. Premature development of various cardiovascular diseases occurs if Bp is high. If untreated, 50% of the hypertensive patients die of coronary artery disease or congestive cardiac failure, about 33% of stroke and 10 – 15% of renal failure. A meta-analysis of nine major prospective studies shows a direct continuous and apparently independent association of diastolic BP with both coronary artery disease and stroke

1. **Hypertensive Complications:**

    Accelerated malignant phase

    Hemorrhagic stroke

    Congestive heart failure

    Nephrosclerosis

    Aortic dissection

2 **Atherosclerotic Complications:**

    Coronary artery disease

    Sudden death

    Arrhythmias, Atherothrombotic Stroke, Peripheral vascular stroke

CALCIUM AND ESSENTIAL HYPERTENSION:

Humans with essential hypertension and genetic animal models of hypertension is shows low serum ionized calcium , increased urinary calcium excretion, and increased parathyroid hormone (PTH) concentration.

Calcitriol metabolism and bone mineralization are also altered in hypertension. These alterations in systemic calcium metabolism may be linked to factors responsible for the elevated blood pressure.

Cytosolic free calcium tends to be increased in most cells that have been studied from hypertensive humans and animals.

This raised levels may be due to an intrinsic defect in renal calcium handling.[40] Administration of supplemental dietary calcium tends to suppress PTH, calcitriol, and intracellular free calcium

In hypertensive patients there is a defect in excreting the digitalis like natriuretic factor which inhibits ouabain sensitive Na^+-K^+ATPase causing intracellular sodium accumulation. This increased intracellular sodium causes intracellular calcium accumulation in the vascular smooth muscle cells leading to an increase in contractility.[41]

There exists numerous relationship between calcium and sodium as stated by Blaustein.

1. Inhibition of N^{+}-K^{+} Exchange pumps would depolarise muscle fibres and thereby increase calcium entry through voltage sensitive calcium channels.
2. An increase in intracellular sodium will result in a sodium electrochemical gradient between sarcoplasm and external medium causing reduced extrusion of calcium from the cell.
3. An increase in intracellular sodium in the presynaptic terminal of sympathetic neurons promoting calcium dependant noradrenaline release causing release of calcium from cellular stores.
4. A very small rise in intracellular sodium, theoretically is adequate to cause enough rise in intracellular calcium, to increase the resting vascular smoo

Defects of Calcium at Cellular level in Humans:

Several defects in cellular calcium concentration, membrane binding, and transport kinetics have been identified in red blood cells (RBCs), platelets, and adipocytes of persons with essential hypertension, including reduced calcium buffering and sodium-calcium exchange.

In RBCs of hypertensive persons, there is 25 to 30% reduction in calcium binding to inside surface which leads to increased permeability of the cell to sodium and partial inhibition of Na^{+}-K^{+} ATPase activity.[42]

While calmodulin content and distribution in RBCs from hypertensive subjects have been found to be normal, the ability of calmodulin to activiate Ca^{2+}-ATPase is impaired, since the affinity of the calcium pump for calcium is reduced and the maximal activity of the pump is lower. It was also demonstrated that basal (unstimulated) Ca^{2+}-ATPase activity is decreased in RBC membranes of hypertensive subjects compared with that in matched control subjects.

Those with higher intracellular free calcium concentrations were associated with lower extracellular calcium levels, which demonstrates the dichotomy that can exist between these calcium pools. .

The possibility that a generalized defect does exist is supported by two additional observations: the intracellular alcium concentrations are elevated in RBCs of hypertensive persons and adipocytes obtained from hypertensive subjects exhibit similar alterations of intracellular calcium.[42]

Effects of reduced calcium intake:[11]

Various studies showed an association between dietary calcium intake and blood pressure however, the potential benefit of treating hypertension with increased dietary intake of calcium remain controversial.

Previous analyses of the NHANES I and II data have yielded conflicting findings regarding the influence of various dietary variables on blood pressure, particularly calcium.

Many cross-sectional studies have shown relations between dietary calcium intake and blood pressure.

Data from the Western Electric Heart Study showed that calcium intake was inversely related to the incidence of elevated DBP (95 mmHg or greater) but not of elevated SBP (160 mmHg or greater). A recent report of a large cohort study of women showed that dietary calcium intake was inversely related to hypertension among women

Increased urinary calcium excretion:[43]

The total and fractional urinary calcium excretion is elevated in subjects with essential hypertension.

Consistent with these reports is a population survey that demonstrated a positive correlation between urinary calcium excretion and blood pressure among 9321 men.

Although dietary calcium was not measured in the survey, the greater urinary calcium excretion was thought to be reflective of a greater dietary intake of calcium.

The likelihood of this cause-and effect relationship's holding is inconsistent with the epidemiological data summarized above, which report decreased intake of calcium by hypertensive persons.

In addition, in an intervention trial, which assessed urinary calcium and dietary calcium intake in hypertensive subjects had observed that lower intakes were associated with higher excretion rates.

Whether the excessive urinary calcium excretion reflects an enhanced intestinal absorption of a decreased oral intake or a decreased ability of the kidney to reabsorb the cation is controversial. However the pattern of increased PTH levels and urinary cyclic AMP, lower serum ionized calcium values and reduced serum phosphorus levels appears to argue strongly against the former and in favour of the latter possibility.

Supporting literatures:

Some epidemiological studies are discussed here to enlighten the present study.

Kar K at al[44] has done study on 47 Hypertensive patients and showed there is reduced level of serum calcium than normotensives patients and there is decrease in Serum calcium as the age advances in comparison to controls and concluded there is role of Ionised Calcium in Hypertension

Yogesh R Pawade at al[45] has done study concluded there is effect on calcium metabolism in Essential Hypertension and and it can also related as prognostic marker.

Uday S B and Prashant H[46] has Studied 100 hypertensive patients and studied level of S. Calcium in it showing reduced level in comparison to controls in essential hypertenive cases

K. Sudhakar et al.[47], in their study enrolled one hundred and seventeen confirmed untreated essential hypertensive patients and their 77 first degree relatives (33 siblings and 44 offsprings). The mean total serum calcium levels in males and females were significantly decreased in hypertensive group when compared with normotensive controls. In the first-degree relatives also the total serum

Fu, Y., Wang, S.,et.[48]lassessed the relationships between plasma and intracellular Ca^{2+} ,Mg^{2+} and blood cell membrane ATPase activity in normotensive and hypertensive subjects, showed a significant decreased activity of ATPase along low with calcium and higher cytosolic calcium levels

AR Folsom et al.[49]showed. Hypertensive subjects had lower mean serum levels of ultrafilterable calcium, and ionized calcium than normotensives.

Grobbee DE et al[50]. in his research article “Calcium metabolism and familial risk of hypertension” stated that there is circumstantial evidence that disturbances of calcium metabolism are implicated in primary hypertension.

He also stated that in the “Dutch Hypertension and Offspring Study”, young normotensive subjects were selected on the basis of presence or absence of familial predisposition for hypertension. The findings showed that disturbances in calcium metabolism were present in the early phase of primary hypertension and may precede the development of high BP. Moreover, they suggested that changes in calcium metabolism may be a characteristic of familial hypertension and could reflect a genetic basis for calcium sensitive hypertension. The presence of a relatively reduced serum calcium and increased plasma PTH level in the offspring of hypertensive parents indicates that calcium balance in prehypertensive subjects is maintained at a higher level of circulating PTH

METHODOLOGY

1. SOURCE OF DATA:

The information for the study will be collected from patients admitted to BLDEDU'S Shri B.M Patil Medical college Hospital and Research center, Vijayapur from November 2016 to June 2018.

