STUDY OF VITAMIN D STATUS IN HYPERTENSION AND IT'S COMPLICATIONS

DISSERTATION SUBMITTED TO THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY, CHENNAI

In partial fulfilment of the requirements for the degree of

M.D. BRANCH – I

Registration No.: 201711369

(GENERAL MEDICINE)

DEPARTMENT OF GENERAL MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

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MAY-2020

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This is to certify that the dissertation entitled "**STUDY OF VITAMIN D STATUS IN HYPERTENSION AND IT'S COMPLICATIONS"** submitted by **Dr.M.SOWMIYA**, to the Tamilnadu Dr. M.G.R Medical University, Chennai, in partial fulfillment of the requirement for the award of M.D. Degree Branch – I (General Medicine) is a bonafide research work carried out by her under direct supervision & guidance.

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I solemnly declare that the dissertation entitled "**STUDY OF VITAMIN D STATUS IN HYPERTENSION AND IT'S COMPLICATIONS"** is done by me at Tirunelveli Medical College Hospital, Tirunelveli Under the guidance and supervision of Prof.Dr.S.ALAGESAN,M.D,DM. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

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CERTIFICATE – II

This is to certify that this dissertation work entitled **"STUDY OF VITAMIN D STATUS IN HYPERTENSION AND IT'S COMPLICATIONS"** of the candidate **Dr.M.SOWMIYA** with registration Number **201711369** for the award of **M.D.** Degree in the branch of **GENERAL MEDICINE (I)** is personally verified by me in the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows 0 **percentage** of plagiarism in the dissertation.

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PROTOCOL TITLE: STUDY OF VITAMIN-D STATUS IN HYPERTENSION AND ITS COMPLICATIONS
PRINCIPAL INVESTIGATOR: Dr.M.SOWMIYA, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: PG STUDENT
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Dear Dr.M.SOWMIYA, MBBS, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 15.12.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of The Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of The validity
4. An annual status report should be submitted.
5. The TIREC will monitor The study
6. At The time of PI's retirement/leaving the institute, The study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in The original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and The revised budget form should be submitted.
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   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in The protocol must be informed.

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ACKNOWLEDGEMENT

I wish to express my heartfelt gratitude to our Dean Prof.Dr. S. M. .Kannan M.S., MCh., Tirunelveli Medical College for allowing me to do the study in this institution.

I would like to express my humble thanks to our professor & Head of the Department Prof .Dr .M.Ravichandran M.D., Department of General Medicine.

I express my sincere thanks to my renowned teacher and my guide Dr.S.Alagesan,MD,DM.Professor,Department of General Medicine, Tirunelveli Medical College for his guidance, valuable suggestions and constant encouragement throughout the study.

I am greatly obliged to Dr.T.Grashia,MD, Dr.N.M.SAhmed MD, Dr.T.Vinotha,MD, Assistant Professors, Dept .of General Medicine for their valuable suggestions in preparing this dissertation.

I thank my seniors, my family and the almighty who were beside me in the successful completion of this dissertation.

CONTENT

ABBREVIATIONS

ACE	:	Angiotensin Converting Enzyme
ADA	:	American Diabetes Association
AGE	:	Advanced Glycosylation End products
BMI	:	Body Mass Index
CAD	:	Coronary Artery Disease
CO	:	Cardiac Output
CVA	:	Cerebro Vascular Accident
DALY	:	Disablity Adujsted Lifetime Year
DASH	:	Dietry Advice to Stop Hypertension
ECG	:	Electrocardigram
ECHO	:	Echocardiography
HT	:	Hypertension
LVH	:	Left Ventricular Hypertrophy
RAS	:	Renin Angiotensin System
SVR	:	Systemic Vascular Resistance
T2DM	:	Type 2 Diabetes Mellitus

INTRODUCTION

Hypertension is the most common treatable condition which can be easily diagnosed right from the primary health center which when properly treated can prevent a lot of major complications like myocardial infarction, stroke, renal failure and eventually death.

There are many risk factors which has been identified as a cause of hypertension like obesity, smoking, alcoholism, dyslipidemia. So these factors are now individually approached to reduce the burden of hypertension in the society as a whole.

Vitamin D has long been studied as an important biological molecule which exerts multiple physiological effects. The important function of vitamin D is the maintenance of calcium and phosphate level in the blood to maintain the bone homeostasis.

In recent years it has been studied to have multiple extra skeletal roles. One of the important roles is of which is its importance in hypertension and its complications. Many observational studies has found a significant relationship between vitamin D deficiency and hypertension.

This study is aimed at clarifying the relationship between the above two.

AIMS AND OBJECTIVES

- To compare vitamin D level in hypertensive and normotensive patients
- To compare Vitamin D level in newly diagnosed hypertensive patients and in those with long standing hypertension
- To find out the relationship between vitamin D deficieny and complications of hypertension.

MATERIALS AND METHODS

STUDY CENTRE: Tirunelveli medical college, Tirunelveli.

STUDY DURATION: 2 years

STUDY DESIGN: Case control study

SAMPLE SIZE: 50 patients : 50 controls.

INCLUSION CRITERIA:

Patients with newly diagnosed systemic hypertension attending hypertension OPD and those who are admitted in the medical wards with complications of hypertension and willing to participate in the study after getting informed consent.

EXCLUSION CRITERIA:

- All cases of secondary hypertension
- Patients already taking Vitamin D supplements
- Patients already taking Calcium supplements
- Patients who are not willing to participate in the study
- Patients who are diagnosed to have chronic kidney disease.
- Patient who are diagnosed to have chronic liver disease.

DATA COLLECTION METHODS:

Collection of data as per proforma with consent from patients with systemic hypertension in Tirunelveli medical college medicine wards and in hypertension OPD

SELECTION CRITERIA:

SYSTEMIC HYPERTENSION:

DEFINATION OF HYPERTENSION ACCORDING TO JNC 8

- Systolic blood pressure more than or equal to 140
- Diastolic blood pressure more than or equal to 90

DIABETES:

DIAGNOSTIC CRITERIA ACCORDING ADA RECCOMENDATIONS

- Random blood sugar of 200mg/dl with symptoms of diabetes
- Fasting blood sugar of more than or equal to 126mg/dl
- Postprandial blood sugar of more than or equal to 200
- HBA1c more than or equal to 6.5 %

Random is defined as with no regard to time since last meal. Fasting is defined as no food intake for at least 8 hours.

OBESITY

Body mass index of more than 25kg/sq.m.

MICROVASCULAR COMPLICATIONS

Retinopathy – Retinal changes in fundus examination.

Nephropathy – Presence of microalbumin by urine dipstick method

Left ventricular hypertrophy - presence of LVH in ECG and /or Echocardiography

MACROVASCULAR COMPLICATIONS

Coronary artery disease – History, Ecg, ECHO abnormalities.

Cerebrovascular accidents - History, Examination and Imaging studies

VITAMIN D ESTIMATION:

METHOD – CALORIMETRIC METHOD:

Estimation is done using 25(OH) vitamin D Enzyme Linked Immunosorbant Assay (ELISA) kit.

Dissociation buffer is added to wells coated with donkey anti-sheep IgG antibody. Samples and standards are then added to it to dissociate vitamin D from its binding protein. It is followed by addition of a solution of alkaline phosphatase conjugated 25(OH) vitamin D3 followed by sheep monoclonal antibody to 25(OH) vitamin D.

The mixture is incubated at room temperature, during which the antibody binds the vitamin D in the sample in a competitive manner and by itself is conjugated with anti sheep IgG antibody. The plate is then washed leaving the complex bound with vitamin D from sample. A substrate containing pNpp solution is then added, which initiates an alkaline

phosphatase catalysed reaction that generates an yellow colour in the solution. The resulting yellow colour is read at 450nm. The amount of signal is inversely proportional to the amount of 25(OH) vitamin D in the sample.

REFERENCE VALUES:

Normal level of vitamin D : 30-100 ng/ml

Insufficiency : 6 – 29ng/ml

Deficiency : <6 ng/ml

Toxicity : > 100ng/ml

REVIEW OF LITERATURE

INTRODUCTION

Overview

The cardiovascular system plays a Vital role in sustaining the metabolic demands of all organs by the pumping action of heart. The blood pressure and blood flow can be determined by cardiac output(CO) and systemic vascular resistance (SVR). The cardiac output can be determined by the pumping activity of the heart. There are number of factors which results in the alteration of CO or SVR leading on to alteration from the normal blood pressure.

Most guidelines defines hypertension as systolic BP more than 140 mmHg or diastolic BP more than 90 mmHg, where as normal BP is 120/80 mmHg or lower. The BP level between these 2 ranges is termed as prehypertension or borderline hypertension. Now a days most of the people living in developed as well as developing countries throughout the world will develop hypertension at some point of their lifetime.

The balance between cardiac output and systemic vascular resistance can be influenced by many factors. CO is determined by the pumping action of the heart and volume of blood which is circulating in the body. Sodium regulation and fluid handling ability of the kidney plays a vital role in maintaining the blood volume of the body. Since kidney plays a vital role in balancing the fluid and sodium content of the body, even the

modest impairment of kidney function will cause significant alteration in the fluid volume regulation. SVR depends on blood vessels and it's wall thickness and vasomotor tone. Moreover environmental factors, metabolic factors and humeral milieu can also affects SVR.

Hypertension may be secondary to certain specific causes in 5- 10 % of cases. Correction of underlying cause will completely revert hypertensive patients to normotensive in case of patients who are all having secondary hypertension. In case of primary or essential hypertension, there may be no specific cause. Many factors such as lifestyle changes, age, genetic predisposition, environmental changes may contribute to development of hypertension. Irrespective of its cause, hypertension should be treated to reduce the risk of morbidity and mortality associated with it. At initial stages hypertension may be unnoticed and usually it is not symptomatic. Therefore routine monitoring of BP is necessary to make the diagnosis as early as possible. That's why it may be called as 'silent killer'.

Complications associated with hypertension:

Cardiovascular diseases	Other
Congestive cardiac failure.	Chronic kidney disease
Stroke	Hypertensive nephrosclerosis
Myocardial infarction	End stage renal disease
Left ventricular hypertrophy	Retinopathy
Peripheral arterial disease	

Long standing hypertension causes LV remodelling and ventricular hypertrophy. If not treated it may lead to increased risk of death from cardiovascular disease like myocardial infarction, congestive heart failure and some other complications. Effective treatment of hypertension can reverse the end organ damage and ceases progression of the disease. This is why we need to treat hypertension aggressively to maintain BP at normal levels.

Hypertension and cardiovascular disease.

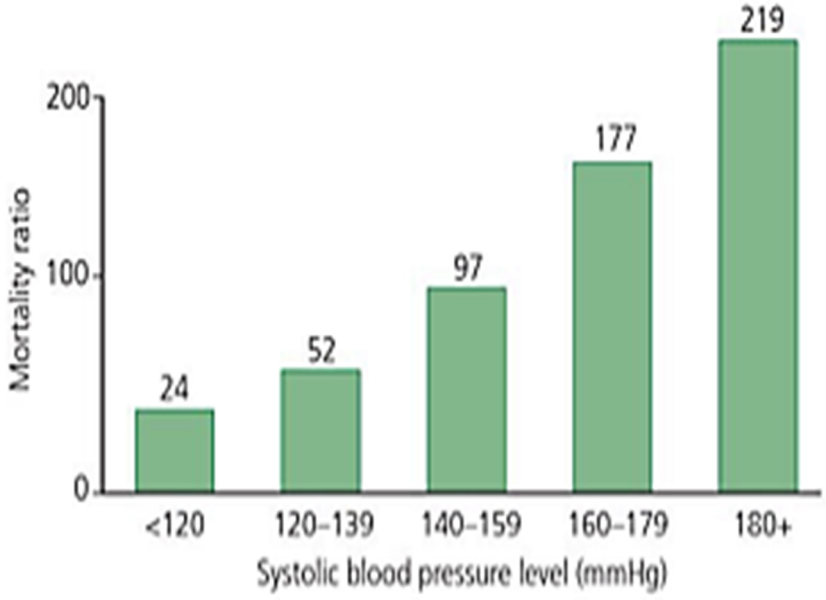
Nowadays CVD becomes the major Global health hazard worldwide. The spectrum of coronary vascular disease includes coronary artery disease, stroke heart failure and other peripheral vascular diseases.Apart from cigarette smoking, diabetes and dyslipidemia, hypertension is considered to be the major risk factor for the development of premature CVD.

Framingham heart study quotes that hypertension is the prime cause for heart disease among men. It has been estimated that 20 % of the first myocardial infarction can be attributed by hypertension in both men and women globally. When compared to men, women with long standing hypertension will end up in stroke rather than myocardial infarction as in men. Most of the trials proves that hypertension is the prime risk factor for predicting hemorrhagic and ischemic stroke.

CARDIOVASCULAR DISEASE AND PREHYPERTENSION:

CVD risk factors are not only pertained to hypertensive patients by traditional definition. Prehypertension can be referred as range of BP between Normal (120/80mmHg) and hypertensive patients (140/90mmHg). Most of the studies conclude that prehypertension is also one of the risk factor for developing the coronary artery disease and stroke. But these studies failed to relate prehypertension with this vascular events since patients with prehypertension are also having additional risk factors such as diabetes mellitus, increased body weight, elevated serum cholesterol level. The relationship between the prehypertension and the CVD can be supported by the antihypertensive therapy. Treatment of patients with prehypertension will have reduced risk of developing the CVD as compared with patients without taking treatment for prehypertension.

The body tries to adapt to higher arterial pressures which leads to disease of the cardiovascular system. The arterial and the vascular tree have some structural changes due to elevated BP which is referred to as remodeling or hypertrophy which causes damage to the organ systems. Due to the higher sheer stress caused by hypertension the larger vessels will undergo arteriosclerosis. This process of arteriosclerosis depends upon the age of the patient, since elder patients have increased risk than the younger patients. Hypertension also plays a vital role in the development of atherosclerosis. A common problem seen in patients with hypertension is the left ventricular hypertrophy (LVH) which occurs due to the thickening of the left ventricle , changes in the left ventricle geometry and increased LV mass. LVH is the preceding risk factor for the development of heart failure, myocardial infarction and Cardiac arrhythmias. Chronic hypertension will be the sole cause for congestive heart failure in majority of the patients.



EPIDEMIOLOGY

"Rule of halves":

Hypertension is one of the 'iceberg' disease. Rule of halves states that 'in the early 1970s , only half of the general population in the developed countries were aware of hypertension, in that only half of them gets treated for hypertension, in that only half of them were adequately treated.

INCIDENCE:

Due to the variability of readings among the population and chronicity of the condition, the concept of incidence in Hypertension has limited value. It has been estimated that 1.13 billion population has been prevailing with hypertension globally in 2015.It has been estimated that overall prevalence of hypertension is 30-40 percent. Genderwise, around 24 and 20 percent in males and females respectively. The prevalence of hypertension is irrespective of the income status globally, i.e., its prevalence can be seen in lower, middle and higher income countries. Prevalence of hypertension in more common in the elderly age groups that is age more than 60 years. This contributes around 60 percent in the total hypertensive population. Due to the sedentary life style and increased weight in the population, it was estimated that the prevalence of hypertension would be increased by 15-20 percent by the year 2025. Hypertension is the leading cause for premature deaths and Disability

adjusted life years (DALY) for more than 200 million population. Although there are recent advances in the modern medicine, DALYs have been increased in the recent past due to the ineffective control of blood pressure and lack of awareness among the population.

