CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS

A DISSERTATION SUBMITTED TO

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU

in partial fulfilment of the requirements

FOR THE AWARD OF THE DEGREE OF

DOCTOR OF MEDICINE - BRANCH I

(GENERAL MEDICINE)

Registration No: 200120104016

DEPARTMENT OF GENERAL MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 627011

MAY 2023

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS"** submitted by Dr.RUBAN RAJ.R, 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.

Place: Tirunelveli
Date: 17/12/2022

Prof.Dr.R.PERIASAMY, M.D
Professor of Medicine,
Unit Chief,
Department of General Medicine
Tirunelveli Medical College,
Tirunelveli.

Dr. R. Periyasamy MD.,
Reg.No. 51232
Professor of Medicine
Tirunelveli Medical College
Tirunelveli

CERTIFICATE BY THE HEAD OF THE DEPARTMENT

I hereby certify that this dissertation entitled "**CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS**" is a record of work done by Dr. Ruban Raj.R, in the Department of General Medicine, Tirunelveli Medical College, Tirunelveli, during her postgraduate degree course period from 2020- 2022. This work has not formed the basis for previous award of any degree.

Date : 17/12/2022
Place : TIRUNELVELI

17/12/22

Prof. Dr. S ALAGESAN. MD DM,
Professor & Head of the Department,
Department of General Medicine,
Tirunelveli Medical College.

for

Dr. S. Alagesan, MD.,
Reg. No. 43658
Prof. & HOD of Medicine
Tirunelveli Medical College Hospital,
Tirunelveli.

CERTIFICATE BY THE HEAD OF THE INSTITUTION

I hereby certify that this dissertation entitled **"CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS"** is a record of work done by Dr.Ruban Raj.R, in the Department of General Medicine, Tirunelveli Medical College, Tirunelveli, during her postgraduate degree course period from 2020- 2022. This work has not formed the basis for previous award of any degree.

Date : 12/12/2022
Place : TIRUNELVELI

Prof. Dr. M.RAVICHANDRAN. MD
The Dean,
Tirunelveli Medical College,
Tirunelveli.

DEAN
TIRUNELVELI MEDICAL COLLEGE
TIRUNELVELI - 11

COPYRIGHT

DECLARATION BY THE CANDIDATE

I solemnly declare that the dissertation entitled **"CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS"** is done by me at Tirunelveli Medical College Hospital, Tirunelveli under the guidance and supervision of Prof.Dr.R.Periasamy M.D. The Tamilnadu Dr. M.G.R. Medical University, Chennai shall have the rights to preserve , use and disseminate this dissertation in print or electronic format for academic / research purpose.

Date: 13/12/2021
Place : Tirunelveli

R. Ruban

Dr.RUBAN RAJ.R, MBBS
Registration no: 200120104016
Postgraduate Student,
M.D General Medicine,
Department of General Medicine,
Tirunelveli Medical College
Tirunelveli.

ACKNOWLEDGEMENT

I wish to express my heartfelt gratitude to our Dean **Prof Dr.M.Ravichandran M.D.,** 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, **Dr.S.Alagesan, MD, DM,** Department of General Medicine whose valuable guidance and constant help have gone a long way in the preparation of this dissertation.

I express my sincere thanks to my renowned teacher and my guide Chief **Dr.R.Periasamy,M.D.** 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.K.S.Dakshinamoorthy M.D , Dr. E.Sheik Mohammed Raja M.D.,** Assistant Professors, Department of General Medicine for their valuable suggestions in preparing this dissertation.

Date: 17/12/2022
Place : Tirunelveli

R.Ruban

Dr.RUBAN RAJ.R, MBBS
Registration no: 200120104016
Postgraduate Student,
M.D General Medicine,
Department of General Medicine,
Tirunelveli Medical College
Tirunelveli.