2. METHOD OF COLLECTION OF DATA:

Information will be collected through prepared proforma from each patient. Qualifying patients will be undergoing detailed history, clinical examination and laboratory investigations and will be matched for sex and age(within 5 year)[11]

- **Inclusion Criteria:**

  1. Patients with newly detected or untreated primary hypertension.
  2. The classification of blood pressure in adults as PER JNC8(2).
  3. Patients whose age is above 18 yr are included.Both sexes are included.

- **Exclusion Criteria:**

  1. Patients already on antihypertensive drugs
  2. On drugs that alters calcium levels
  3. Patients with renal disease (alsonephrosis, nephritis)
  4. Pregnant females
  5. With Encocrie disorders like Diabetes Mellitus, Thyroid and Parathyroid disorder,
  6. Patients with Acute Diarrhoeal disease, steatorrhoea
  7. Ischemic Heart Disease

3. TYPE OF STUDY: Comparative

4. SAMPLE SIZE:

With the anticipated mean difference and common SD [2.3(0.07) & 2.25(0.09)](6) of serum calcium among Grade I and Grade II at 95% confidance level and 80% power the sample size worked out in each group is 42 by following formula

$$n = \frac{(Z_{\alpha}+Z_{\beta})^2 * 2SD^2}{MD^2}$$

Zα - Z value at 95% confidence interval

Zβ - Z value at βerrors = 80%

SD - common standard deviation

MD – mean difference of two parameters

Hence 42 cases will be included in 3 group (Stage I, Stage II and control)

Total sample size = 126

Statistical Analysis

1. Mean +/- SD^2
2. Statistical tests like students t test / Mann whitney U test.

It was done using Software SPSS version 17

RESULTS

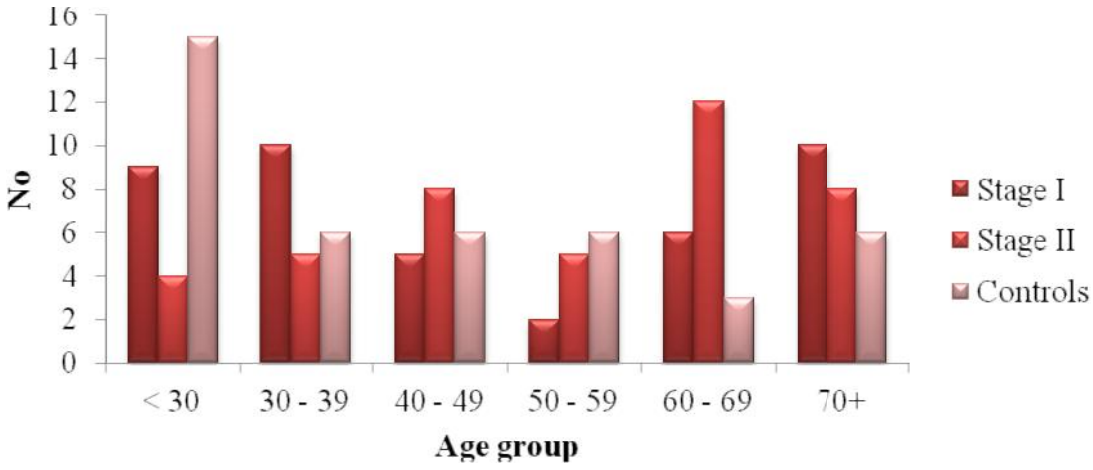
A Study of serum total calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and following results were obtained.

AGE DISTRIBUTION:

TABLE 2: DISTRIBUTION OF CASES BY AGE

AGE(YEARS)	STAGE I		STAGE II		CONTROLS	
	N	%	N	%	N	%
< 30	9	21.4	4	9.5	15	35.71
30 - 39	10	23.8	5	11.9	6	14.28
40 - 49	5	11.9	8	19.04	6	14.28
50 - 59	2	4.7	5	11.9	6	14.28
60 - 69	6	14.28	12	28.57	3	7.1
70+	10	23.8	8	19.04	6	14.28
Total	42	100	42	100	42	100

FIGURE 4: DISTRIBUTION OF CASES BY AGE

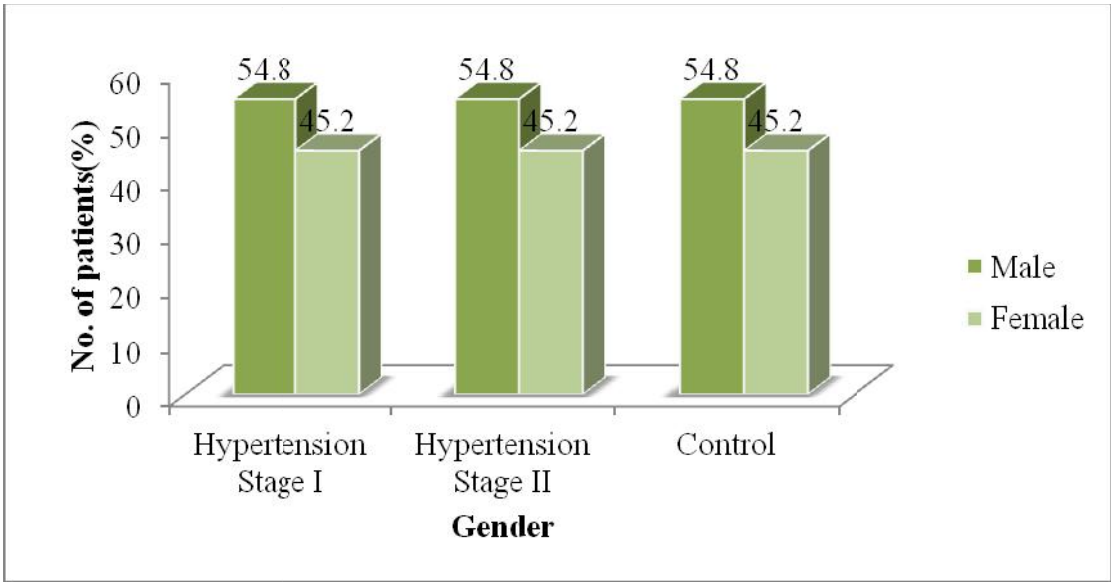


GENDER:

TABLE 3: DISTRIBUTION OF CASES BY GENDER

GENDER	STAGE I		STAGE II		CONTROL	
	N	%	N	%	N	%
Male	23	54.8	23	54.8	23	54.8
Female	19	45.2	19	45.2	19	45.2
Total	42	100.0	42	100.0	42	100.0

FIGURE 5: DISTRIBUTION OF CASES BY GENDER



Here number of male and female cases were same in all 3 groups which was 23 and 19 respectively and were compared.

DISTRIBUTION OF CASES BY HABITS OF:

TABLE 4: SMOKING AND/OR TOBACCO CHEWING

Smoking And/or Tobacco	Hypertension Stage I		Hypertension Stage II		Control	
	No. of patients	Percentage	No. of patients	Percentage	No. of patients	Percentage
Yes	21	50.0	13	31.0	9	21.4
No	21	50.0	29	69.0	33	78.6
Total	42	100.0	42	100.0	42	100.0