PREVALENCE IN INDIA:

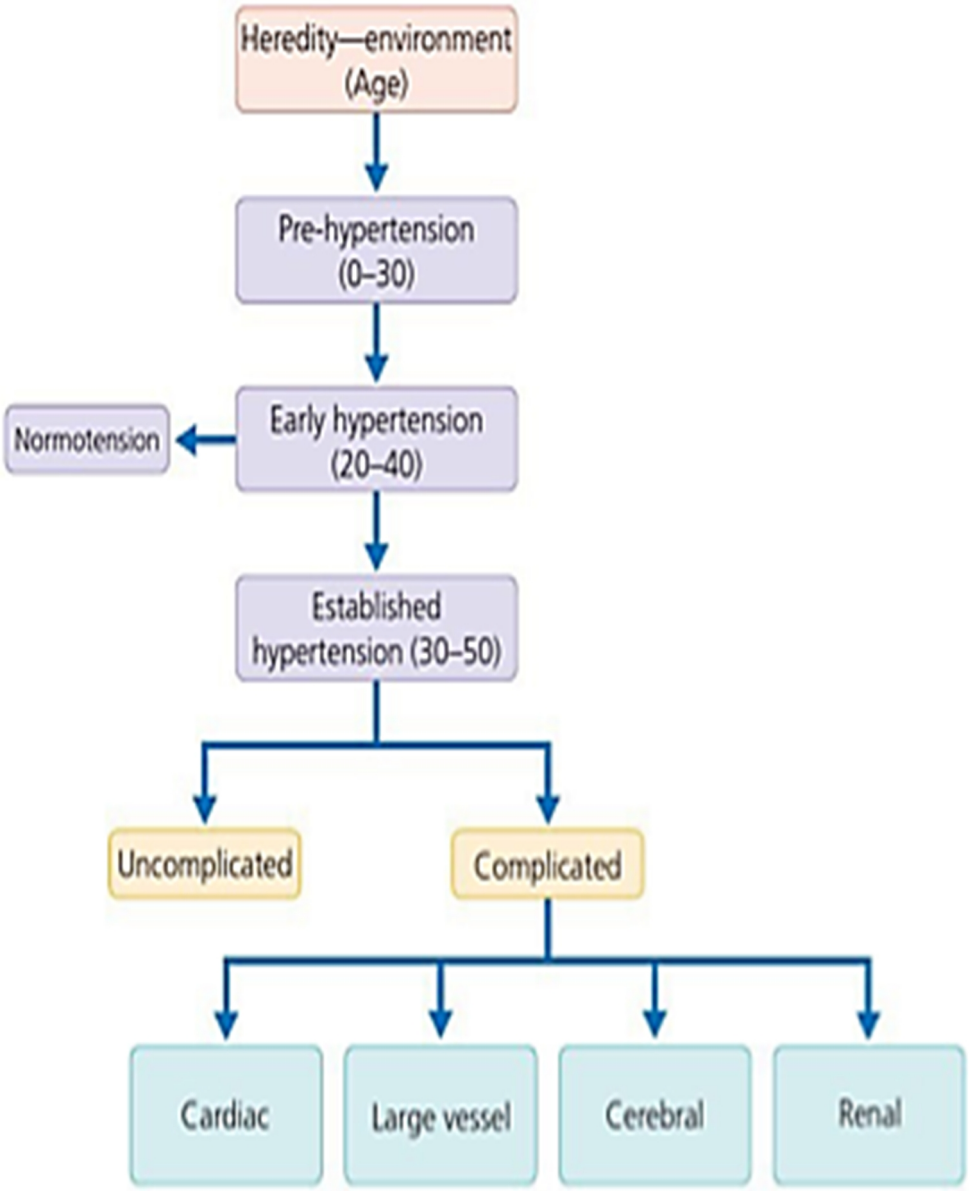
In the year 2015, National family health survey conducted a study on hypertension. The study reveals that prevalence of hypertension was somewhat higher in men than women in the age group of 15-49 years. Among men 15% where hypertensive, 43% have normal blood pressure and the same percentage have pre hypertensive and only 1% were on antihypertensive medications. The study also reveals that the prevalence of hypertension increases with age for both men and women.

Prevalence of hypertension increases consistently with the increased body mass index for both men and women. 38% of obese men and 29% of obese women were found to have hypertension. At the age group of 15-49, prevalence of hypertension ranges from 8% in Bihar to 18% in Sikkim and Assam for women. For men it ranges from 6 % in Delhi to 31% in Sikkim. For men and women, the North Eastern states have a higher prevalence than the national average.

Tracking" of Blood pressure

In a community, if the blood pressure levels were followed up from the early childhood to adult life, those who have low blood pressure at

their early childhood period tends to have lower blood pressure in their adult age and those who were having high blood pressure in their childhood period tends to have high level of blood pressure in their adult age. This phenomenon of persistence of rank order of blood pressure has been called as "Tracking". This knowledge can be applied in identifying the children and adolescents who were all at risk of developing hypertension.



Risk factors for hypertension:

According to WHO scientific group, risk factors for hypertension can be classified into Non modifiable and Modifiable risk factors.

1. Non- modifiable risk factors

- Age- blood pressure consistently rises as the age increases
- Sex- Men will be affected more common than women, but women in post menopausal age group have higher risk
- Genetic factors
- Ethnicity- Black Americans of African origin have higher blood pressure when compared to whites.

2. Modifiable risk factors

- Obesity- Central obesity which has been indicated by increased waist to hip ratio. Central obesity has better correlation with elevated blood pressure.
- Salt intake: Numerous studies states that increased salt intake per day that is more than 7 to 8g/day has been better correlated with the elevated blood pressure.
- Saturated fat
- Dietary fibre: Studies states that consumption of decreased amount of dietary fibre will lead on to hypertension.
- Alcohol: High intake of alcohol for the prolonged period will leads to elevated blood pressure

- Heart rate: When the normotensive and untreated hypertensive population matched for age and sex are compared, hypertensive group have somewhat higher heart rate than the normotensive patient. This reflects that the untreated hypertension may have increase sympathetic activity.
- Physical activity: Decrease in the physical activity will leads to elevated blood pressure. So hypertension is more common with the population with sedantary lifestyle.
- Environmental stress

All studies reveals that patients with hypertension have increased level of catecholamine than the normotensive population. This supports that hypertension can be due to the over activity of the sympathetic nervous system.

- Socio economic status

Nowadays hypertension can be seen in both higher and lower socioeconomic status.

- Other factors

Oral contraception remains one of the cause for hypertension in some population because of its estrogen component. Some of the other factors such as noise, vibration, temperature and humidity may require further investigations.

Vitamin D deficieny is also being investigated as causal factor for hypertension. The pathogenesis studied in correlating these two factors is involving the rennin angiotensin system.

MECHNISMS OF HYPERTENSION:

To understand the mechanism of hypertension, we need to know the factors affecting the normal and elevated blood pressure. The two main factors are cardiac output and peripheral vascular resistance. Cardiac output inturn is a product of stroke volume and heart rate. Stroke volume depends on the myocardial contractility and the size of the vessel. Peripheral vascular resistance depends on the anatomical and functional alterations in the vessel lumen of the arteriolar and small arteries.

INTRAVASCULAR VOLUME:

The intravascular volume depends on the extra cellular volume and the interstitial volume of the blood. This volume is primarily maintained by extra cellular sodium. so, as the sodium intake increases the intravascular volume and the proportional cardiac output also increases. But, most of the organs have autoregulatory regulation of blood pressure, so the resistance of the blood vessels in the specific organs increases to combat the increase flow. In long course of time, the resistance increases and the cardiac output falls. This hypothesis is not proved yet. Contrary to

this hypothesis is that non chloride forms of sodium have minimal effect on blood pressure

Another hypothesis is that as the sodium load increases, there occurs pressure natriuresis to maintain the sodium balance at the expense of increased blood pressure. The best model for the fact that intravascular volume increases the blood pressure is that volume overload status in end stage renal disease due to defective excretion of sodium resulting in secondary hypertension. This fact is further supported by the thing that most of this resistant hypertension secondary to ESRD respond well to the dialysis.

AUTONOMIC NERVOUS SYSTEM :

This mechanism play an another important role in the pathophysiology of hypertension. The sympathetic nervous system acts via the neurotransmitters such as epinephrine, nor epinephrine and dopamine .The epinephrine acts more on the beta 1 receptors whereas alpha receptors are more sensitive to norepinephrine. Chronic state of excessive catecholamines such as pheochromocytoma causes down regulation of alpha receptors which is responsible for the paradoxical orthostatic hypotension in these individuals. The alpha 1 receptors are post synaptic in nature which modulates smooth muscle contraction and vasoconstriction while the alpha 2 receptors are pre synaptic in location which decreases the synthesis of norepinephrine thus lowering the blood pressure.

Many reflexes modulating the blood pressure are present. One such is baroreceptor reflex .The baroreceptors are present in the carotid sinus , aortic arch and the left ventricle. As the blood pressure increases, these receptors gets activated causing reflex reduction in heart rate and blood pressure. However, when blood pressure is persistently high, these receptors gets downregulated and they uplift the setting point of blood pressure.

Hypertension related to obesity and obstructive sleep disorders are also due to increased sympathetic over activity. Hypertension in pheochromocytoma patients and the control of it after the removal of tumour is the live example for the role of adrenergic system in the pathophysiology of hypertension. This leads on to the novel treatment strategy of baroreceptor activation through electrical stimulus in cases of resistant hypertension.

THE RENIN- ANGIOTENSIN SYSTEM (RAS) : A CENTRAL REGULATOR OF BLOOD PRESSURE

The RAS cascade and its functions

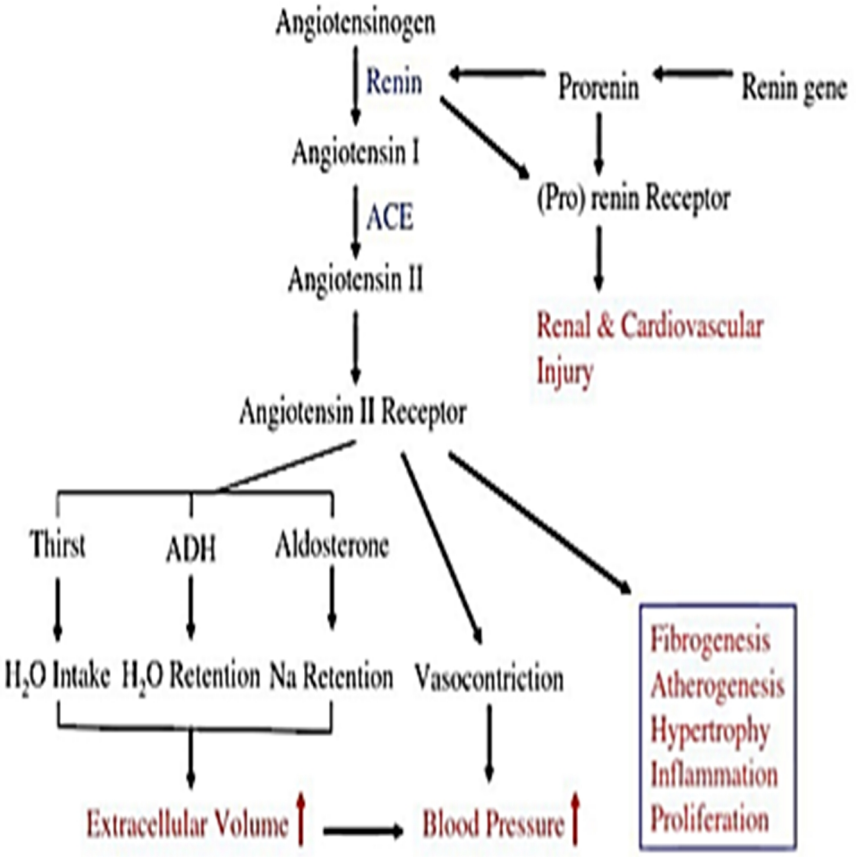
RAS consists of multiple components which makes it as a systemic endocrine regulatory cascade. Angiotensinogenn (AGT) which is the predominent substrate of this cascade is produced mainly in the liver. The rate limiting step of RAS cascade is cleavage of AGT to Angiotensin (Ang) 1 in the circulation by Renin. Ang 1, an inactive decapeptide is

converted to Ang 2, an active octapeptide by Angiotensin converting enzyme (ACE) which is mainly present in the endothelial cells of blood vessels. Aminopeptidase A and N cleaves Ang2 further and produces Ang3 and Ang4. ACE2 , an ACE analog converts Ang2 to Ang (1-7) and this enzyme plays vital role in cardiac function.

Ang2 plays a central role in blood pressure regulation and it is also the central biological effector of RAS. Ang2 through its action on smooth muscle cells of the vasculature, it increases the tone of the vessel and it is considered as the important vasoconstrictor and thus it increases the peripheral vascular resistance. It also promotes the secretion of aldosterone from the adrenal cortex. Ang2 stimulates the release of vasopressin otherwise called as antidiuretic hormone from the posterior pituitary which helps retention of water by the kidney. Vasopressin also enhances the sensation of thirst by the activation of central nervous system and thus it increases the water intake. Thus activation of RAS cascade causes increased extracellular volume and systemic vascular resistance. Over activation of RAS cascade in combination with cardiac output and increased peripheral vascular resistance results in hypertension. Ang2 has other physiological and pathological activities in addition to blood pressure control. Fibrogenesis, atherogenesis, inflammation, cell hypertrophy and proliferation are some of the activities in which Ang2 plays the role. So, excessive activation of Ras cascade results in deleterious effects.

RAS have also been present in many tissues apart from systemic RAS, which includes brain, blood vessels, kidney, heart and reproductive system. Tissue- specific RAS gets activated by paracrine fashion and sometimes it causes tissue damages.

Several G protein coupled receptors widely present in the body mediates the actions of Ang2. There are two Angiotensin receptors - Type 1 receptor (AT1) and Type 2 receptor (AT2). AT1 activation mediates most of the actions such as vasoconstriction, sodium retention, hypertrophy. AT2 activation results in vasodilation, natriuresis and growth inhibition. Hypertension and its complications are due to over activation of the RAS mediated by AT1.



Renin, the Rate- limiting Enzyme of RAS cascade:

Renin consists of two beta-sheet domains in which the active site resides between these two domains. Renin is highly specific for AGT and it is also species-specific. Renin is secreted as an inactive precursor prorenin by the juxtaglomerular cells from the media of afferent arteriole in glomerulus. Renin is readily secreated through exocytosis, since it is stored in the secretary granules. Usually the plasma concentration of prorenin is much higher than that of renin i.e., 10-100 times than that of renin. Some of the studies have shown that prorenin can be activated by some endopeptidases like trypsin, cathepsin B. But how these endopeptidases activates prorenin and what is its physiological role is clearly understood. High renin activity can leads to activation of RAS cascade which in turn causes hypertension and other complications of hypertension.

Renin receptor is identified initially in the mesangial cells and vascular smooth muscle cells. This receptor binds both renin and prorenin with high affinity. Binding of renin or prorenin to its receptors initiates intracellular signalling and phosphorylation processes independent of Ang2 production. Increased renin/prorenin and over activation of its receptors leads to synthesis some profibrotic cytokines such as TGF-beta which causes detrimental effects. This process is independent to Ang2.

Since renin plays the central role in RAS cascade, its production and action are tightly regulated. The factors which regulates the renin secretion are

1. Renal perfusion pressure
2. Renal sympathetic activity
3. Tubular NaCl load

- Reduced Renal perfusion causes increased renin secretion. This is mediated by the baroreceptors present in the juxtaglomerular apparatus.
- Juxtaglomerular apparatus have increased sympathetic nerve endings, its stimulation results in renin synthesis.
- In case of tubular control for renin release, there is an inverse relationship between renin secretion and tubular sodium chloride load. The macula densa which is the part of the distal tubule lies adjacent to the JG cells senses sodium chloride load and influences the renin secretion. Some of the local bioactive molecules such as nitric oxide, prostaglandins, adrenomedullin stimulates renin secretion whereas Ang2, vasopressin, adenosine, endothelin suppresses renin secretion. The feedback inhibitor of renin production is Ang2. It exerts its action through AT1 receptor. Multiple transcriptional factors such as cAMP, retinoic acid, cytokines, endothelin 1 are involved in the secretion and regulation of renin by altering the gene expression.

Since RAS cascade plays the major role in regulation of blood pressure, it has been the major target for the treatment of hypertension. ACE Inhibitors(ACEI), Ang2 type 1 receptor blockers (ARB) and renin inhibitors major class of drugs used in the treatment of hypertension which intervene the RAS. ACEI's and ARB's are the widely used Anti hypertensive drugs. There are some undesired side effects associated with ACEI and ARB which reduces its efficacy. They are

- Ang1 can be converted to Ang2 by some other enzymes like chymase rather than ACE.
- Since ACE metabolizes Bradykinin also. ACE inhibition causes elevation of bradykinin which results in adverse effects.
- Blocking of type 1 receptors by using ARBs leads to increased availability of Ang2 to Type 2 receptor leads to various unwanted effects.
- Chronic treatment with ACEI's leads to compensatory increase in renin concentration. This is due to the disruption in the feedback inhibition loop of renin metabolism which leads to increase in the production & secretion Renin. This phenomenon is called as " ACE escape". This adverse effect of increased renin concentration has also been found with Renin inhibitors (Aliskiren). Therefore for the adequate control of Blood pressure for the prolonged period, we

need an agent which blocks the compensatory increase of renin thereby enhancing the efficacy of RAS inhibitors.

VASCULAR MECHANISMS:

The vascular diameter and the compliance of the arterioles and arteries plays a key role in maintaining the blood pressure. Resistance to the blood flow is inversely propotional to the fourth power of radius.so, a small change in diameter of the blood vessel contributes much to the increase in blood pressure. So ,any anatomical and functional changes in the vessel wall reflects in the blood pressure. Low grade inflammation, vascular fibrosis lead on to the stiffening of arteries thus decreasing its elasticity and increases its pressure.

There is a definite difference between the central aortic pressure measured invasively and the brachial artery pressure. In hypertension, there is increase in aortic systolic pressure and decrease in the aortic diastolic pressure, thus increasing the pulse pressure. This is calculated by an index called as **aortic augmentation index which is the ratio of central aortic pressure and the pulse pressure**. It is considered as a marker of arterial stiffening which correlates well with the all cause mortality due to blood pressure.

Many ion channels are involved in the pathophysiology of hypertension. One such is the Na-H+ exchanger. The activity of this channel is found to be augmented in hypertension. The proposed mechanisms for its role are,

the increased sodium entry enhances the Na+-Ca2+ exchanger which increases the intracellular calcium and thus increasing the vascular tone. The other mechanism is that the resultant increase in pH increases the calcium sensitivity of the contracting unit. They also increase the growth of vascular smooth muscle cells.

Vascular endothelium does its role in maintaining blood pressure by secreting vasoactive substances such as nitric oxide, a vosodialator and endothelium, a potent vasoconstrictor. Alterations in the secretion of these substances is documented in hypertensive patients. But it is not known whether it is a cause or effect of hypertension.