TIRUNELVELI MEDICAL COLLEGE

INSTITUTIONAL RESEARCH ETHICS COMMITTEE

CERTIFICATE OF REGISTRATION & APPROVAL OF THE TIREC REF NO: 1998/GM/2021

PROTOCOL TITLE: CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS
PRINCIPAL INVESTIGATOR: DR.R. RUBANRAJ MBBS
DESIGNATION OF PRINCIPAL INVESTIGATOR: RESIDENT
DEPARTMENT & INSTITUTION: GENERAL MEDICINE, TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear DR. R. RUBANRAJ MBBS, Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 06.07.2021.

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.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d. If there are any amendments in the trial design, these must be incorporated in the protocol and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
   e. Approval for amendment changes must be obtained prior to implementation of changes.
   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.

STANDS APPROVED UNDER SEAL

31/8/21

Dr.K.Shantaraman, MD
Member Secretary, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

CERTIFICATE – II

This is to certify that this dissertation work entitled **"CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS"** of the candidate **Dr.Ruban Raj.R** with Registration Number **200120104016** for the award of M.D. Degree in the branch of GENERAL MEDICINE (I). I personally verified 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 5 percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal

Dr. R. Periyasamy MD.,
Reg.No. 51232
Professor of Medicine
Tirunelveli Medical College
Tirunelveli

Document Information

Analyzed document	CORRELATION BETWEEN SERUM CALCIUM LEVELS AND BLOOD PRESSURE AMONG NEWLY DIAGNOSED ESSENTIAL HYPERTENSION PATIENTS.docx (D153186432)
Submitted	12/13/2022 5:20:00 AM
Submitted by	Ruban Raj
Submitter email	drrubanraj@gmail.com
Similarity	5%
Analysis address	drrubanraj.tnmg@analysis.urkund.com

Sources included in the report

W	URL: http://repository-tnmgrmu.ac.in/6221/1/200100306sidharthan.pdf Fetched: 7/4/2022 12:14:06 PM	5
W	URL: https://www.iaimjournal.com/wp-content/uploads/2022/02/iaim_2022_0902_02.pdf Fetched: 11/30/2022 9:35:03 PM	2
W	URL: http://repository-tnmgrmu.ac.in/6224/1/200100307anand.pdf Fetched: 11/16/2021 5:23:48 AM	3
W	URL: https://www.ijmedicine.com/index.php/ijam/article/viewFile/3127/2147 Fetched: 12/1/2022 11:13:49 AM	8
W	URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4093982/ Fetched: 12/11/2022 5:29:54 PM	1

Entire Document

INTRODUCTION Hypertension is one of the major risk factor for cardiovascular morbidity and mortality. It affects 1 billion people globally. Hypertension doubles the risk of cardiovascular disease including congestive heart failure, coronary artery disease, renal failure, peripheral arterial disease ,ischaemic and hemorrhagic stroke. In India, hypertension poses substantial burden on cardiovascular health status and health care system. Hypertension is responsible for 57% of stroke death and 29% of death due to coronary vascular disease1,2 .In India the prevalence of hypertension is 59.9% and 69.9% per 1000 males and females respectively in urban population ,35.5% and 35.9% per 1000 males and females respectively in rural population49. Numerous studies have shown association between serum calcium level and essential hypertension. There is decreased serum ionised calcium, increased intracellular calcium and increased urinary excretion of calcium in essential hypertensive patients. National Health And Nutritional Examination survey (NHANES) conducted a largest study in this topic and concluded that there is a threshold of about 400-600mg per day of dietary calcium. At levels below this threshold there is a increased risk of high blood pressure, also the cardiovascular benefits increases at higher intake. Objective of this study is to estimate corrected calcium level and total serum calcium level in newly detected essential hypertensive patients, to compare its relationship with factors age, gender, lifestyle ,family history of hypertension, alcohol, smoking and BMI and to determine the correlation of corrected calcium levels and total serum calcium levels with systolic blood pressure and diastolic blood pressure in patients with essential hypertension .