FIGURE 6:SMOKING AND/OR TOBACCO CHEWING

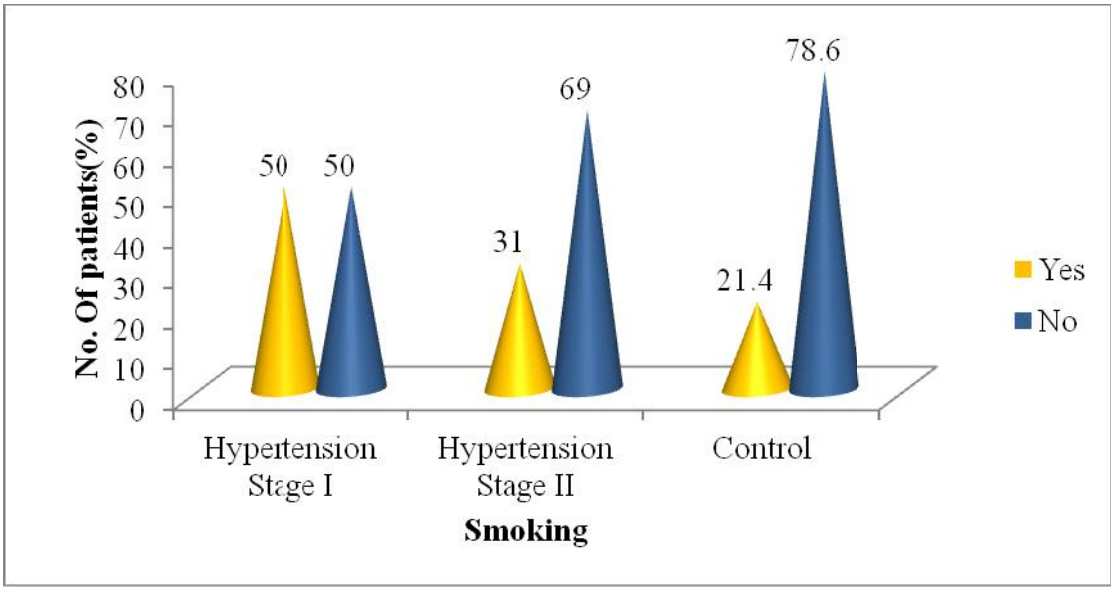


TABLE 5: HABIT OF ALCOHOL CONSUMPTION

Alcohol consumption	Hypertension Stage I		Hypertension Stage II		Control	
	No. of patients	Percentage	No. of patients	Percentage	No. of patients	Percentage
Yes	8	19.0	8	19.0	12	28.6
No	34	81.0	34	81.0	30	71.4
Total	42	100.0	42	100.0	42	100.0

FIGURE 7: HABIT OF ALCOHOL CONSUMPTION

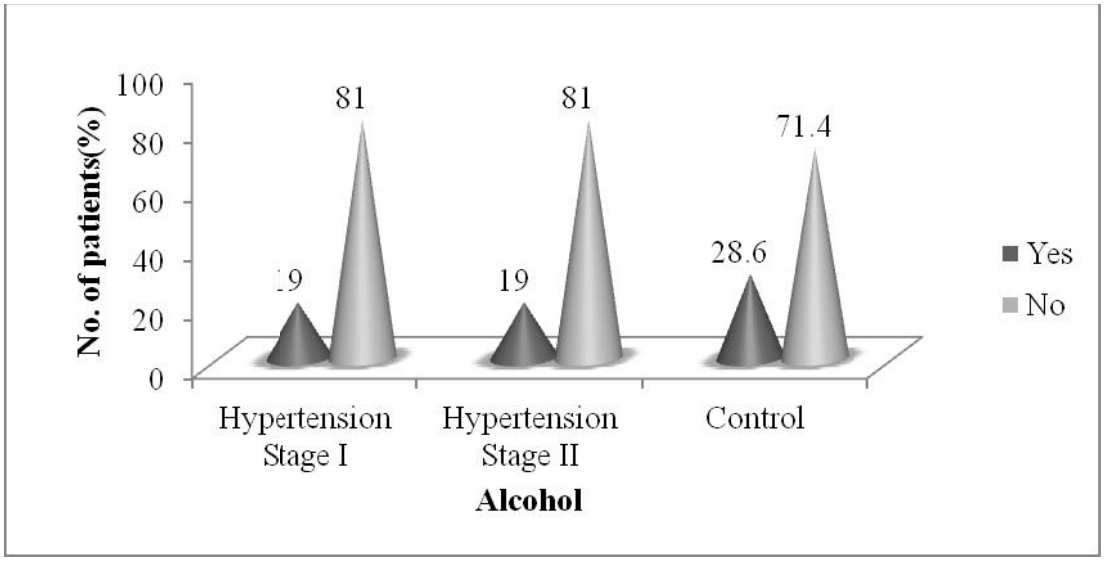
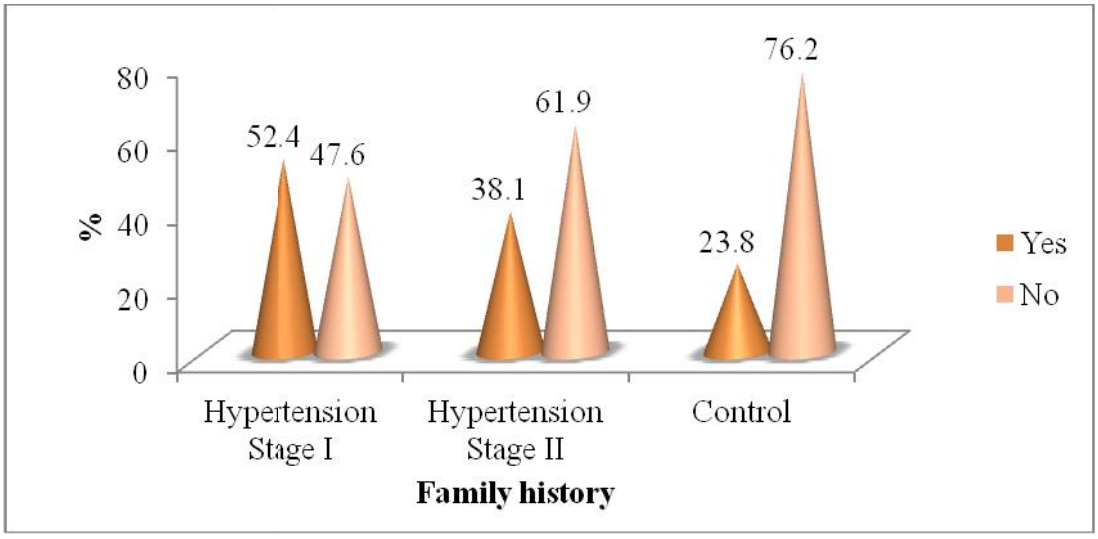


TABLE 6: FAMILY HISTORY OF HYPERTENSION:

Family History	Hypertension Stage I		Hypertension Stage II		Control	
	No. of patients	Percentage	No. of patients	Percentage	No. of patients	Percentage
Yes	22	52.4	16	38.1	10	23.8
No	20	47.6	26	61.9	32	76.2
Total	42	100.0	42	100.0	42	100.0

FIGURE 8: FAMILY HISTORY OF HYPERTENSION



In the study history of smoking and/or tobacco chewing in Stage I hypertensives was 50% and in stage II hypertensives it was 31%. History alcohol consumption in Stage I hypertensives and in stage II hypertensives was same 19%. Family history of essential hypertension in Stage I hypertensives was 52.4% and in stage II hypertensives it was 38.1%.