INFLAMMATION:

Increased circulatory levels of autoantibodies are found in essential hypertension patients. Inflammation has resulted in increase in reactive oxygen species generation which decreases the endothelial nitric oxide production. The ROS also plays a significant role in pressure natriuresis.

So here I conclude the major pathophysiological mechanisms of hypertension.

END ORGANS DAMAGE IN HYPERTENSION:

HEART:

Heart is the most commonly affected organ in hypertension. The pathological consequences can be due to left ventricular hypertrophy, systolic or diastolic dysfunction, accelerated atherosclerosis of the

coronary vessels, microangiopathic complications and sometimes with rhythm disturbances such as atrial fibrillation. Among, these diastolic dysfunction of the heart is earliest complication of hypertension.

BRAIN :

Stroke is the second most common cause of death in the world and hypertension is the prime cause for it. Eighty percent of patients experience ischemic stroke while the reminder causes hemorrhagic stroke. There is direct definite correlation between the incidence of stroke and the presence oh hypertension in patients more than 65 years of age.

Other than stroke, hypertension is also attributed for the cognitive decline in elderly patients. An association has been found between the middle age hypertension and late age cognitive decline. The mechanisms involved are beta amyloid deposition, infarcts due to occlusion of a major cerebral artery or multiple subcortical small vessel infarcts.

Hypertensive encephalopathy, a result of malignant hypertension characterised by severe headache, nausea, vomiting, focal neurological deficits, altered sensorium which can progress to stupor, coma and death if left untreated. It is because of the failure of auto regulation of blood pressure in the brain during malignant hypertension. It is important to distinguish hypertensive encephalopathy from other causes of altered sensorium in these patients.

KIDNEY :

Kidney can be both the cause and effect of hypertension. Renal diseases are the important cause of secondary hypertension. The pathophysiology underlying this is the impaired excretion of salt and water and increased secretion of renin and sympathetic over activity. The damage to the kidneys depend on the systolic than a diastolic blood pressure.

Hypertension and atherosclerosis mainly affects the afferent arterioles of the glomerulus resulting in hyperfiltration, glomerular hypertrophy and nephron loss which further increases the blood pressure thus perpetuating a vicious cycle of kidney damage and hypertension.

Pathologically, the afferent arterioles demonstrates fibrinoid necrosis which can sometimes affects the glomerular tufts too. Clinically, it is evident by the presence of micro or macro albuminuria.

PERIPHERAL ARTERIES:

Like kidneys, the peripheral arteries can also be the cause as well as effect of hypertension. Hypertension causes accelerated atherosclerosis of the peripheral arteries which forms the basis of myocardial infarction and stroke. Ankle brachial index is the ratio of blood pressure of ankle and the arm. It is a noninvasive marker for peripheral vascular disease. Ankle brachial index less than 0.9 is indicative of peripheral vascular disease and less than 0.8 is indicative of isolated systolic blood pressure.

HYPERTENSION DEFINATION :

Clinically, hypertension is defined as the level of blood pressure at which initiation of antihypertensive therapy prevents the complications associated with increased blood pressure.

BLOOD PRESSURE CLASSIFICATION:

Blood pressure classification.	Systolic, mmhg.	Diastolic, mmhg.
Normal	**< 120**	**<80**
Prehypertension	**120-139**	**80-89**
Stage 1	**140-159**	**90-99**
Stage 2	**>_160**	**>_100**
Isolated systolic hypertension	**>_140**	**<_90**

Ambulatory blood pressure monitoring is preferable to once a day clinical blood pressure measurement. Blood pressure seems to be little high in the morning for about 20 mmhg and dips in the night. Absence of midnight dipping in the blood pressure is associated with increased cardiovascular events.

. Illustrative examples of possible discrepancies in the measurement of blood pressure.

BP measurement method	Threshold for stage 1 hypertension	Threshold for stage 2 hypertension
Clinic BP reading	140/90 mm Hg	160/100 mm Hg
Ambulatory BP reading	135/85 mm Hg	150/95 mm Hg

WHITE COAT HYPERTENSION:

Increase in office BP but ambulatory BP monitoring being in normal range is called as white coat hypertension. These people are not associated with all the risks associated with hypertension

MASKED HYPERTENSION:

Normal office BP but increased ambulatory blood pressure is called as masked hypertension. These patients are associated with all the complications associated with hypertension.

An appropriate sized cuff should be used for the accurate measurement of blood pressure. The arm circumference and the cuff length should be as follows

Arm circumference	Cuff name	Cuff size
22-26 cm	Small adult	12 x 22 cm
27-32 cm	Adult	16 x 30 cm
35-44 cm	Large adult	16 x 36 cm
45-52 cm	Adult thigh	16 x 42 cm

SECONDARY CAUSES OF HYPERTENSION:

1. Renal causes :

Parenchymal renal diseases, renal tumours, renal cysts such as ADPKD OR ARPKD, obstructive uropathy

2.Renovascular causes:

Atherosclerosis of the renal arteries, Fibromuscular dysphasia of the renal arteries

3.Endocrine causes :

Primary hyper aldosteronism, Cushing syndrome, pheochromocytoma, Congenital adrenal hyperplasia, licorice ingestion,Hypothroidism,Hyperthyroidism,Acromegaly,Hypercalcemia.

4.Coarctation of aorta

5.Obstructive sleep apnoea

6.Neurogenic causes:

Acute intermittent porphyria, increased intracranial tension, acute cord transaction, psychogenic, familial dysautonomia.

6.Drug induced :

Steroids,Oral contraceptive pills,cyclosporine, Tricyclic anti depressants,erythropoietin, NSAIDS, MOA inhibitors, Cocaine, Nasal decongestants.

7.Rare Mendalian forms of hypertension.

APPROACH TO HYPERTENSION:

The initial assessment for hypertension includes complete history, physical examination and relavent lab investigations.

HISTORY:

History includes duration of hypertension, family history of hypertension, treatment history and its responsiveness, personal history of smoking, alcoholism, dietry pattern, history relavent to the evidence of secondary hypertension such as history of renal diseases, spells of anxiety, sweating and palpitations, symptoms of hyperthyroidism or hypothyroidism, history of any chronic drug intake.

PHYSICAL EXAMINATION:

The relevant clinical examination includes height of the individual, blood pressure in all the 4 limbs, checking for orthostatic hypotension, fundus

examination for retinopathy screening, abnormal vascular bruits, heart rate and rhythm.

LABORATORY INVESTIGATIONS:

Renal function tests, Urinalysis to look for micro or macroalbuminuria, serum electrolytes, thyroid profile, lipid profile, fasting blood sugar and ECG

TREATMENT OF HYPERTENSION:

NON PHARMACOLOGICAL METHODS:

These primarily includes life style modifications such as weight loss, quiting of smoking and alcoholism, reduction of dietry sodium intake and increased potassium intake.

Weight loss of around 10 kg is associated with reduction in BP of about 3 to 6 mmhg. A regular excercise of around 30 minutes per day for 6 days a week is advised. Reducing salt intake to 4 to 7 grams per day is associated with reduction of blood pressure of about 3 to 4 mmhg. Increased potassium supplementation also reduces the mortality due to stroke, dietry protein restriction reduce the renal complications of hypertension.

DASH (DIETRY ADVICE TO STOP HYPERTENSION) is a trial which advices that a diet rich in vegetables, fruits and low fat dietary products associated with reduced salt intake has a role in reduction of blood pressure.

PHARMOCOLOGICAL THERAPY:

The choice of the pharmacological agent depends on the age of the patient, severity of hypertension, other comorbidities present, cost and frequency of the medications and its adverse effect profile.

DIURETICS:

Thiazides reduce the blood pressure effectively when used alone or in combination with other antihypertensives by inhibiting the Na+/cl- pump in the distal convoluted tubule. The adverse effects are hypokalemia, hyper urecemia, insulin resistance, increased cholesterol. Loop diuretics are generally reserved for use in renal failure, congestive heart failure and edematous patients.

RAAS INHIBITORS:

These includes ACE inhibitors and ARBs. ACE inhibitors prevent the conversion of angiotensin 1 to angiotensin 2 while the ARBs selectively block the AT1 receptors and mitigate the action of angiotensin. Both these drugs effectively lowers the blood pressure. This class is also believed to reduce the risk of diabetes in high risk hypertensive patients.

The adverse effects include functional renal insufficiency due to efferent arteriolar dialation especially in subjects taking NSAIDS, and those who are in dehydration and congestive heart failure. Hyperkalemia, angioedema, chronic cough are other side effects.

A new blockades for RAAS has been found to be due to direct thrombin inhibitor called as Alisakiren. But it is not considered as first line antihypertensive as of now.

ALDOSTERONE ANTAGONISTS:

This group includes non selective aldosterone antagonist spirinolactone and selective antagonist eplerenone. These drugs are more useful in conditions of secondary hypertension due to primary hyperaldosteronism and cases with associated heart failure, in whom it has mortality benefit. Adverse effects include gynaecomastia, menstrual abnormalities, impotence which can be overcome by selective antagonists.

BETA BLOCKERS:

They decrease the blood pressure by decreasing the cardiac output by reduction in heart rate and contractility of the heart. They are particularly helpful in cases with reduced ejection fraction as they decrease the mortality and hospitalisation of those patients.

ALPHA BLOCKERS :

They reduce the blood pressure by binding to the post synaptic alpha receptors there by causing vasodilation and decrease in blood pressure. But they have no proven cardiovascular benefits. They are preferred in patients with concomitant benign prostatic hypertrophy and in pheochromocytoma.

SYMPATHOLYTIC DRUGS :

These drugs reduce the pre synaptic sympathetic outflow thus reducing the adrenergic drive and causes vasodilation. These drugs are effective antihypertensives but are limited by adverse effects such as dry mouth, sleepiness, many drug interactions, withdrawal rebound hypertension.

CALCIUM CHANNEL BLOCKERS :

They reduce the blood pressure by reducing the vascular tone by inhibiting L-type calcium channel and reduces the vasoconstriction.T hey are of two class including dihydropyridines and non dihyrdopyridines. The latter group causes pedal edema due to capillary vasodilation, flushing and headache.

DIRECT VASODIALATORS:

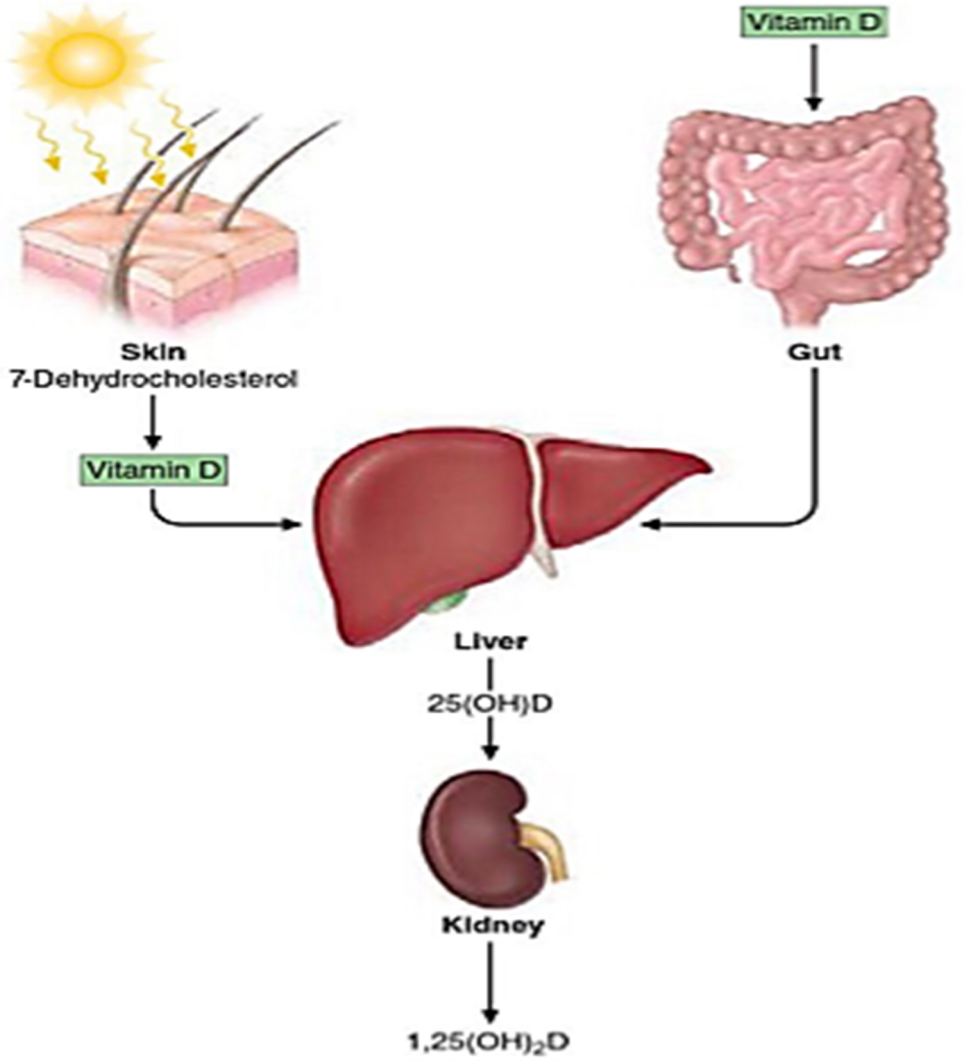
They reduce the blood pressure by direct vasodilator action but they concominantly increase the reflux sympathetic over activity as well as renin secretion.so they are not used as first line drugs. But when they are used along with beta blockers and diuretics they are very effective. Hydralizine, Nitroprusside, Minoxidil belongs to this class which are frequently used in hypertensive emergencies and refractory hypertension.

RESISTANT HYPERTENSION :

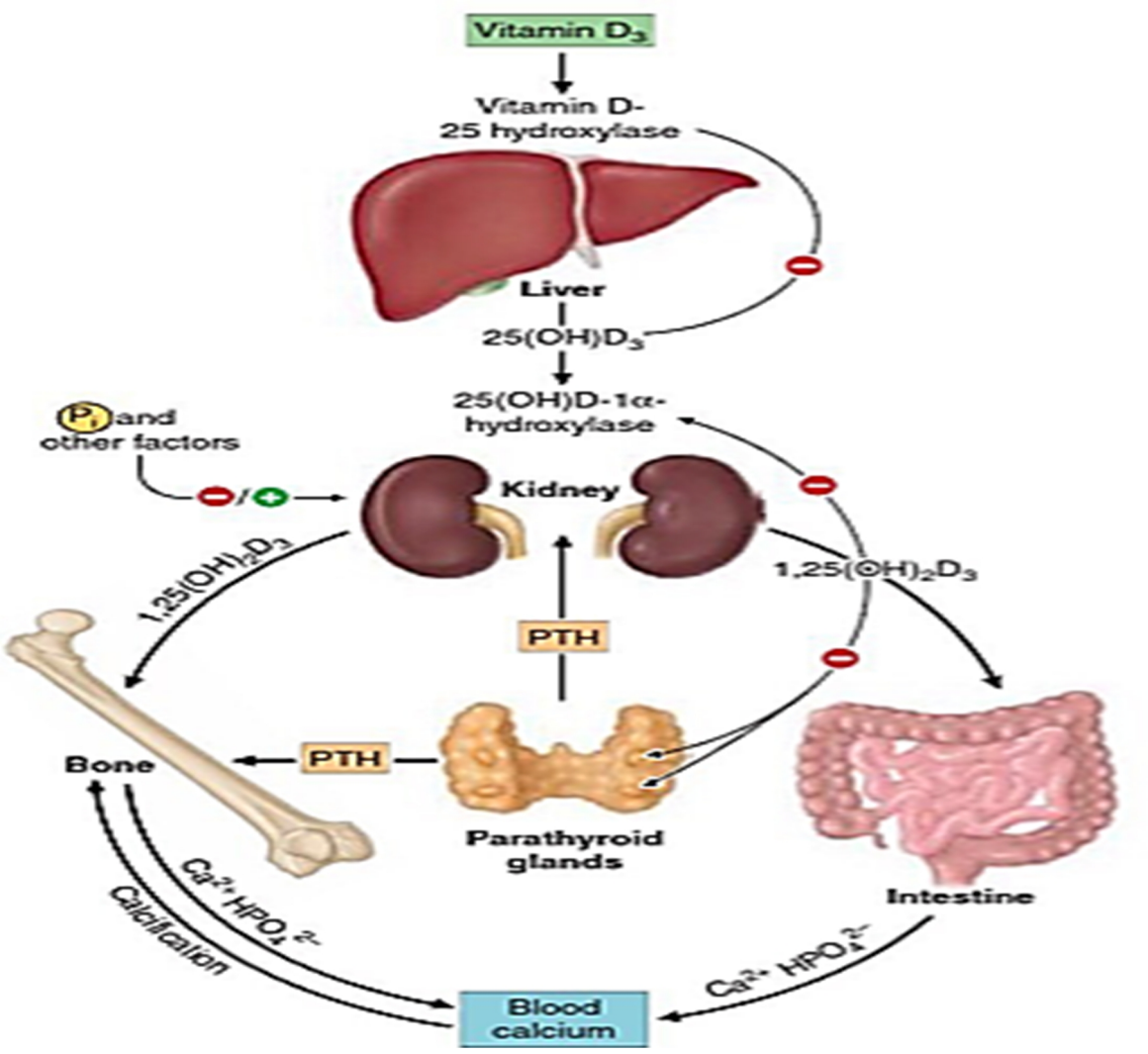
It is defined as blood pressure more than 140/90 mmhg inspite of taking 3 or more antihypertensives including a diuretic. Secondary hypertension and pseudo hypertension has to be ruled out in these patients.

VITAMIN D

Vitamin D is essential for stimulation of absorption of calcium from the gut. It is activated first in the liver to form 25 hydroxy vitamin D and then it undergoes another hydroxylation in the proximal tubules of kidney to form 1,25 hydroxy vitamin D3 which is the final active form.



ACTIONS OF VITAMIN D IN CALCIUM HOMEOSTASIS :



Apart from these known skeletal actions of vitamin D, it has been linked in many extra skeletal diseases such as multiple sclerosis, type 2 diabetes, role in cardiovascular diseases, role in hypertension, chronic kidney disease, Rheumatoid arthritis, Respiratory infections and obstructive airway diseases. Here we will briefly discuss about its role in hypertension.

VITAMIN D REGULATION OF RENIN-ANGIOTENSIN SYSTEM

Vitamin D: Negative Endocrine Regulator of the Renin- Angiotensin system.

Until two decades ago the relationship between 1,25 (OH)2 D (Calcitriol - active form of Vitamin D) and Plasma Renin activity was unclear. It was Li et al. who first demonstrated that calcitriol influences the regulation of Renin production and secretion through Gene expression. Calcitriol functions as the negative endocrine regulator of Renin. This theory was demonstrated by Vitamin D receptor (VDR) - Null mutant mice. VDR Null mutant mice develops elevated plasma levels of Renin due to the lack of VDR - mediated Vitamin D signaling. Hyperreninemia was evidenced by mRNA and protein levels which results in dramatic elevation of Renin level. These mutant mice develops higher blood pressure and cardiac hypertrophy. These effects can be corrected by ACEI or ARB. Moreover, plasma renin levels are found to be significantly reduced in wild-type mice receiving several doses of calcitriol injection. These findings strongly supports that calcitriol functions as the negative regulator of plasma renin levels in vivo.

This phenomenon can also be supported by another genetic mutant mice model Zhou et al. demonstrated this genetic study. Cyp27b1 is the gene responsible for the functional activity of the enzyme 1 alpha hydroxylase. It is the rate limiting enzyme in the Vitamin D biosynthesis.

Like VDR knock out mice, Cyp27b1 knock out mice also develops hyperreninemia and leads on to hypertension and cardiac hypertrophy. In this model, these adverse effects are treated by exogenous calcitriol supplementation in addition to ACEI and ARBs.

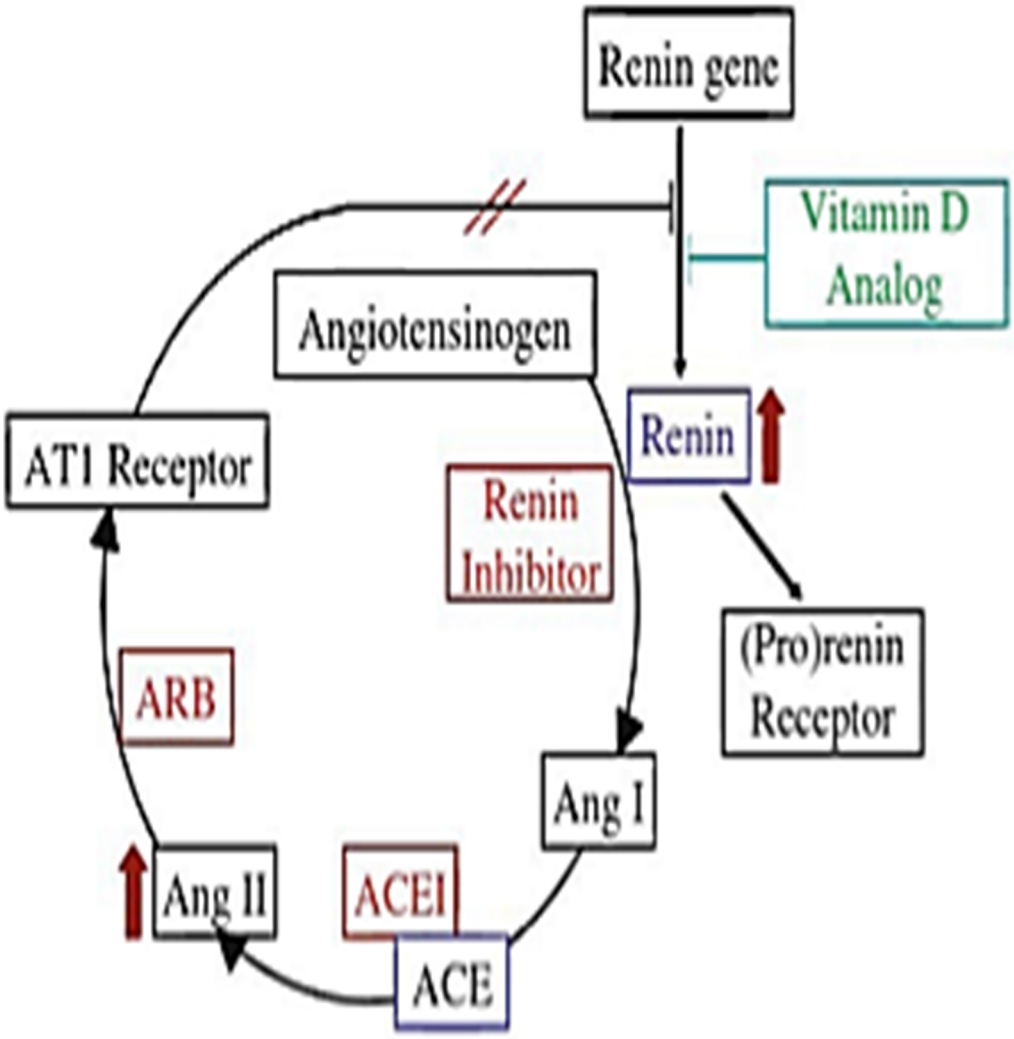
This phenomenon was further confirmed by Kong et al. They produced a transgenic mice with over expression of human VDR in the juxtaglomerular cells. The plasma renin levels are found to be significantly depressed in these transgenic mice without changes in the serum calcium or parathormone levels. These data states that calcitriol suppresses Renin expression in vivo independent of parathormone and calcium.

Based on these experiments, It was found that prolonged Vitamin D insufficiency leads to elevated blood pressure, whereas supplementation of vitamin D may be beneficial to the cardiovascular system by decreasing the blood pressure.

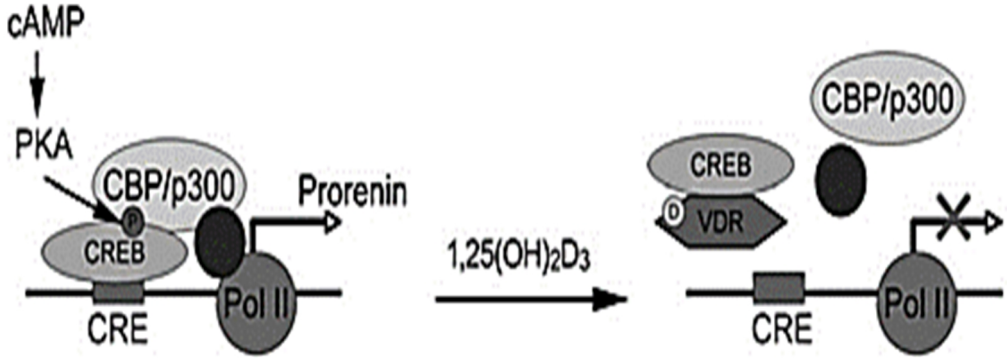
Mechanism of Renin suppression

VDR is a ligand- activated transcriptional factor. It regulates both positive and negative transcriptions. Vitamin D response element (VDRE) mediates most of the positive regulations by VDR. There are numerous mechanisms for negative regulations. Intracellular cAMP stimulates the renin expression when the sympathetic nerve activity is high or when there is low tubular sodium chloride concentration. Calcitriol targets the cAMP

signaling pathway and that's how it suppresses the Renin expression. This was first demonstrated by Yuan et al.



The cAMP signals through the cyclic AMP response element (CRE). CRE then interacts with some transcription factors like ATF/CREB/CREM bZIP. Interacellularly ATP is converted into cAMP and this cAMP binds with protein kinase A (PKA) which causes phosphorylation. This results in the recruitment of co-activators to promote gene transcription.



CAMP response element has been shown to play a vital role in the gene expression of renin. Calcitriol suppresses the renin gene transcription by direct inhibition of CRE - mediated trancriptional activity.

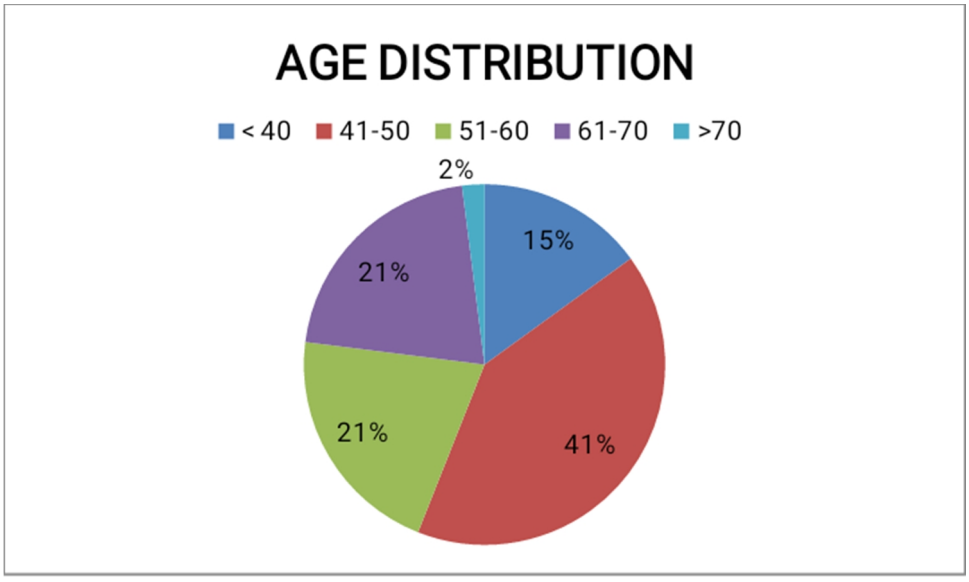
It has been proved that calcitriol suppresses the Renin expression by blocking the cAMP pathway and thereby preventing the deleterious effects due to hyperreninemia.

RESULTS

TOTAL PATIENTS–100

Table 1: AGE DISTRIBUTION

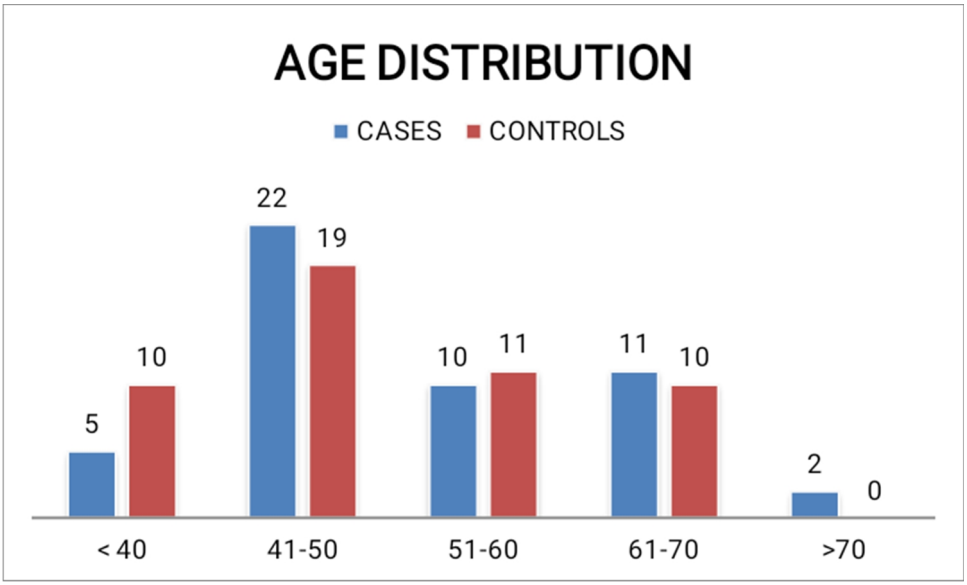
AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
<40	15	15%
41-50	41	41%
51-60	21	21%
61-70	21	21%
>70	2	2%



The Age of the cases as well as control are comparable

Table 2: AGE DISTRIBUTION : CASE VS CONTROL

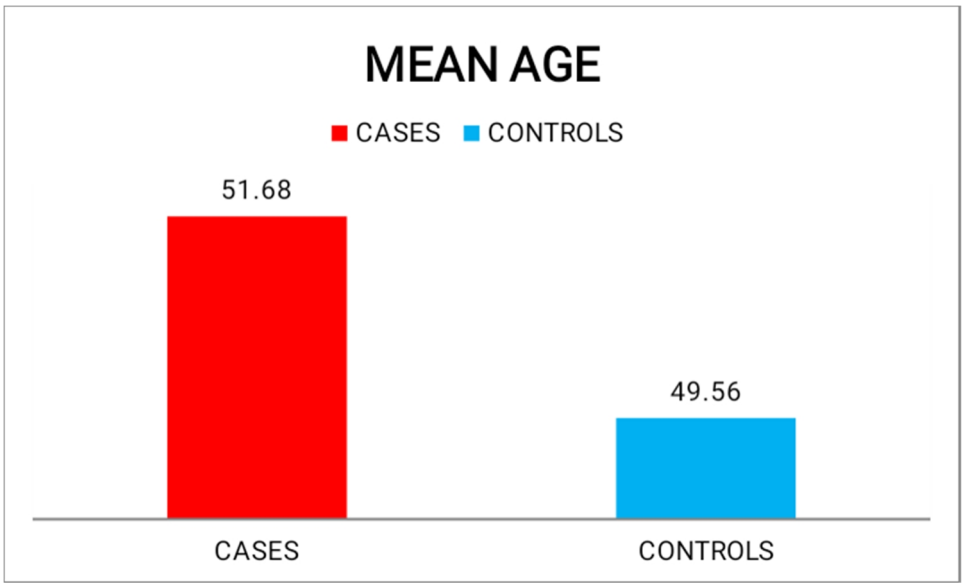
AGE IN YEARS	CASES	CONTROLS
<40	5	10
41-50	22	19
51-60	10	11
61-70	11	10
>70	2	0



The mean age of case is 51 and the control is 49

Table 3: MEAN AGE: CASE VS CONTROLS

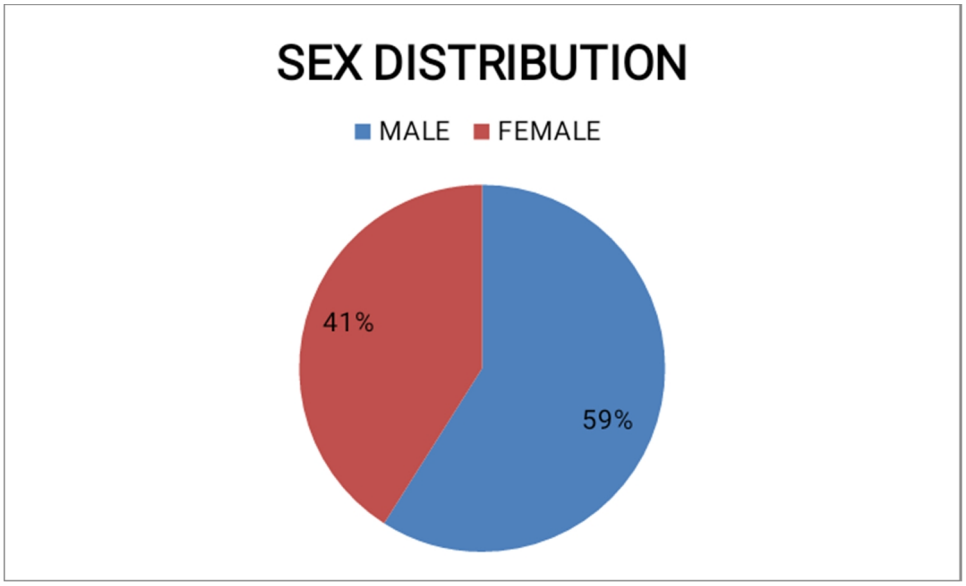
GROUP	AGE IN YEARS	
	MEAN	SD
CASES	51.68	9.89
CONTROLS	49.56	10.56
UNPAIREDTTEST		
PVALUE-0.303		
NONSIGNIFICANT		