So, history of smoking and/or tobacco chewing was associated most followed by family history of essential hypertension

TOTAL SERUM CALCIUM LEVELS:

TABLE 7: DISTRIBUTION OF CASES BY NORMAL AND LOW SERUM CALCIUM IN TOTAL CASES OF HYPERTENSION

S.Calcium (mg/dl)	Hypertensive		Control	
	No. of patients	Percentage	No. of patients	Percentage
< 8.5	48	57.14	4	9.5
8.5 +	36	42.86	38	90.5
Total	84	100.0	42	100.0

TABLE 8: DISTRIBUTION OF CASES BY NORMAL AND LOW SERUM CACIUM IN BOTH STAGES OF HYPERTENSION

S.Calcium (mg/dl)	Hypertension Stage I		Hypertension Stage II		Control	
	No. of patients	Percentage	No. of patients	Percentage	No. of patients	Percentage
< 8.5	22	52.4	26	61.9	4	9.5
8.5+	20	47.6	16	38.1	38	90.5
Total	42	100.0	42	100.0	42	100.0

FIGURE 9: GRAPHICAL DISTRIBUTION OF CASES BY NORMAL AND LOW SERUM CALCIUM IN TOTAL CASES OF HYPERTENSION

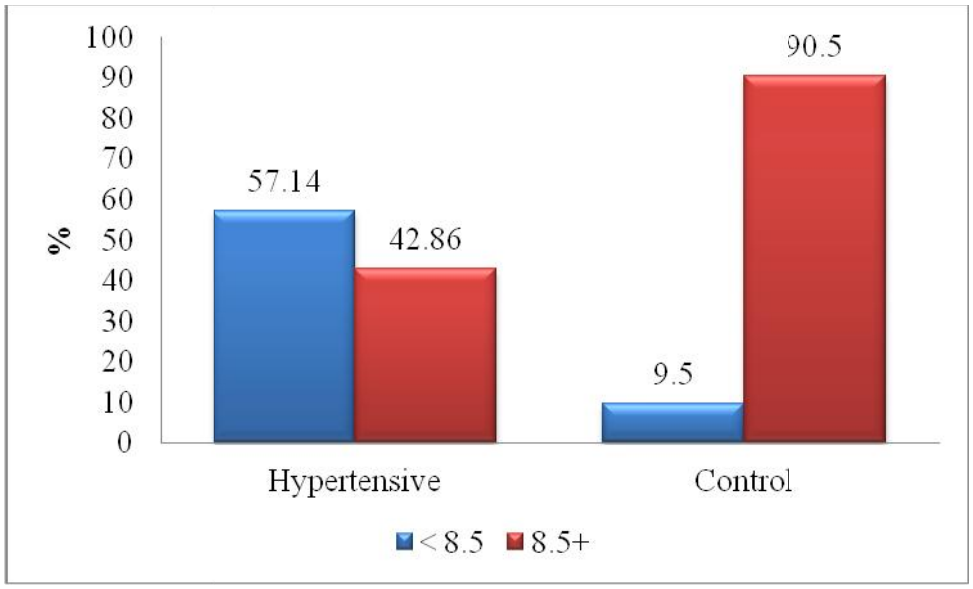
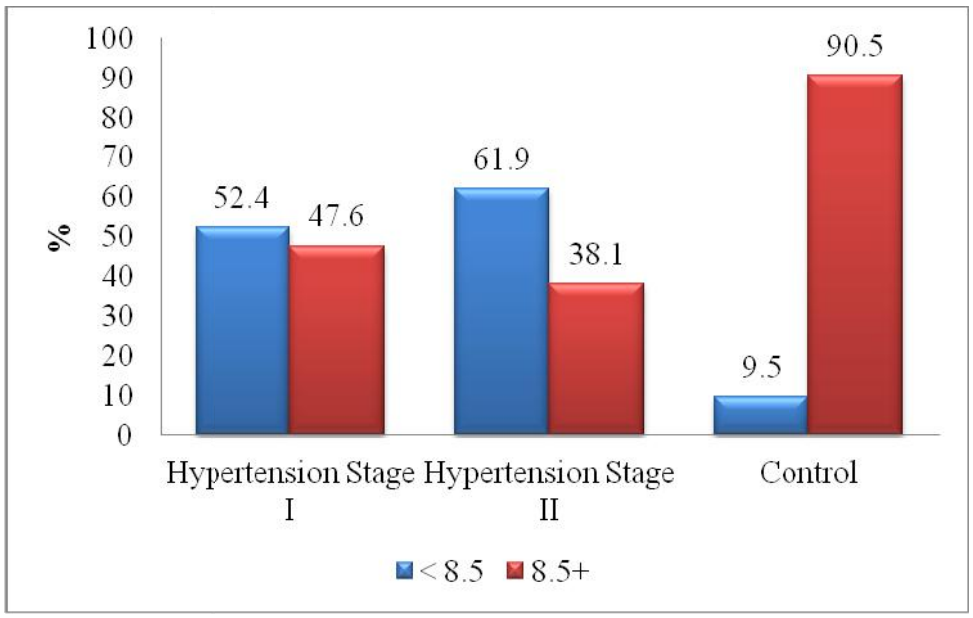


FIGURE 10: GRAPHICAL DISTRIBUTION OF CASES BY NORMAL AND LOW SERUM CALCIUM IN DIFFERENT STAGES OF HYPERTENSION



In the study S Calcium value of 8.5 – 11 mg/dl is taken normal.

Out of 84 Hypertensive patients, 48 (57.14%) had low S. Calcium (<8.5mg/dl) and 36 (42.86%) had normal S. Calcium level. Out of 42 cases of Stage I Hypertension 22 (52.4%) has low S. Calcium. Out of 42 cases of Stage II Hypertension 26 (61.9%) has low S. Calcium level. Out of 42 controls only 4 (9.5%) has low S. Calcium level.

Here, overall >50 % of Hypertensive cases has low S. Calcium level. And number of cases with low S. Calcium were more in Stage II than in Stage I group.

TABLE 9: S. CALCIUM LEVELS INTOTAL HYPERTENSIVES CASES

Groups	Serum calcium (mg/dl)			
	Minimum	Maximum	Mean	Std. Deviation
Hypertensive	6.8	13.4	8.408	1.07
Control	7.9	11.0	9.190	0.7827

TABLE 10: S.CALCIUM INDIFFERENT STAGES OF HYPERTENSION

Hypertension	Serum calcium (mg/dl)			
	Minimum	Maximum	Mean	Std. Deviation
Stage I	7.7	10.5	8.626	0.6012
Stage II	6.8	13.4	8.190	1.3668
Control	7.9	11.0	9.190	0.7827