The mean age of case is 51 and the control is 49

Table 4: SEX DISTRIBUTION

SEX	NO OF PATIENTS	PERCENTAGE
MALE	59	59%
FEMALE	41	41%



The study constitutes 59% of males and 41 % of females

Table 5: SEX DISTRIBUTION

SEX	CASES	CONTROLS
MALE	29	30
FEMALE	21	20

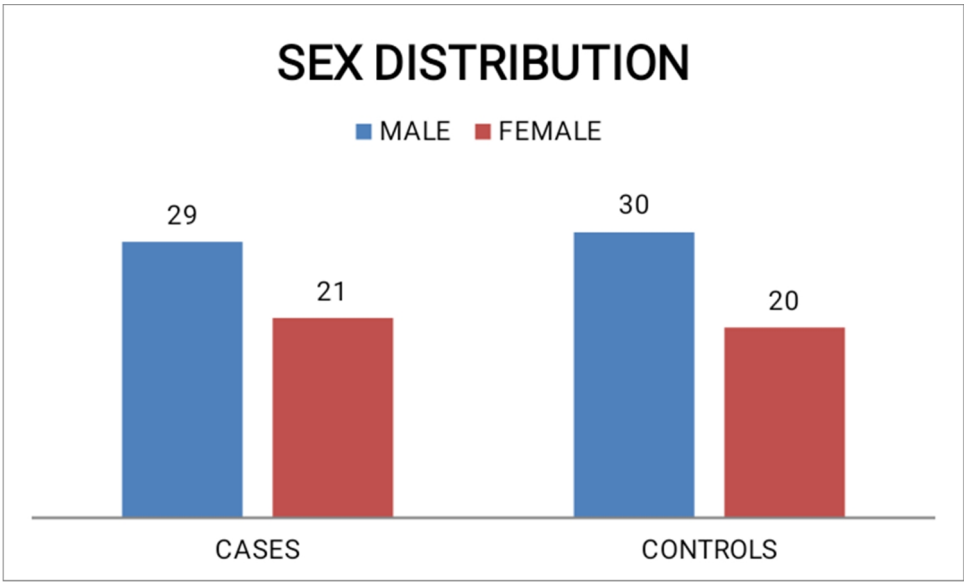
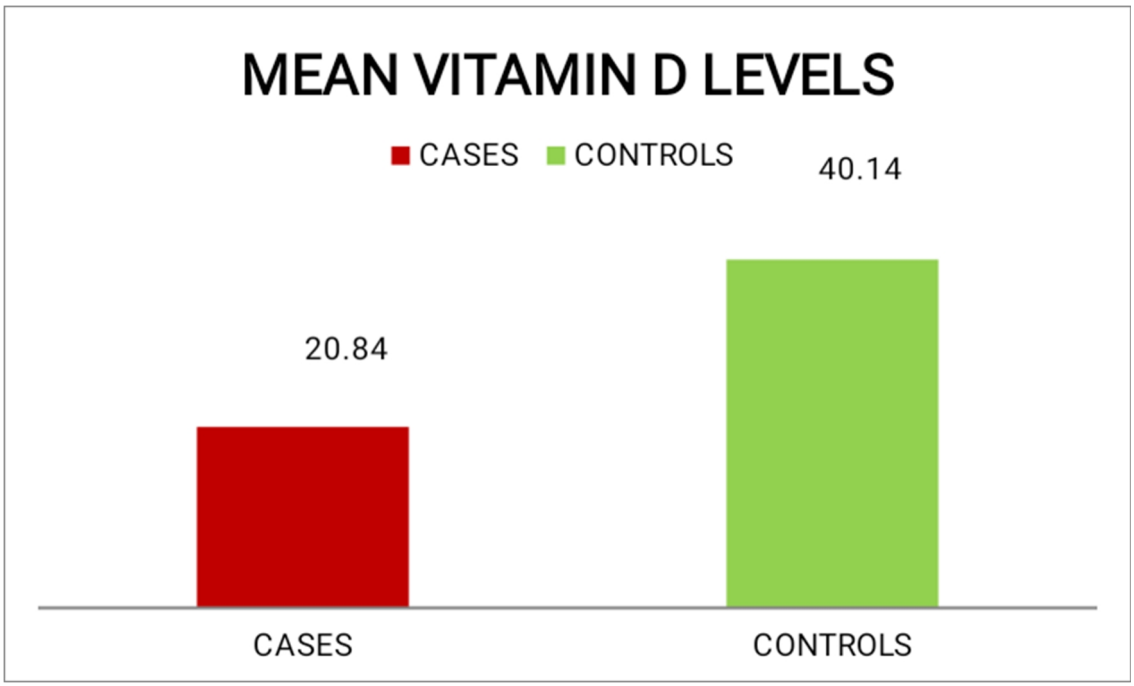


Table 6: MEAN VITAMIN D LEVELS

GROUP	VITAMIN D LEVELS	
	MEAN	SD
CASES	20.84	6.48
CONTROLS	40.14	15.27
UNPAIRED T TEST		
PVALUE-0.001		
SIGNIFICANT		



The mean vitamin D level in cases is 20.84 and that of controls is 40.14 with a significant p value of 0.001

AMONG CASES (N=50)

Table 7: AGE DISTRIBUTION

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
<40	5	10%
41-50	22	44%
51-60	10	20%
61-70	11	22%
>70	2	4%

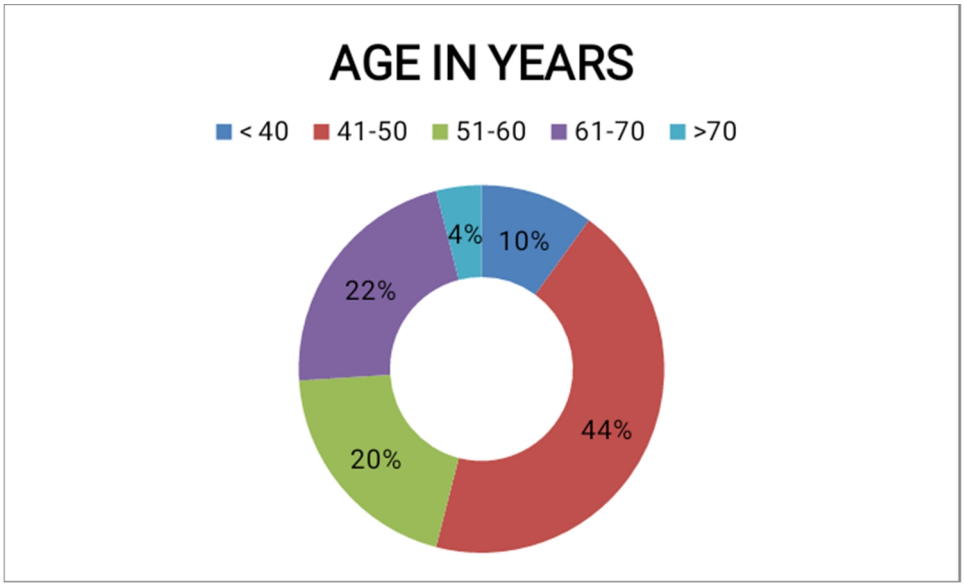


Table 8: SEX DISTRIBUTION

SEX	NO OF PATIENTS	PERCENTAGE
MALE	29	58%
FEMALE	21	42%

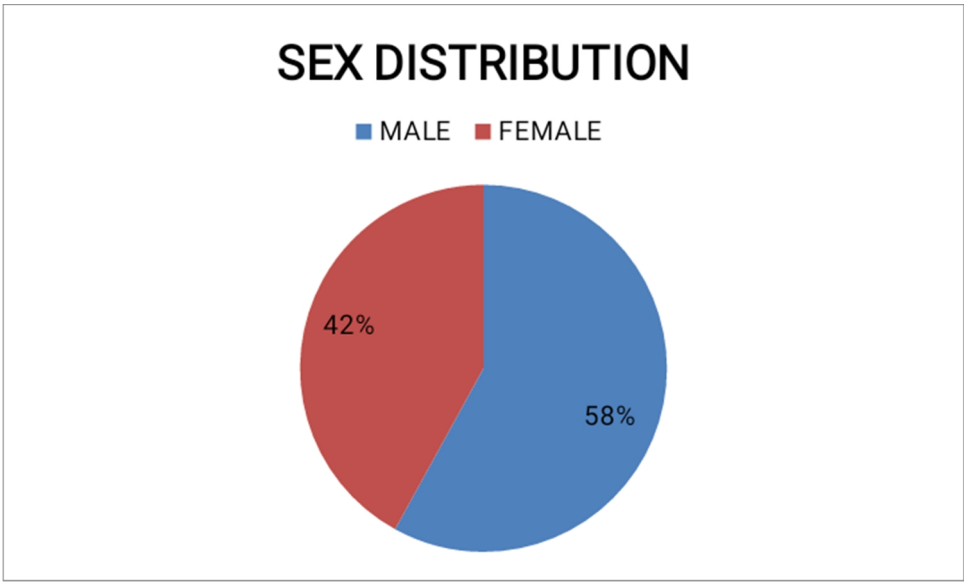
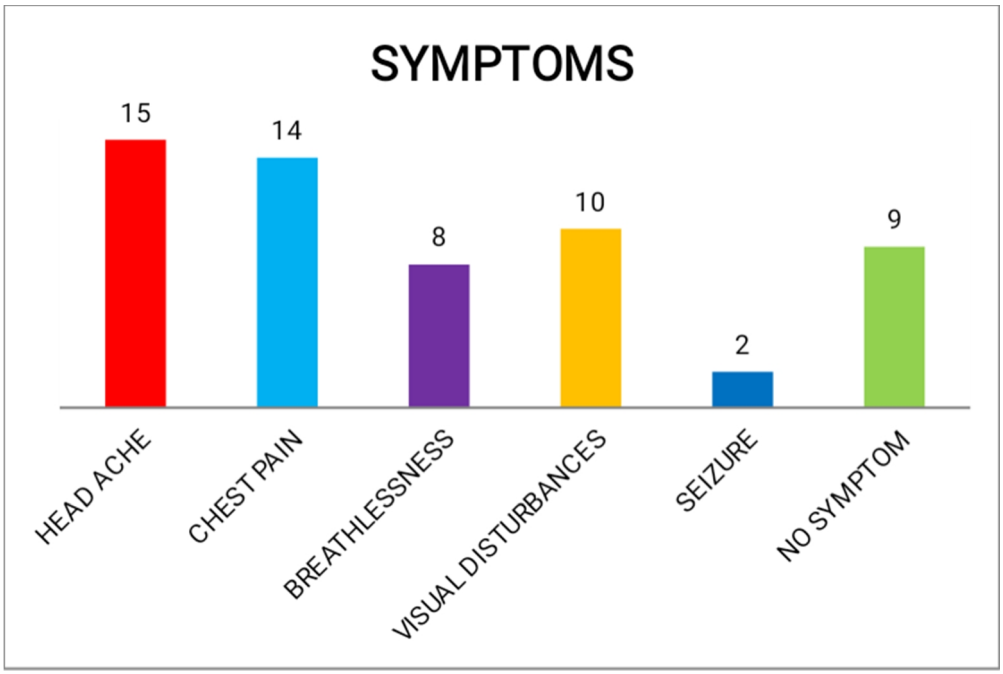


Table 9: SYMPTOMS

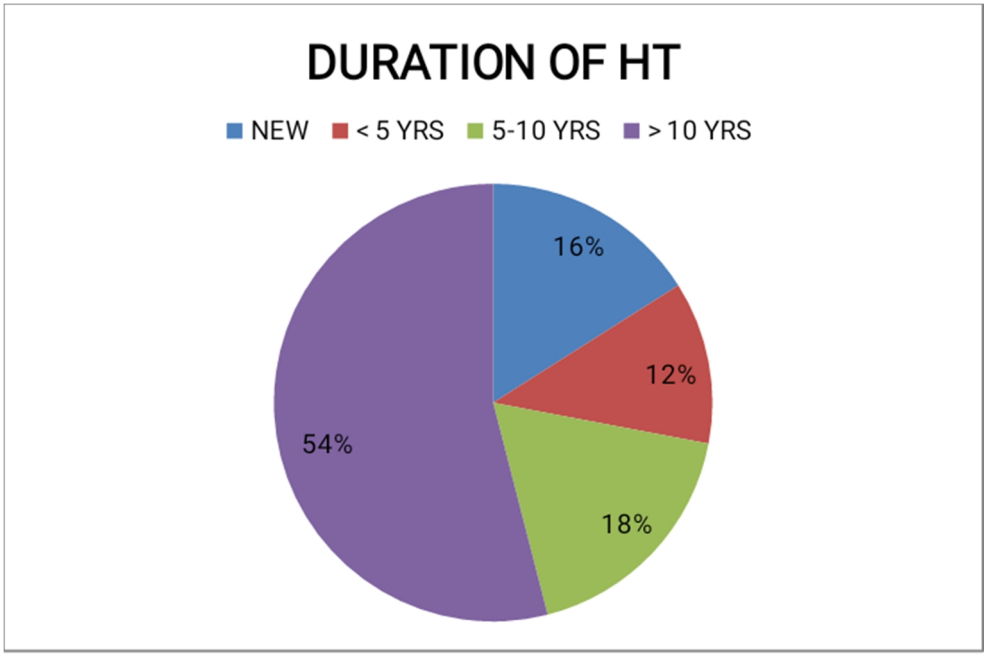
SYMPTOMS	NO OF PATIENTS	PERCENTAGE
HEADACHE	15	30%
CHESTPAIN	14	28%
BREATHLESSNESS	8	16%
VISUALDISTURBANCES	10	20%
SEIZURE	2	4%
NOSYMPTOM	9	18%



The most common presenting symptom of hypertension in the cases studied being headache

Table 10: DURARION OF DISEASE

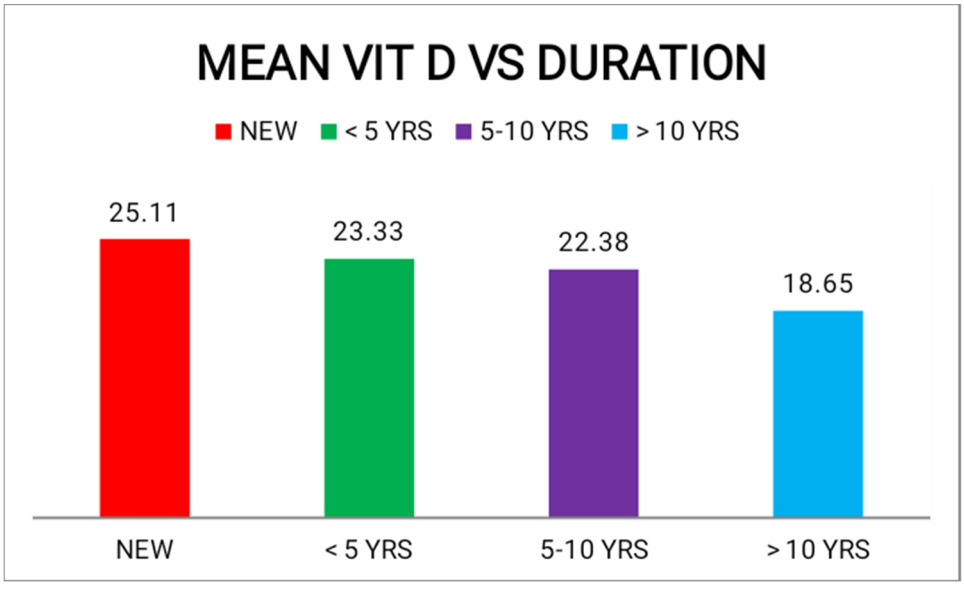
DURATION OF HT	NO OF PATIENTS	PERCENTAGE
NEW	8	16%
<5YRS	6	12%
5-10YRS	9	18%
>10YRS	27	54%



In 54% percentage of patients the duration of hypertension being more than 10 years

Table 11: DURATION OF HT : VITAMIN D LEVELS

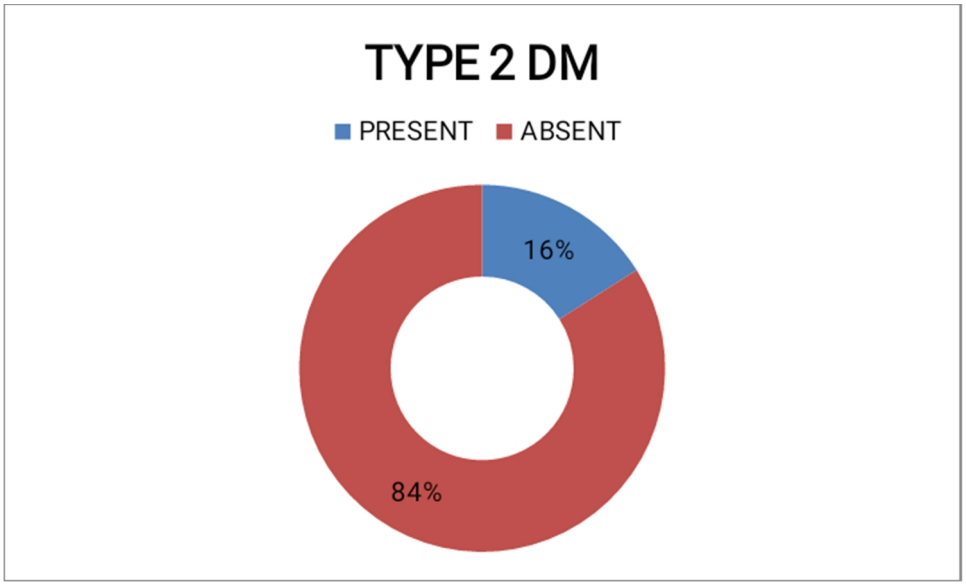
DURATION OF HT	VITAMIN D LEVELS	
	MEAN	SD
NEW	25.11	7.71
<5YRS	23.33	6.56
5-10YRS	22.38	7.06
>10YRS	18.65	4.92
ANOVA		
PVALUE-0.034		
SIGNIFICANT		



There is significant correlation between duration of hypertension and the level of vitamin D with p value of 0.034

Table 12: COMORBIDITIES : TYPE 2 DIABETES MELLITUS

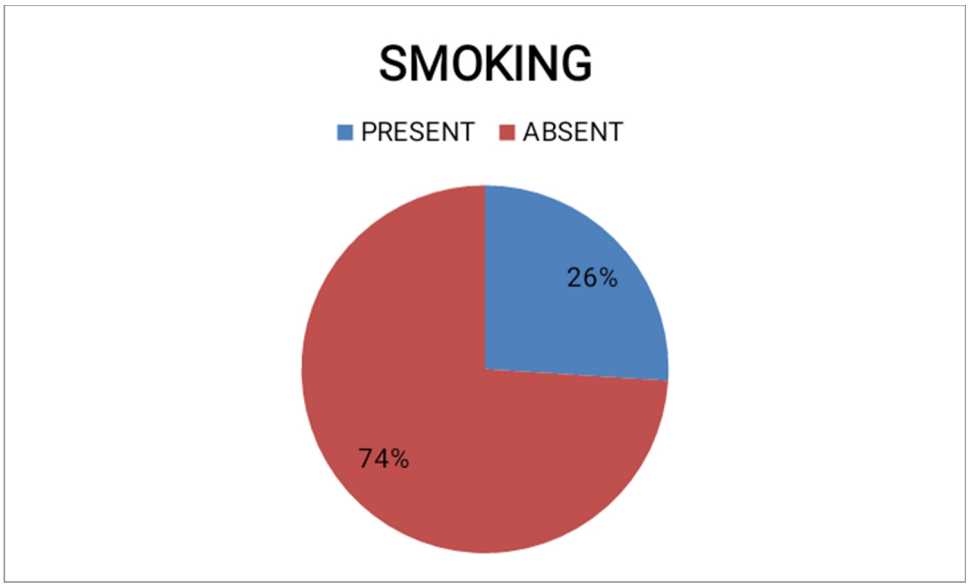
TYPE 2 DM	NO OF PATIENTS	PERCENTAGE
PRESENT	8	16%
ABSENT	42	84%



In 16 percent of patients studied,type 2 diabetes was also present

Table 13: SMOKING HABIT

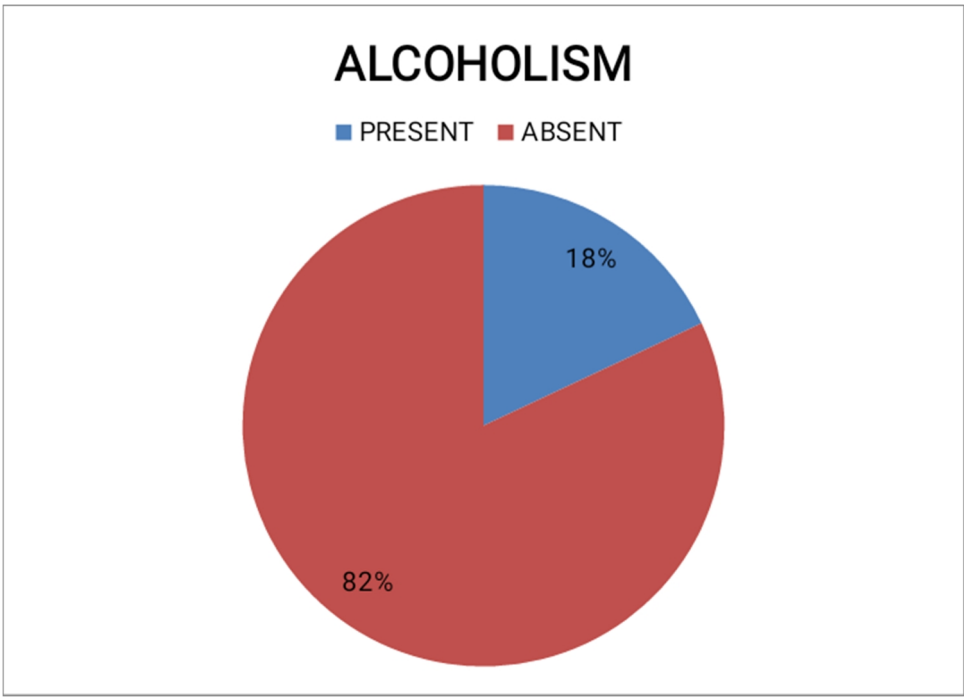
SMOKING	NO OF PATIENTS	PERCENTAGE
PRESENT	13	26%
ABSENT	37	74%



26 percent of patients studied were smokers

Table 14: ALCOHOLISM

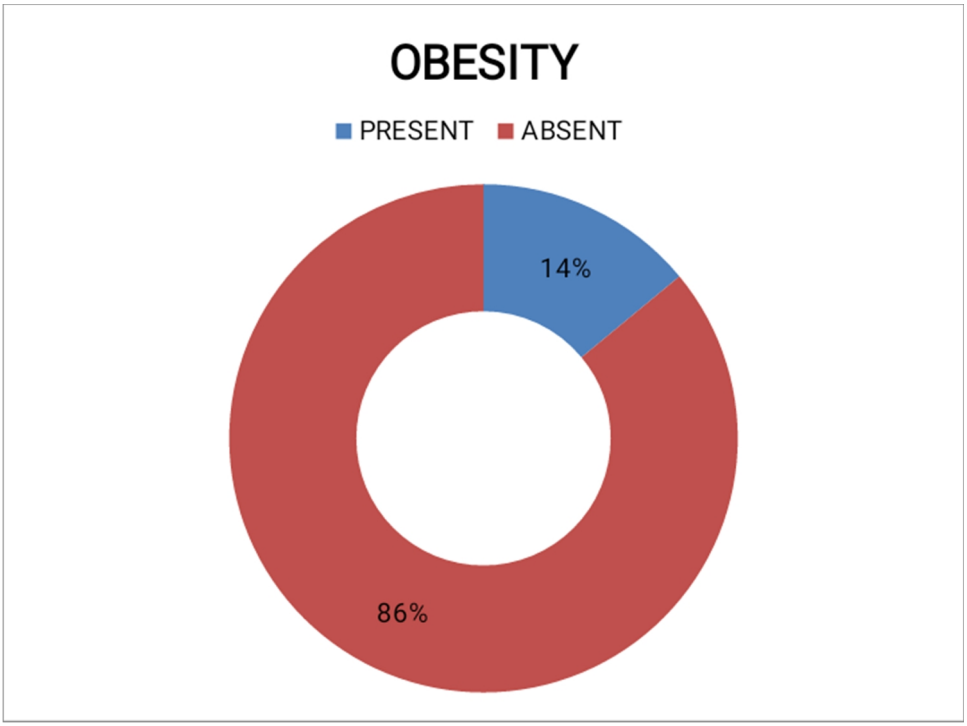
ALCOHOLISM	NO OF PATIENTS	PERCENTAGE
PRESENT	9	18%
ABSENT	41	92%



18 percent of patients studied were alcoholics

Table 15: OBESITY

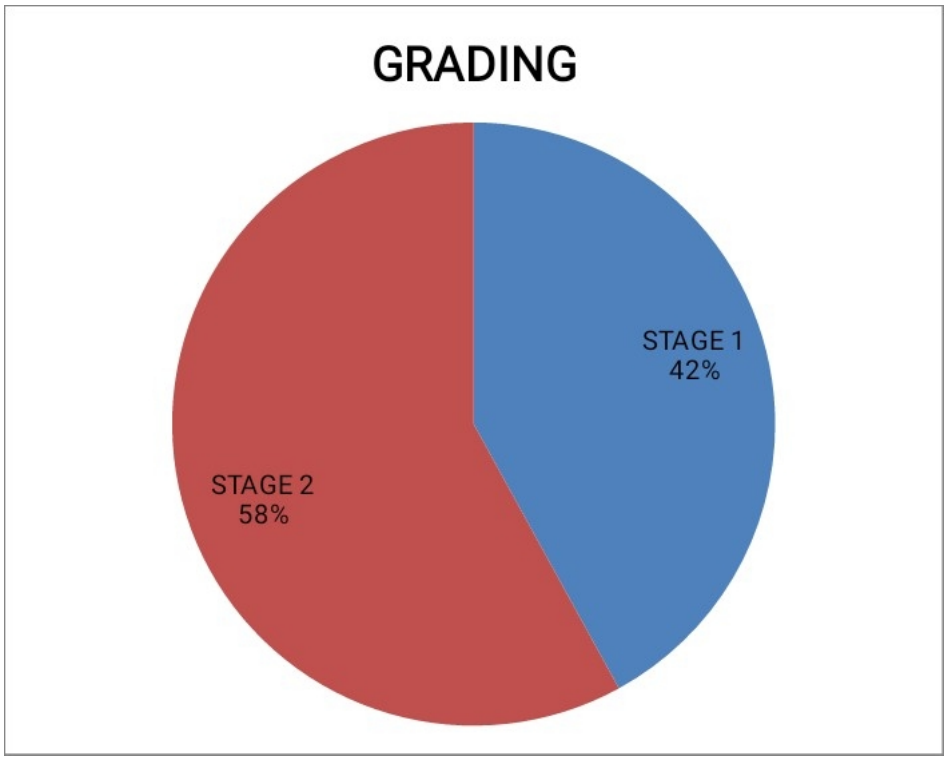
OBESITY	NO OF PATIENTS	PERCENTAGE
PRESENT	7	14%
ABSENT	43	86%



7 percent of patients studied were obese

Table 16: GRADING

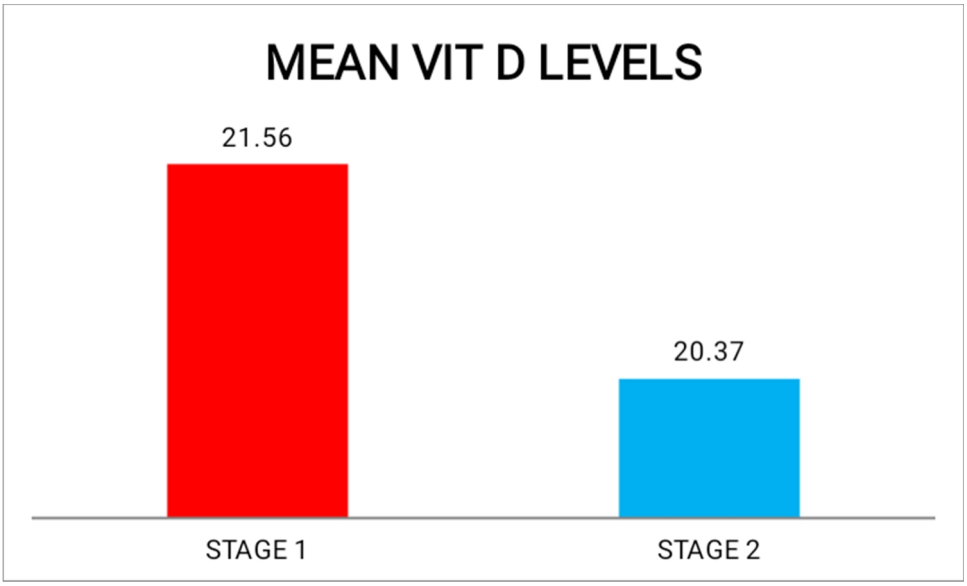
GRADING	NO OF PATIENTS	PERCENTAGE
STAGE1	21	42%
STAGE2	29	58%



58 percent of patients studied had stage 2 hypertension and 42 percent of patients studied had stage 1 hypertension

Table 17: GRADING VS VITAMIN D LEVELS

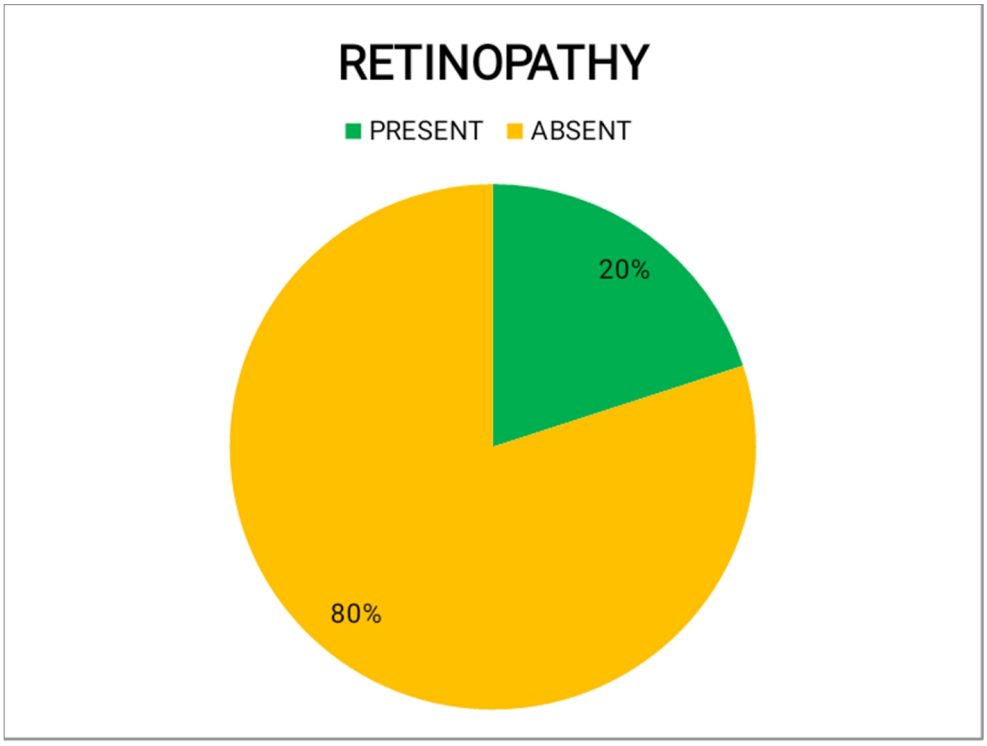
GRADING	VITAMIN D LEVELS	
	MEAN	SD
STAGE1	21.56	6.03
STAGE2	20.37	6.81
UNPAIREDTTEST		
PVALUE-0.398		
NONSIGNIFICANT		



There is no significant correlation between the vitamin D levels and staging of hypertension

Table 18: RETINOPATHY

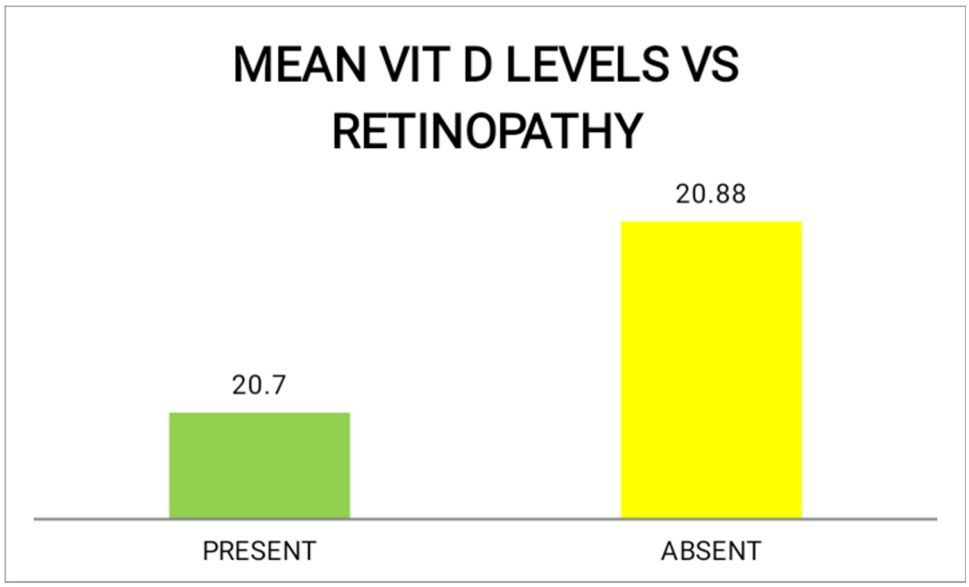
RETINOPATHY	NO OF PATIENTS	PERCENTAGE
PRESENT	10	20%
ABSENT	40	80%