TABLE 11: MEAN S. CALCIUM IN CASES HAVING LOW S. CALCIUM

S. Calcium(mg/dl)	Mean	
< 8.5	Hypertension Stage I	Hypertension Stage II
	8.182±0.18	7.34±0.58

FIGURE11:MEAN SERUM CALCIUM IN ALL PATIENTS IN EACH GROUP

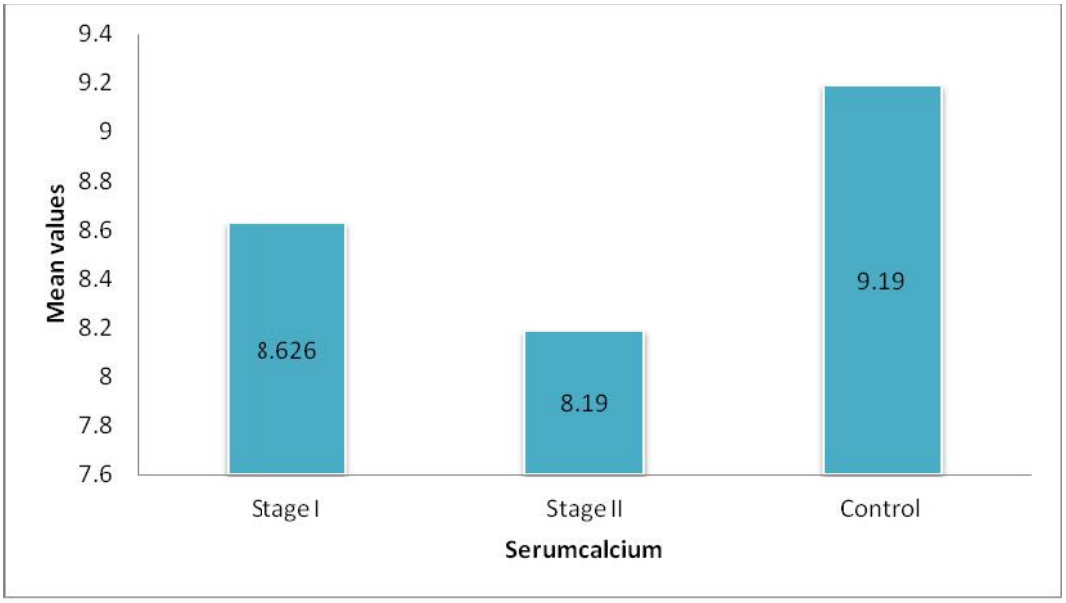
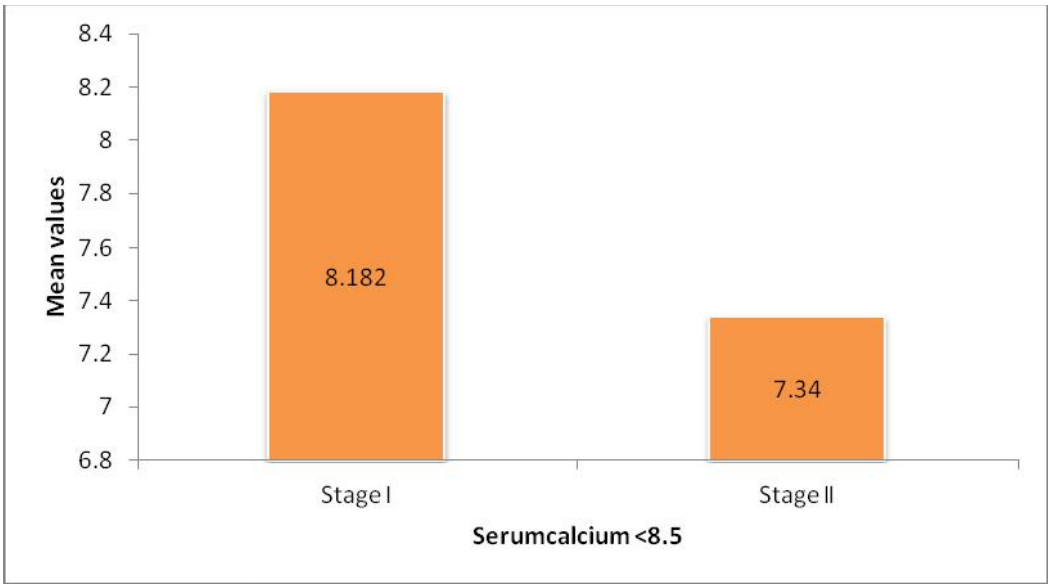


FIGURE 12: MEAN SERUM CALCIUM IN CASES WITH LOW CALCIUM



In total Hypertensives cases mean ± SD of S. Calcium was 8.408 ± 1.07.

In all Stage I Hypertensive case mean ± SD of S. Calcium was 8.626 ± 0.6012

In all Stage II Hypertensive case mean ± SD of S. Calcium was 8.190 ± 1.3668

In all normotensives cases mean ± SD of S. Calcium was 9.190 ± 0.7827

In cases with low calcium mean ± SD of S.Calcium in Stage I cases was 8.182±0.18 and in Stage II cases it was 7.34±0.58.

Here, study shows average Serum Calcium is low in Hypertension. And when comparing all cases of Stage I and Stage II Groups, average S. Calcium is Normal in Stage I and Low in Stage II. But in comparison to control group both Stages has low S. Calcium Level. When the cases with Low S.Calcium is compared in both Stages, Stage II hypertensives patients has more reduction in S. Calcium level than Reduction in S. Calcium in Stage I.

TABLE 12: S. CALCIUM LEVEL IN EACH GENDER IN TOTAL CASES

All Hypertensive cases	Serum calcium(mg/dl)		**Mann Whtney U test** P=0.9606*
	Male	Female	
	Mean±SD	Mean±SD	
	8.45±1.14	8.36±0.99	

TABLE 13: S. CALCIUM IN EACH GENDER IN BOTH STAGES

	Serum calcium(mg/dl)		Mann Whtney U test
	Male	Female	
	Mean±SD	Mean±SD	
Stage I	8.522±0.49	8.753±0.70	P=0.220*
Stage II	8.374±1.55	7.968±1.11	P= 0.543*

*P value of <0.05 is statistically significant

Here Serum calcium level was compared between male and female in all cases and Different stages,too. There was no statistically significant difference of S. Calcium level was observed between male and female hypertensive cases.

TABLE 14: COMPARISON OF SERUM CALCIUM LEVELS BETWEEN ALL HYPERTENSIVE CASES AND CONTROLS

Groups	Serum calcium (mg/dl)		Unpaired t test
	Mean	Std. Deviation	
Hypertensive	8.408	1.07	P = 0.001*
Control	9.190	0.7827	
Total	8.669	1.0494	

*P value is 0.05 is statistically significant.

TABLE 15: COMPARISON OF SERUM CALCIUM BETWEEN HYPERTENSION STAGE I, STAGE II AND CONTROL GROUPS

Hypertension	Serum calcium		Kriskalwallis test
	Mean	Std. Deviation	
Stage I	8.626	0.6012	P = 0.001*
Stage II	8.190	1.3668	
Control	9.190	0.7827	
Total	8.669	1.0494	

Comparison between	Significant value
Stage I and Stage II	P=0.126
Stage I and Control	P=0.032*
Stage II and Control	P=0.0001*

*P value is 0.05 which is statistically significant

Hence, low Serum Calcium level in hypertensive patient is statistically Significant in comparison to controls

Low Serum Calcium level in Stage I hypertension and Stage II Hypertension is statistically Significant in comparison to controls.

But low calcium level in all cases of Stage I is not statistically significant when compare with Stage II. But the mean value is much low in Stage II and when cases with low Serum calcium are compared it is statistically significant.

DISCUSSION

Hypertension is one of the leading causes of death and disability among adults all over the world and emerging health problem in India41.Essential hypertension is a heterogeneous disorder, with different patients having different causal factors that lead to high Blood Pressure, Alterations in the intracellular free Calcium regulation as well as disturbances of extracellular calcium homeostasis have been observed in patients with essential hypertension.[4]

Considering the above study was conducted in BLDEDU's Shri BM Patil Medical College and Research centre over a period of 2 year in which A Study of serum calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and the results were obtained and compared.

Lian IA and Asberg A[51], did a study which has concluded that Unadjusted Total cacium has better diagnostic accuracy than commonly used adjustment formulas, so clinician should stop use of this formulas. In our study corrected S. Calcium levels were not obtained and compared.

In our study mean age in hypertensive patients was 50.80 ± 19.38 and in controls it was 43.19 ± 19.171. There was no significant difference was obtained in relation to age in both the Stage of Hypertension but Jorde.,et al.[52], has noticed that there was a significant decrease in serum calcium with increasing age in men as age increases there is significant decrease in S. Calcium levels while in women it increases with age

Our study showed there was no significant difference in relation to gender (p value <0.9606) in both Stages which was supported by study by AR Folsom et al(49)

In our study while comparing S. Caclium values in different groups with each other, the observation was that overall > 50 % of Hypertensive cases has low S. Calcium level. And number of cases with low S. Calcium were more in Stage II than in Stage I group. Out of 42 controls only 4 (9.5%) has low S. Calcium level. In total Hypertensives cases mean ± SD of S. Calcium was 8.408 ± 1.07 mg/dl while in normotensives cases it was 9.190 ± 0.7827 mg/dl hence difference of 0.782 ± 0.2873.

G. Ranjani[43] showed similar difference of S. Calcium levels in which Hypertensive Patient has mean Serum Calcium of 8.9160 ± 0.62529 mg/dl and 9.7042 ± 0.79350 mg/dl in normotensives and difference was 0.7882 0.16821 mg/dl which were statistically significant as in our study.