20 percent of patients studied had hypertensive retinopathy

Table 19: RETINOPATHY VS VITAMIN D LEVELS

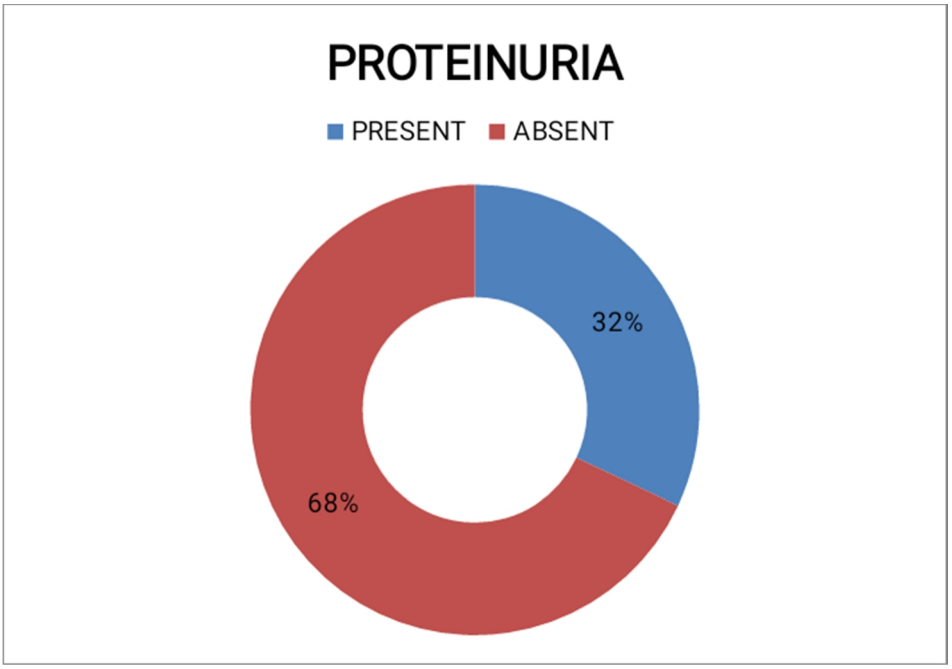
RETINOPATHY	VITAMIN D LEVELS	
	MEAN	SD
PRESENT	20.7	7.31
ABSENT	20.88	6.35
UNPAIRED T TEST		
PVALUE-0.940		
NONSIGNIFICANT		



There is no significant correlation between the vitamin D levels and presence of retinopathy

Table 20: PROTEINURIA

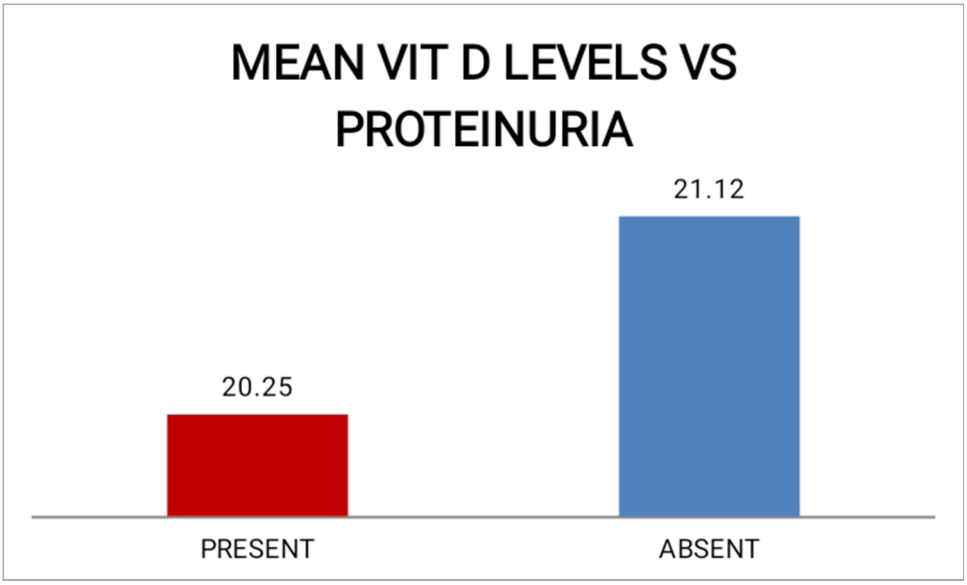
PROTEINURIA	NO OF PATIENTS	PERCENTAGE
PRESENT	16	32%
ABSENT	34	68%



Proteinuria was present in 32 percent of patients

Table 21: PROTEINURIA VS VITAMIN D LEVELS

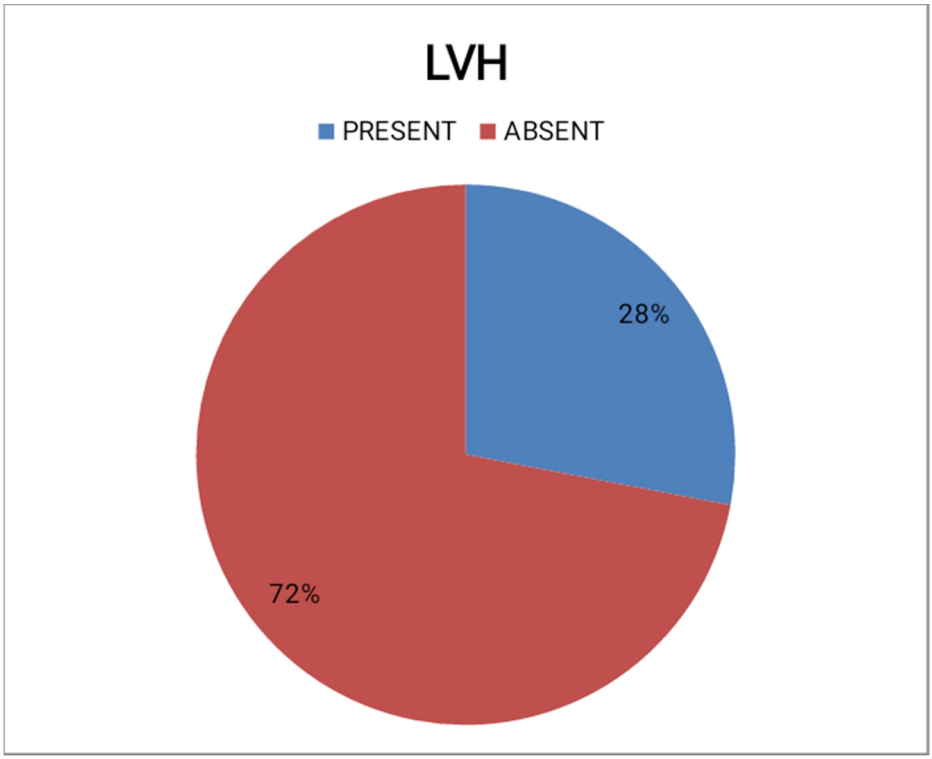
PROTEINURIA	VITAMIN D LEVELS	
	MEAN	SD
PRESENT	20.25	8.45
ABSENT	21.12	5.44
UNPAIREDTTEST		
PVALUE-0.663		
NON SIGNIFICANT		



There is no significant correlation between the vitamin D levels and Proteinuria

Table 22: LEFT VENTRICULAR HYPERTROPHY

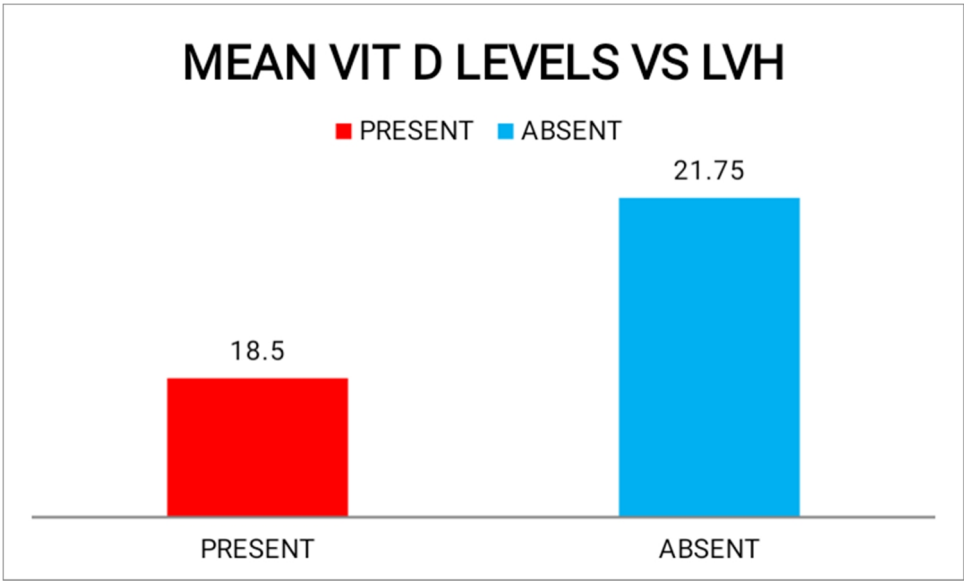
LVH	NO OF PATIENTS	PERCENTAGE
PRESENT	14	28%
ABSENT	36	72%



Left ventricular hypertrophy was present in 28 percent of patients.

Table 23: LVH VS VITAMIN D LEVELS

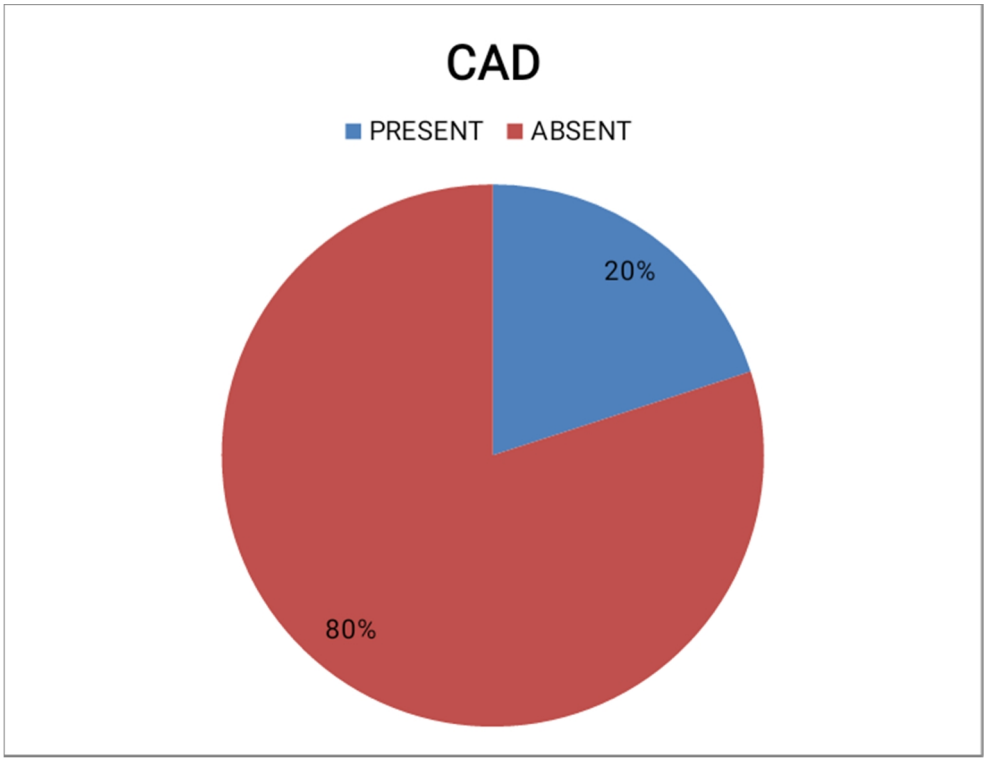
LVH	VITAMIN D LEVELS	
	MEAN	SD
PRESENT	18.5	7.03
ABSENT	21.75	6.4
UNPAIRED T TEST		
P VALUE-0.112		
NON SIGNIFICANT		



There is no significant correlation between the vitamin D levels and presence of left ventricular hypertrophy

Table 24: CORONARY ARTERY DISEASE

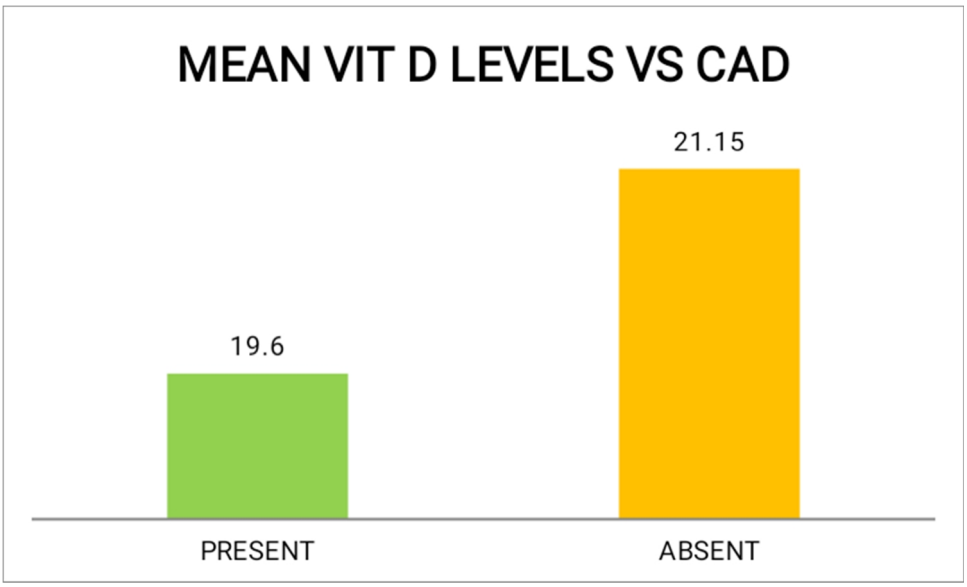
CAD	NO OF PATIENTS	PERCENTAGE
PRESENT	10	20%
ABSENT	40	80%



Coronary artery disease was present in 20% of patients studied

Table 25: CAD VS VITAMIN D LEVELS

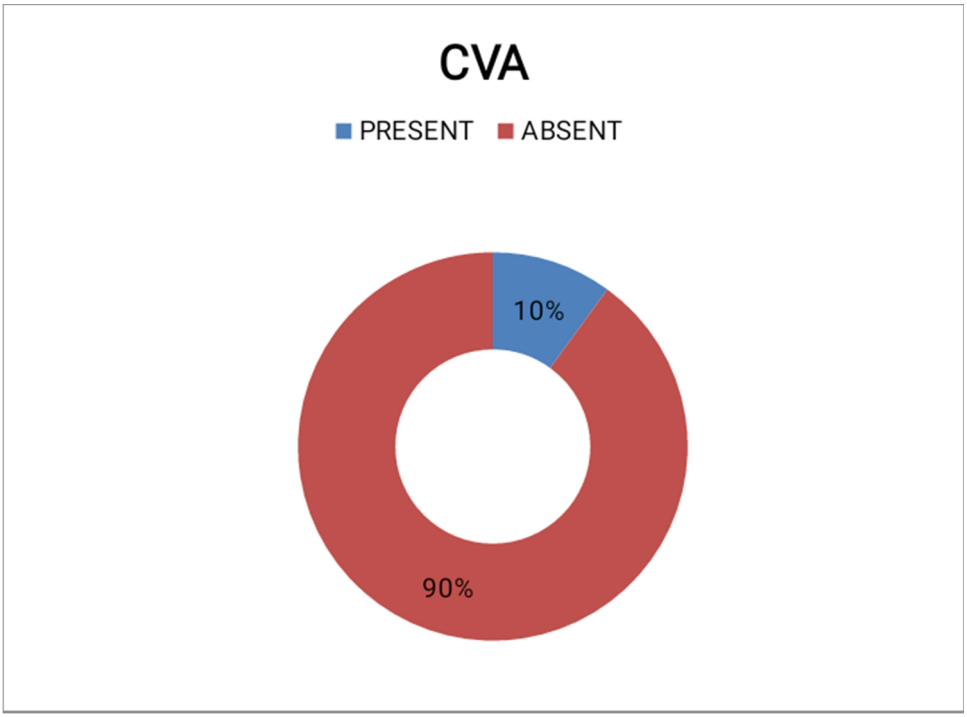
CAD	VITAMIN D LEVELS	
	MEAN	SD
PRESENT	19.6	8.48
ABSENT	21.15	5.97
UNPAIRED T TEST		
PVALUE-0.504		
NONSIGNIFICANT		



There is no significant correlation between the vitamin D levels and presence of coronary artery disease

Table 26: CEREBRO VASCULAR ACCIDENT

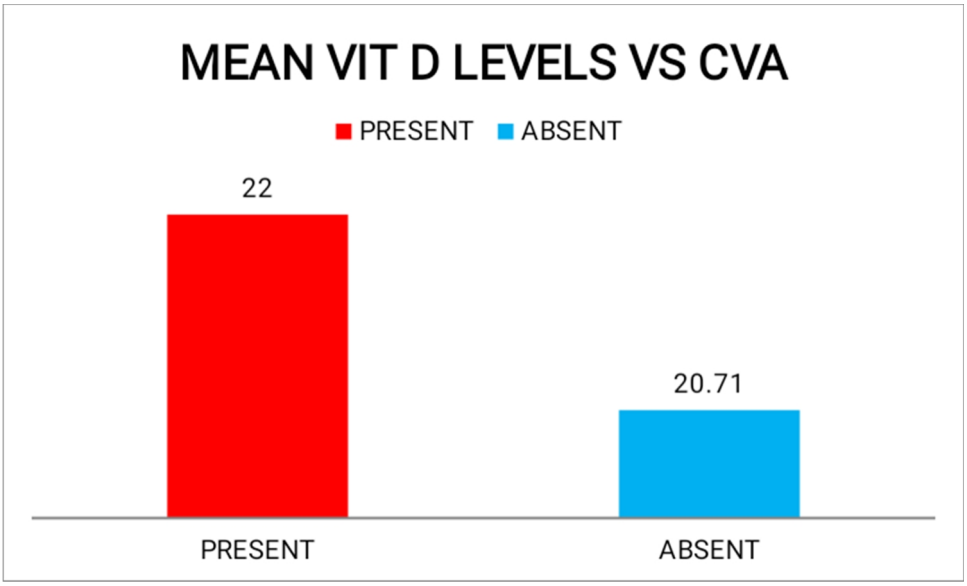
CVA	NO OF PATIENTS	PERCENTAGE
PRESENT	5	10%
ABSENT	45	90%



Cerebral vascular accident was present in 10 percent of patients studied

Table 27: CVA VS VITAMIN D LEVELS

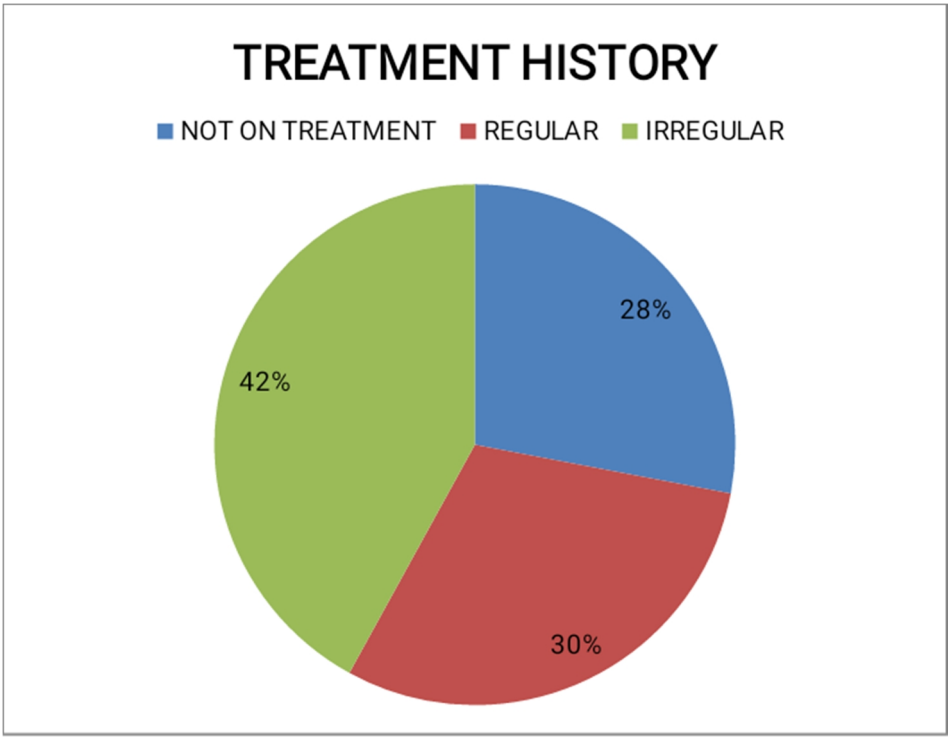
CVA	VITAMIN D LEVELS	
	MEAN	SD
PRESENT	22	4.18
ABSENT	20.71	6.71
UNPAIREDTTEST		
PVALUE-0.678		
NONSIGNIFICANT		



There is no significant correlation between the vitamin D levels and incidence of CVA in these patients.

Table 28: TREATMENT HISTORY

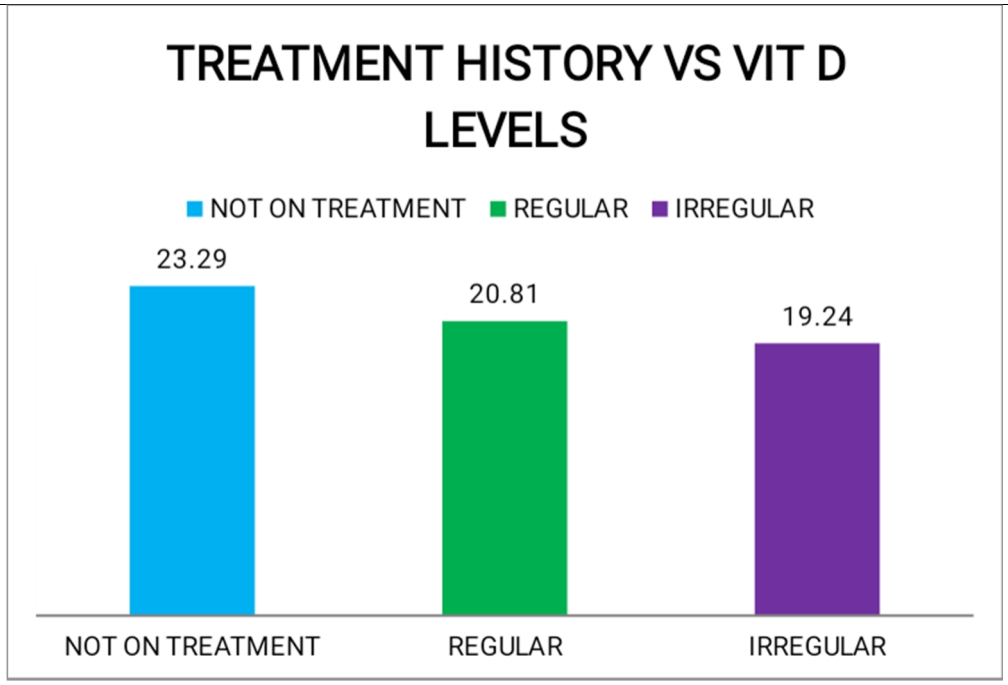
TREATMENT HISTORY	NO OF PATIENTS	PERCENTAGE
NOT ON TREATMENT	14	28%
REGULAR	15	30%
IRREGULAR	21	42%



30 percent of patients studied were on regular treatment. 42 percent of patients studied were on irregular treatment and 28 percent of patients studied were not on treatment.

Table 29: TREATMENT HISTORY VS VITAMIN D LEVLES

TREATMENT HISTORY	VITAMIN D LEVELS	
	MEAN	SD
NOTONTREATMENT	23.29	5.88
REGULAR	20.81	5.97
IRREGULAR	19.24	7.45
ANOVA		
PVALUE-0.197		
NONSIGNIFICANT		



There is no significant correlation between the vitamin D levels and treatment history.

DISCUSSION

Our study included a total of about 50 patients with age and sex matched controls of 50 normotensives. About 41 percent of patients in the study belonged to the age group of 41 to 50 years who constituted the major part of the study.59 percent patients were male and 41 percent were females. There was no statistical difference between age and sex of the patients in cases as well as control.

In our study statistical significance found between the vitamin D level and hypertension. Vitamin D level was found to be significantly lower in the hypertensive population on comparing with the normotensives. The mean vitamin D level in hypertensives was 20.84 while in the normotensives it was 40.14.

This was similar and in accordance with the study conducted by Shalini Priya et al, in Kings George medical university, Lucknow, India.

The most common presenting symptoms of hypertensives in our study was headache which constituted about 30 percent. About 54 percentage of cases were hypertensive for more than 10 years. Interestingly, there was statistical correlation between the vitamin D levels

and the duration of hypertension signifying the deficiency of vitamin D status with chronicity of hypertension.

A study of Alpsoy et al found an inverse correlation between the vitamin D level and risk of hypertension. They also reported the association between vitamin D deficiency and increased rennin angiotensin aldosterone activity. All the three measurements such as systolic, diastolic and mean arterial pressure was higher in vitamin D deficient group.

In our study 16 percentage of patients were diabetics,26 percentage of patients were smokers,18 percentage of paients were alcoholics and 14 percentage of patients were obese. As it is a cross sectional study, these can be the confounding factors for results.

Among the 100 patients studied,42 percentage patients were having stage 1 hypertension and 58 percentage patients were having stage 2 hypertension and there is no correlation between the level of vitamin D and staging of hypertension.

Several studies published in developed countries signify that an inverse relationship exist between the intimal artery thickness and vitamin

D levels. They also argue about the relationship between the vitamin D levels and risk of CAD and left ventricular mass.

But in our study we found no statistical significance between the vitamin D level and complications of hypertension like retinopathy, proteinuria, left ventricular mass, coronary artery disease and cerebrovascular accidents.

Also there is no significant correlation between the treatment history and vitamin D levels.

SUMMARY

- Vitamin D level is significantly lower in hypertensives on comparing with the age and sex matched controls of normotensives.
- There is inverse correlation between the chronicity of hypertension and the level of vitamin D
- There is no significant correlation found between the level of vitamin D and complications of hypertension such as hypertensive retinopathy, nephropathy, risk of coronary artery disease and left ventricular mass which might be attributed to other confounding factors such as other comorbidities and treatment history

CONCLUSION

Vitamin D levels are significantly lower in hypertensive patients when compared to the normotensives and it also correlates with the chronicity of hypertension. But we could not find the correlation between vitamin D levels and complications of hypertension.

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PROFORMA

AGE

SEX

IP NO:

Duration of hypertension:

SYMPTOMS PRESENT :

No symptoms

Headache

Giddiness

Chest pain

Breathlessness

Visual disturbance

Seizures

Othsers if any

PAST HISTORY:

T2DM

CAD

CVA

CKD

Chronic drug intake

Other significant medical history

PERSONAL HISTORY:

Smoking

Alcoholism

ANTHROPOMETRY:

Height in cm

Weight in kgs

FUNDUS EXAMINATION:

For retinopathy

BP:

INVESTIGATIONS:

URINALYSIS

ECG

ECHOCARDIOGRAPHY

VITAMIN D LEVEL

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்டஅறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
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மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....

sl.no	Age	Sex	Symptoms						Duration of hypertension				Risk factors				ng of hyperte		Complications					Treatment			vitamin D level
			No symptoms	Headache	Chest pain	Breathlessness	Visual disturbance	Seizures	Newly diagnosed	<5 years	5 to 10 years	> 10 years	T2DM	Smoking	Alcoholism	Obesity	Stage 1	Stage 2	Retinopathy	Proteinuria	LVH	CAD	CVA	Not on treatment	Regular	Irregular	
1	44	M	P	A	A	A	A	A	A	A	A	P	A	P	P	P	A	p	A	p	p	A	A	A	A	p	12
2	41	F	A	P	A	A	A	A	A	A	A	P	P	A	A	A	p	A	A	A	A	A	A	A	p	A	20
3	46	M	A	A	P	P	A	A	A	A	P	A	A	P	A	A	A	p	A	A	p	A	A	A	A	p	17
4	53	F	A	A	A	P	A	A	A	P	A	A	A	A	A	A	p	A	A	A	A	A	p	p	A	A	29
5	65	F	A	A	P	P	A	A	A	A	A	P	A	A	A	A	A	p	A	p	p	p	A	A	A	p	8
6	31	F	A	P	A	A	A	A	P	A	A	A	A	A	A	A	p	A	A	A	A	A	A	p	A	A	32
7	70	M	A	A	A	A	P	P	A	A	P	A	A	P	P	A	A	p	p	A	A	A	A	A	A	p	30
8	63	F	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	p	p	p	A	p	A	A	p	A	11
9	62	M	A	A	P	P	A	A	A	A	A	P	A	A	A	A	p	A	A	A	A	A	A	A	A	p	14
10	72	M	A	P	A	A	A	A	P	A	A	A	A	A	P	P	p	A	A	A	A	A	A	p	A	A	22
11	35	F	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	p	p	p	P	p	A	p	A	A	26
12	39	M	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	p	p	A	A	A	A	A	p	A	16
13	44	M	A	A	P	A	A	A	A	A	A	P	A	P	A	A	A	p	A	A	A	A	A	A	A	p	18
14	49	M	P	A	A	A	A	A	A	A	A	P	A	A	P	A	p	A	A	A	A	A	A	A	p	A	22
15	66	F	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	p	A	p	p	p	A	A	A	p	33
16	53	M	A	A	P	P	A	A	A	P	A	A	A	A	A	A	p	A	A	A	A	A	A	A	p	A	31
17	46	M	A	P	A	A	A	A	P	A	A	A	A	P	A	A	p	A	A	A	A	A	p	p	A	A	20
18	57	M	P	A	A	A	A	A	A	A	A	P	A	P	A	A	p	A	A	A	A	A	A	A	A	p	12
19	62	F	A	A	A	A	P	A	A	P	A	A	A	A	A	p	A	p	p	p	p	p	A	p	A	A	14
20	71	M	A	P	A	A	A	A	A	P	A	A	P	P	A	A	p	A	A	A	A	A	A	A	A	p	22
21	48	M	P	A	A	A	A	A	A	A	A	P	A	A	P	A	p	A	A	A	A	A	A	A	p	A	16
22	51	F	A	A	P	P	A	A	P	A	A	A	A	A	A	A	p	A	A	A	A	A	A	p	A	A	14
23	53	F	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	p	A	A	A	A	A	p	A	A	20
24	47	M	A	P	A	A	A	A	A	A	A	P	A	P	A	A	A	p	A	p	p	p	A	A	A	p	12
25	62	M	P	A	A	A	A	A	P	A	A	A	A	P	A	p	p	A	A	A	A	A	A	p	A	A	24
26	39	F	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	p	A	A	A	A	A	A	A	p	22
27	44	M	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	p	A	A	A	A	A	A	p	A	24
28	48	M	P	A	A	A	A	A	A	A	A	P	P	A	A	A	p	A	A	p	A	A	A	A	A	p	21
29	47	F	A	A	P	A	A	A	A	A	A	P	A	A	A	A	p	A	A	A	A	A	A	A	p	A	20
30	52	M	A	P	A	A	A	A	A	A	A	P	A	P	A	A	p	A	A	A	A	A	A	A	A	p	22
31	44	M	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	p	A	A	A	A	p	A	A	p	18
32	62	F	A	A	A	A	P	P	A	A	P	A	A	A	A	A	A	p	P	p	p	p	A	A	A	p	16
33	43	M	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	p	A	p	A	A	A	A	p	A	12
34	49	M	A	A	A	A	P	A	P	A	A	A	A	P	A	A	A	p	p	A	A	A	A	p	A	A	34
35	62	F	A	A	A	A	P	A	A	A	A	P	P	A	A	A	A	p	p	A	p	A	A	A	p	A	18
36	69	M	A	A	P	A	A	A	P	A	A	A	A	P	A	p	A	p	A	A	p	A	A	p	A	A	12

sl.no	Age	Sex	Symptoms						Duration of hypertension				Risk factors				ng of hyperte		Complications					Treatment			vitamin D level
			No symptoms	Headache	Chest pain	Breathlessness	Visual disturbance	Seizures	Newly diagnosed	<5 years	5 to 10 years	> 10 years	T2DM	Smoking	Alcoholism	Obesity	Stage 1	Stage 2	Retinopathy	Proteinuria	LVH	CAD	CVA	Not on treatment	Regular	Irregular	
37	57	M	A	A	A	A	P	A	A	A	A	P	P	A	P	A	p	A	p	p	A	A	A	A	A	P	21
38	48	M	A	A	P	P	A	A	A	A	P	A	A	A	A	A	p	A	A	p	A	A	A	p	A	A	36
39	44	F	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	p	A	A	A	A	A	A	p	A	22
40	62	F	P	A	A	A	A	A	A	A	A	P	A	A	A	A	A	p	A	p	A	A	A	A	A	p	26
41	38	F	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	p	p	A	p	A	A	P	A	A	21
42	42	M	A	A	P	A	A	A	A	A	A	P	P	A	P	A	A	p	A	p	A	p	A	A	p	A	26
43	48	M	A	A	A	A	A	A	A	A	A	P	A	P	A	A	p	A	A	A	A	A	p	A	A	p	21
44	50	F	A	A	P	A	A	A	A	P	A	A	A	A	A	A	p	A	A	A	A	A	A	A	p	A	18
45	48	M	A	P	A	A	A	A	A	A	P	A	A	A	A	p	A	p	A	A	p	A	A	A	p	A	28
46	46	M	P	A	A	A	A	A	A	A	A	P	A	A	P	A	p	A	A	A	A	A	A	A	A	p	20
47	56	F	A	A	A	A	P	A	A	A	A	P	P	A	A	A	A	p	A	A	A	A	A	A	A	p	19
48	52	M	A	A	P	P	A	A	A	A	A	P	A	A	P	A	A	p	A	p	A	p	A	A	p	A	28
49	60	F	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	p	A	A	p	A	A	A	A	p	20
50	44	F	P	A	A	A	A	A	A	A	P	A	P	A	A	p	A	p	A	p	p	p	p	p	A	A	22

sl no	Age	Sex	Vitamin D
1	30	F	41
2	38	M	44
3	53	M	36
4	46	F	50
5	50	M	32
6	42	F	60
7	56	M	51
8	60	F	62
9	46	F	30
10	61	F	62
11	32	M	56
12	44	M	48
13	49	M	49
14	52	M	33
15	62	M	31
16	56	M	22
17	49	M	34
18	44	F	18
19	48	F	14
20	51	F	32
21	39	M	16
22	62	M	38
23	37	M	46
24	70	M	52
25	58	M	22
26	64	M	18
27	66	M	44
28	62	M	48
29	48	M	55
30	44	M	62
31	69	F	29
32	56	M	58
33	32	F	22
34	43	F	18
35	49	M	12
36	33	M	53
37	56	M	60
38	37	M	41
39	43	F	28
40	52	F	22
41	41	F	56
42	34	M	68
43	49	M	44
44	50	F	42
45	63	F	38
46	70	M	30
47	42	F	48

sl no	Age	Sex	Vitamin D
48	39	M	62
49	55	F	48
50	46	F	22