K. Sudhakar et al[47], They the study first of all in Indian population, serum calcium levels were measured in 117 subjects and 77 first degree relatives. Serum Calcium levels were decreased in hypertensive which were statistically significant.

Strazzullo P et al.[53], showed there is elevated fractional urinary calcium excretion in cases ofPrinary hypertension and had obtained significant reduction in Total S. Calcium levels, but no significant reduction inIonized calcium levels.

Tillman DM and Semple PF[45], showed that there is disturbance of calcium metabolism in hypertension, and although result of Ionized calcium, Total Serum Calcium concentration in the hypertensive was not significant, there was significant correlation between total calcium and systolic pressure

Wright GL, Rankin was a study in rats showed a lower serum ionized and total serum calcium concentrations in spontaneously hypertensive rats

In all Stage I Hypertensive case mean ± SD of S. Calcium was 8.626 ± 0.6012 mg/dl (p = 0.032) while in Stage II Hypertensive it was 8.190 ± 1.3668 mg/dl (p = 0.0001). This results were significantly low than normotensives. But comparing both

Stage of Hypertension mean was lower in stage II but it is not significantly low. So level of S. Calcium has inverse relation with Hypertension severity.

KamleshJha M[11] support this observation of inverse relation between Calcium levels and Severity of disease. But they have studied Ionised Calcium. In Stage I hypertensives mean was 2.30 ± 0.072 mmol/l which was significantly lower ($p<.0001$) than that of normotensives, but in comparison to Stage II hypertensivesit was significantly higher ($p=.009$) where mean serum calcium level was 2.25 ± 0.09 mmol/l

There are difference studies which showed that calcium supplementation can alter outcome of disease or not. Jolma at al, a study in ratsshowed increased dietary Calcium reduce the development of hypertension there will be the improved vasorelaxation after Calcium supplementation in NO deficient hypertension. On human populations also several similar studies are done for dietry supplementation in England[54], Oregon[55], Indiana[56] showed reduction in Blood pressure.

The findings have been highly variable across various studies but the largest study (TOHP) - Trials and Hypertension Prevention Study found no significant blood pressure lowering at 600mg per day. Based on the data and experience available, calcium supplementation on increased Dietary intake of calcium rich foods can be recommendednon-specifically for prevention of hypertension, and in osteoporosis it will have. Therefore, intake be maintained at 1.0 to 1.5gm per day is recommanded through dietary intake on supplements for both adolescent and Adults

CONCLUSION

The study concludes:

Hypertensive cases are found to have low S. Calcium level. And number of cases with low S. Calcium were more in Stage II than in Stage I group.

Average Serum Calcium is low in Hypertensive patients. And when comparing all cases of Stage I and Stage II Groups, average S. Calcium is Normal in Stage I and Low in Stage II. But in comparison to control group both Stages has statistically significant low S. Calcium Level.

Low Serum Calcium level in Stage I hypertension and Stage II Hypertension is statistically Significant in comparison to controls.

When the cases with Low S.Calcium is compared in both Stages, Stage II hypertensives patients has more reduction in S. Calcium level than Reduction in S. Calcium in Stage I hence there is inverse relation between blood pressure and Serum Calcium

Our study shows there is correlation between Serum Calcium levels and essential hypertension and also shows Severity of disease and Serum calcium has inverse relationship.

SUMMARY

Hypertension is one of the leading causes of death and disability among adults all over the world and emerging health problem in India. Over 90% of patients with high blood pressure have 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. To know association, study of the levels of serum Calcium in patients with primary hypertension wasdone and correlation with severity was established

Information for the study was collected from patients admitted to BLDEDU'S Shri B.M Patil Medical college Hospital and Research center, Vijayapura from November 2016 to August 2018. Patients were screened and who met inclusion criteria where studied. A Comparative Study was done. serum calcium was done in total 126 patient which were divided equally in 3 groups named Stage I Hypertensives, Stage II Hypertensives, and Controls or Normotensives, 42 patients in each groups and results were obtained compared.

In our study mean age in hypertensive patients was 50.80 ± 19.38 and in controls it waa 43.19 ± 19.171. There was no significant difference of serum calcium was obtained in relation to age in both the Stage of Hypertension. There was no significant difference in relation to gender. In total Hypertensives cases mean ± SD of S. Calcium was 8.408 ± 1.07 mg/dl while in normotensives cases it was 9.190 ± 0.7827 mg/dl.In all Stage I Hypertensive case mean ± SD of S. Calcium was 8.626 ± 0.6012 mg/dl ($p = 0.032$) while in Stage II Hypertensive it was 8.190 ± 1.3668 mg/dl ($p = 0.0001$). This results were significantly low than normotensives. But comparing both Stage of Hypertension mean was lower in stage II but it is not significantly low. So level of S. Calcium has inverse relation with Hypertension severity.

In patients of Essential hypertension mean serum Calcium levels were found to be low in comparison to Normotensives. Further, Stage II Hypertensive patient has more reduced levels of serum calcium than Stage I, hence low Serum Calcium levels were associated as the severity of the disease increases

LIMITATION OF THE STUDY

1. Sample size was small
2. Ionized Calcium, Parathyroid Hormons and Serum renin levels were not done due to constrains
3. Patients with having low Calcium levels are not studied for Effect of Calcium supplements as this is not a follow up study.

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ANNEXURE-I

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04-10-2016 *at* 3pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "Study of Serum calcium in essential Hypertension and its correlation with Severity of the disease"

Name of P.G. student Dr. Jayadeepkumar. D. Dhameliya
Dept of Medicine

Name of Guide/Co-investigator Dr S. N. Bentoor.
Prof of Medicine

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE-II

CONSENT FORM

BLDEDU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR- 586103

TITLE OF THE PROJECT - STUDY OF SERUM CALCIUM IN ESSENTIAL HYPERTENSION AND ITS CO-RELATION WITH SEVERITY OF THE DISEASE

PRINCIPAL INVESTIGATOR - Dr. JAYDEEPKUMAR D. DHAMELIYA

9510456488

P.G.GUIDE NAME - Dr. SANJEEVKUMAR N. BENTOOR

PROFESSOR OF MEDICINE

08352-, Ext-2148

All aspects of this consent form are explained to the patient in the language understood by him/her.

I) **INFORMED PART**

1) PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

4) BENEFITS:

I understand that my participation in this study will help to patient's survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or

videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at anytime.

Dr. JAYDEEPKUMAR D. DHAMELIYA is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. JAYDEEPKUMAR D. DHAMELIYA may terminate my participation in the study after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate

8) INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I

understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Dr. JAYDEEPKUMAR D. DHAMELIYA Date

(Investigator)

II) **STUDY SUBJECT CONSENT STATEMENT:**

I confirm that Dr. JAYDEEPKUMAR D. DHAMELIYA has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

Participant / Guardian Date

_____ _____

Witness to signature Date

ANNEXURE-III

PROFORMA

STUDY OF SERUM CALCIUM IN ESSENTIAL HYPERTENSION AND ITS CO-RELATION WITH SEVERITY OF THE DISEASE

Name:	CASE NO:
Age:	IP NO:
Sex:	DOA:
Religion:	DOD:
Occupation:	
Residence:	

Presenting complaints with duration:

History of present complaints:

Past History:

Family History:

Personal History:

Diet/appetite

Sleep

Bladder and bowel habits:

Addictions

Drug allergy

Treatment History:

General Physical Examination

Height:

Weight:

Body Mass Index:

Vitals

PR:

BP:

RR:

Temp:

Neck:

Upper Limbs:

Chest:

Abdomen:

Lower Limbs:

Skin:

SYSTEMIC EXAMINATION.

- Respiratory System
- Cardiovascular System
- Central Nervous System
- Per abdomen

INVESTIGATIONS

PATHOLOGY

Complete Blood Count Hemoglobin	Gm/dl
Total Count	Cells/cumm
Differencial counts Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Platelets	Cells/cumm
ESR	At the end of one hour
Urine routine	
Urine albumin	
Urine sugar	
Urine Microscopy RBC Pus cells Cast Epithelial cell	

BIOCHEMISTRY

Random Blood sugar	
Serum Creatinine	
Fasting Lipid profile	
Total Cholesterol	
Triglycerides	
HDL	
LDL	
VLDL	
Serum Calcium	
Total Protein	
Serum albumin	

USG ABDOMEN(If done)

ECG

FINAL DIAGONOSIS

STAGE I HYPERTENSIVE PATIENTS

S. NO	NAME	AGE	SEX	IP NO	SMOKING	ALCOHOL	F/H	BP(mmHg)		S. CALCIUM (mg/dl)	RBS	S. CREAT
								SBP	DBP			
1	IBRASAPPA B HATTI	85	M	25734	Y	Y	N	148	92	8.3	93	0.9
2	BASAVARAJ M CHINCHLI	35	M	14440	Y	Y	Y	142	90	8.3	63	1.3
3	SHIVANAND V SALAGARKUR	35	M	14580	Y	N	N	150	92	8.1	110	0.5
4	YANKAPPA BIRADAR	45	M	14759	Y	Y	N	148	94	8.6	125	1.9
5	DHARMARAY S BIRADAR	60	M	15155	Y	N	N	154	96	8.2	156	1.8
6	SHANTAGOUDA S BIRADAR	72	M	22158	Y	Y	Y	148	92	8.3	106	1.6
7	SAHEBGOUDA S BIRADAR	65	M	22212	N	Y	Y	158	92	8	109	1.2
8	SAMEER K DAKHANI	19	M	23066	N	N	Y	150	90	8.6	121	0.9
9	PRASAD K GOBBUR	21	M	2131	Y	N	Y	152	90	8.8	94	0.8
10	SIDDAPPA K KAVALGI	85	M	4134	Y	N	N	148	94	8.9	90	0.6
11	ANAPPA R. TELI	75	M	1853	N	N	N	158	90	8.6	75	0.9
12	SAVALAGAYYA G MATHAPATI	78	M	781	Y	Y	Y	158	94	8.3	105	0.6
13	MADIWALAPPA S CHAUDHARI	85	M	5219	Y	N	N	142	98	8.6	85	1.1
14	SHARNU C KAMANAMANI	29	M	22231	Y	N	Y	142	94	9.7	85	1.3
15	CHANDAPPA P DODAMANI	53	M	23440	Y	N	N	148	94	8.4	110	0.6
16	SRAVAN RKUMAR	24	M	23689	N	N	Y	146	90	8.4	87	0.8
17	RAJSHEKHAR C ROTTI	50	M	23772	Y	Y	N	158	94	8	100	0.9
18	CHANDRASHEKHAR HIREMATH	32	M	24718	N	N	Y	148	90	9.1	100	0.8
19	MALLAPPA S PUJARI	65	M	27418	Y	N	N	154	90	8	88	0.7
20	KANTU V GUNADAL	35	M	19740	Y	N	Y	148	88	8.4	67	1
21	BHIMARAYAGOUDA J REVATAGOUN	90	M	25554	N	N	N	150	92	8.3	108	0.7
22	ABBASALI KHED	36	M	13658	Y	N	Y	144	90	9.9	125	1.3
23	SANTOSH S ASANGI	37	M	20394	Y	N	N	146	92	8.2	118	1

24	YASMIN A NADAF	20	F	19634	N	N	Y	148	94	8.3	96	0.6
25	VILAS G JADHAV	31	F	19653	N	N	Y	158	92	7.7	94	0.8
26	RITA S SUNEJA	49	F	26841	N	N	N	154	92	8	145	0.6
27	MAKTUMBI N BAGEWADI	75	F	15252	N	N	Y	142	84	8	156	0.6
28	BOURAMMA S	60	F	12803	N	N	N	152	88	9.6	93	0.6
29	KALAVATHI H SHIRSHYAD	40	F	4797	N	N	Y	130	90	9.3	76	0.8
30	PARVATI T MALAGOND	62	F	3602	N	N	N	132	90	8.8	163	0.9
31	MAYAWWA S GANDEGUL	40	F	7077	N	N	Y	148	80	8.3	162	0.6
32	KAVITHA T RAJAPUT	37	F	2834	N	N	Y	142	88	9.2	84	0.8
33	KASHIBAI I	71	F	6324	N	N	N	148	88	8.8	96	0.6
34	SHANTABAI S ALUR	75	F	19750	N	N	N	150	94	8.1	77	0.6
35	KAREMMA S PUJARI	35	F	19733	Y	N	Y	152	94	9	77	0.5
36	BASAMMA B BIRADAR	65	F	26614	Y	N	N	158	96	8.3	106	1.1
37	JAYASHREE K INGALE	35	F	26497	N	N	Y	144	90	9.3	108	1.1
38	SHAKUNTALA L CHIMMALAGI	49	F	26257	Y	Y	N	146	92	8.1	174	2
39	RENUKA R JAPLE	28	F	25070	N	N	Y	150	90	8.8	82	0.6
40	SHIVAMMA L CHINCHOLI	18	F	24768	N	N	Y	142	90	8.7	100	0.5
41	PUSHPA Y KAMBLE	20	F	24113	N	N	Y	142	92	10.5	108	0.8
42	CHANDRIKA R MADAR	25	F	19425	Y	N	N	148	92	9.5	105	0.6

STAGE II HYPERTENSIVE PATIENTS

S. NO	NAME	AGE	SEX	IP NO	SMOKING	ALCOHOL	F/H	BP		S.CALCIUM (mg/dl)	RBS	S.CREAT.
								SBP	DBP			
1	SAYED A LASHKAR	23	M	13494	Y	N	Y	178	100	8	76	0.7
2	ADIVEPPA K KAVALDAR	60	M	16135	Y	Y	N	184	112	7.3	103	1
3	EKNATH B BANDARI	68	M	21949	Y	N	Y	188	106	6.8	158	1.3
4	SHANKAR S RATHOD	60	M	22046	N	N	Y	188	116	7.7	101	0.5
5	SHIVARAJ BAGALI	21	M	24631	Y	N	N	190	118	7.8	118	17.4
6	SHIVAPPA D KANTIGOND	83	M	24774	N	N	Y	200	130	7.4	117	1.2
7	ROSHAN M KHAN	25	M	25866	Y	N	Y	232	140	7.7	135	1.2
8	CHANDRASHEKHAR BIRADAR	38	M	26317	Y	N	Y	194	114	6.4	174	2.7
9	SIDDA H TALEWAD	40	M	4754	Y	Y	N	180	130	9.5	102	0.9
10	NARAYAN GORPADE	48	M	4776	N	Y	N	180	100	9.4	181	1
11	ISHWAR L SHARMA	60	M	25006	Y	Y	N	180	110	8	106	0.9
12	NEELKANTAPPA M JANGAMSHETTI	58	M	12090	Y	N	N	180	90	10.1	152	1.3
13	DHARMANNA B PATHANI	62	M	15282	Y	Y	N	180	140	13.4	96	1
14	SADASHIV S BANGARI	45	M	23826	Y	N	Y	210	90	10.2	110	0.8
15	SHIVANAND B TULJANNAUR	40	M	26270	N	Y	N	160	114	7.9	154	1.4
16	BUDANSAB M SARWAD	72	M	23868	N	N	N	196	118	6.8	150	1.7
17	SHARANAPPA Y DODAMANI	73	M	27406	Y	N	Y	174	116	6.8	89	1.5
18	RAVI V ARALI	47	M	22243	N	Y	N	164	112	7.3	122	1.9
19	SANTOSH S ASANGI	36	M	25211	Y	N	N	196	106	7.8	108	0.6
20	SHAHADEV B GITTE	30	M	9111	N	N	N	162	100	8.9	82	1.1
21	IRASANGAPPA S SOLAPUR	66	M	15271	N	N	N	166	100	8.8	166	0.9
22	SAHEBGOND G YELAGI	50	M	28716	N	Y	N	168	100	9.3	106	0.9

23	SIDLINGAWWA B NALA	60	F	6460	N	N	N	200	96	9	111	1
24	REVANSIDDAPPA G BIRADAR	75	M	25098	N	N	N	198	98	9.3	118	1.1
25	KUSUMA G NAIK	22	F	25571	N	N	Y	210	108	6.8	109	0.7
26	MEENAXI M YALAMELI	55	F	26927	N	N	N	170	114	7.6	97	0.6
27	MANJULA K MASALI	65	F	27271	N	N	N	158	100	7.8	151	1.2
28	GOURAMMA A WADAWADUGI	65	F	13838	N	N	N	168	118	6.8	84	1
29	FAATIMA I CARGASTI	75	F	15350	N	N	N	198	130	8.7	108	1.2
30	KASTURIBAI B PAWAR	40	F	20588	N	N	Y	212	140	7.6	121	0.6
31	SUSHILABAI S HALLI	80	F	21394	N	N	N	184	120	7.9	94	0.9
32	RAHEMANBI K MAKANDAR	30	F	23042	N	N	Y	176	110	8.6	117	1.3
33	SUMITRABAI M KAVADE	65	F	23331	N	N	N	190	112	7.3	143	1.5
34	SHREEDEVI B MORATAGI	40	F	24936	N	N	Y	192	114	7.6	118	0.8
35	RUKAMABAI R BADIGER	60	F	2370	N	N	N	170	110	9	101	0.6
36	RAJESHRI V HIREMATH	53	F	8092	N	N	N	250	140	9.5	158	0.8
37	SHANTHAMMA M	45	F	2100	N	N	Y	180	90	8	110	0.6
38	SAROJINI B BHANIKATI	50	F	3979	N	N	Y	180	110	9.8	97	0.8
39	VIMALABAI S CHAVAN	60	F	24772	N	N	Y	200	110	9.6	154	0.8
40	JAKKAMMA S TALAKERI	70	F	22430	N	N	N	200	130	7.9	50	1.8
41	SUMITRABAI KAVADE	70	F	23331	N	N	N	210	118	6.7	75	0.7
42	SANTOSHI S ASANGI	36	F	25211	N	N	Y	192	100	7.8	108	0.6

CONTROLS-NORMOTENSIVE PATIENTS

S. NO	NAME	AGE	SEX	IP NO	SMOKING	ALCOHOL	F/H	BP		S.CALCIUM (mg/dl)	RBS	S.CREAT.
								SBP	DBP			
1	GAURANG B JYAMAGOND	21	M	9920	N	N	Y	118	70	9.8	107	1
2	HANMANTH L KOLKAR	28	M	13016	Y	Y	N	114	80	8.6	114	1.1
3	BASAVARAJ D BENAKI	30	M	16098	Y	N	Y	108	70	9.3	97	1
4	BASANAGOUDA S PATILSASNUR	85	M	18805	N	N	N	118	78	9.5	149	0.7
5	RAJENDRA S RAMAPUR	49	M	20187	N	N	N	118	74	9.2	177	1
6	SHARANAPPA G BADIGER	60	M	22207	N	Y	Y	120	70	9.3	111	1.1
7	YALLAPPA K CHIKKALAGI	24	M	23904	N	N	N	114	72	9.5	71	0.8
8	SHARANAPPA V GIDAVI	81	M	12779	N	Y	N	118	70	8.8	180	0.7
9	AVINASH LAXAMDOUDA	28	M	4404	Y	N	N	114	80	9.7	76	0.8
10	ANIL S JAMSOR	50	M	1419	N	Y	N	132	80	9.3	88	1.4
11	BAPUGOUDA R PATIL	87	M	7341	Y	N	N	116	70	9.3	116	1.1
12	PRABHUSWAMI	39	M	7316	Y	Y	N	110	72	9.8	117	1
13	MALLAPPA B PUJARI	43	M	12521	N	Y	N	104	80	9.5	106	1
14	RAHUL S BIRUNAGI	20	M	23081	N	N	N	118	70	10.4	128	0.8
15	BILIYANSIDDAV CHIKKALAGI	45	M	24626	N	Y	N	122	78	9	107	0.7
16	CHANDRASHEKHAR S HIREMATH	32	M	24718	N	N	N	120	74	9.1	100	0.8
17	BHIMARAYA S MALI	22	M	24792	Y	Y	N	122	82	9.5	93	0.6
18	PRADIP S CHATIRVEDI	24	M	25573	N	Y	N	102	74	8.7	120	0.9
19	SIDDAPPA B GOLLAR	75	M	25468	Y	Y	Y	118	80	8.5	134	0.9
20	BHIMARAY B GAGODYAL	70	M	26339	N	Y	Y	114	70	7.8	83	1.1
21	HANAMANTH S DHANYAL	28	M	26900	Y	N	N	114	80	9	64	0.7

22	MANJUNATH S HUGE	23	M	1498	Y	N	N	108	70	10	82	0.9
23	UTTAM R MOHITE	28	M	25990	N	N	N	116	82	8.5	74	0.8
24	MAHADEVI B TUMBAGI	25	F	24619	N	N	N	124	84	9.9	88	0.6
25	SIHIVAMMA B MASALIKERI	19	F	27080	N	N	Y	118	80	8.9	84	0.9
26	SUSHMITA WAGGI	25	F	17865	N	N	N	112	80	9.9	79	0.6
27	SHARBAMMA B	26	F	25867	N	N	N	102	60	8.9	80	0.6
28	GIRIJA M BIRADAR	24	F	4739	N	N	N	118	80	9.7	94	0.6
29	JARINABANU S GUNDAGI	55	F	4789	N	N	N	118	70	8.8	78	0.6
30	SAYADA ABDUL PARJADE	66	F	4809	N	N	Y	110	70	9.7	98	1.1
31	SHAKUNTALA K KALAKARE	35	F	1174	N	N	Y	128	80	11	108	1
32	SUVARNA M ALUR	37	F	4042	N	N	N	110	70	8.2	118	0.6
33	MAHADEVI M MALIPATIL	45	F	1408	N	N	N	104	70	8.4	96	0.8
34	RATNABAI B RATHOD	60	F	2976	N	Y	N	124	80	7.7	60	1.8
35	MAHADEVI B TUMBAGI	70	F	24619	N	N	N	126	80	9.9	79	0.6
36	LATA AWWANNA	52	F	18847	N	N	Y	108	80	9.3	130	0.6
37	KANTHA S ANAGWAGI	48	F	25867	N	N	Y	108	70	8.8	76	0.9
38	NEELAMMA V BYAKAD	50	F	2738	N	N	N	128	82	9.2	101	0.6
39	KAVITHA T RAJAPUT	37	F	2834	N	N	N	110	84	9.2	84	0.8
40	RAJESHRI V HIREMATH	53	F	8092	N	N	N	118	72	9.5	158	0.8
41	SHANTAMMA M BASARIGIDDAD	45	F	2100	N	N	N	112	86	8.8	110	0.6
42	SAROJINI B BHAVIKATTI	50	F	3979	N	N	N	114	82	9.8	97	0.8