TABLE OF CONTENTS

INTRODUCTION

Hypertension is one of the major risk factor for cardiovascular morbidity and mortality. It affects 1 billion people globally. Hypertension doubles the risk of cardiovascular disease including congestive heart failure, coronary artery disease, renal failure, peripheral arterial disease ,ischaemic and hemorrhagic stroke.

In India, hypertension poses substantial burden on cardiovascular health status and health care system. Hypertension is responsible for 57% of stroke death and 29% of death due to coronary vascular disease[1,2] .In India the prevalence of hypertension is 59.9% and 69.9% per 1000 males and females respectively in urban population ,35.5% and 35.9% per 1000 males and females respectively in rural population[49].

Numerous studies have shown association between serum calcium level and essential hypertension. There is decreased serum ionised calcium, increased intracellular calcium and increased urinary excretion of calcium in essential hypertensive patients. National Health And Nutritional Examination survey (NHANES) conducted a largest study in this topic and concluded that there is a threshold of about 400-600mg per day of dietary calcium. At levels below this threshold there is a increased risk of high blood pressure, also the cardiovascular benefits increases at higher intake.

Objective of this study is to estimate corrected calcium level and total serum calcium level in newly detected essential hypertensive patients, to compare

its relationship with factors age, gender, lifestyle ,family history of hypertension, alcohol, smoking and BMI and to determine the correlation of corrected calcium levels and total serum calcium levels with systolic blood pressure and diastolic blood pressure in patients with essential hypertension .

REVIEW OF LITERATURE

BLOOD PRESSURE:

DEFINITION:

Blood pressure is defined as the lateral pressure exerted by the column of blood against any unit area of the vessel wall. It is always almost measured in millimetres of mercury (mmHg)[3,4].

CLASSIFICATION OF BLOOD PRESSURE[5]:

Blood pressure category	Systolic blood pressure(mmHg)	Diastolic blood pressure(mmHg)
Normal	Less than 120	Less than 80
Elevated	120-129	Less than 80
High blood pressure (hypertension)STAGE 1	130-139	80-89
High blood pressure (hypertension) STAGE 2	140 or HIGHER	90 or HIGHER
Hypertensive crisis	HIGHER THAN 180	HIGHER THAN 120

According to JNC 8(joint national committee) report, in adults over 18 years of age ,systolic blood pressure less than 120 mm of Hg and diastolic blood pressure of less than 80 mm of Hg is normal. Systolic blood pressure between 120-129mm of Hg and diastolic blood pressure less than 80 mm of Hg is considered elevated. Systolic blood pressure between 130-139 and diastolic blood pressure between 80 -89 is defined as stage 1 hypertension. Systolic blood pressure 140 or higher and diastolic blood pressure 90 or higher is defined as stage 2 hypertension.

Epidemiology:

Cardiovascular diseases causes a large proportion of disability and death world wide. Since 1990 the number of people with hypertension worldwide has been doubled with most increase occurring in middle income and low income regions .WHO rates Hypertension as important cause for premature death world wide.

In South Asia hypertension is the one of the most important risk factor for attributable burden of disease.The Global and Regional Burden of Disease and Risk Factors study (2001) , in a systematic analysis of population health data for attributable deaths and attributable disease burden has ranked hypertension as second most common cause. Analysis of world wide data for global burden of hypertension ,20.9% of Indian women and 20.6% of Indian men were suffering from hypertension in 2005 and these rate were projected to go up to 23.6 and 22.9 for Indian women and men respectively by 2025.

Recent studies have shown that prevalence of hypertension to be 10% in rural people and 25% in urban people in India. Difference in socioeconomic conditions could be the reason for difference in hypertension prevalence between rural and urban areas. Lifestyle changes because of economic progress and rapid urbanization also contributes to the increasing trend in epidemics of hypertension in urban regions in India .There is also regional variation in mortality and prevalence of stroke and CHD in India. Highest CHD mortality is seen in south India and higher stroke rates are seen in Eastern India .

Blood pressure control among rural and urban regions in India are poor ranging between 6.5-15% in rural areas and11.6-28.7% in urban areas.

Based on etiology, Hypertension is classified in to following types:

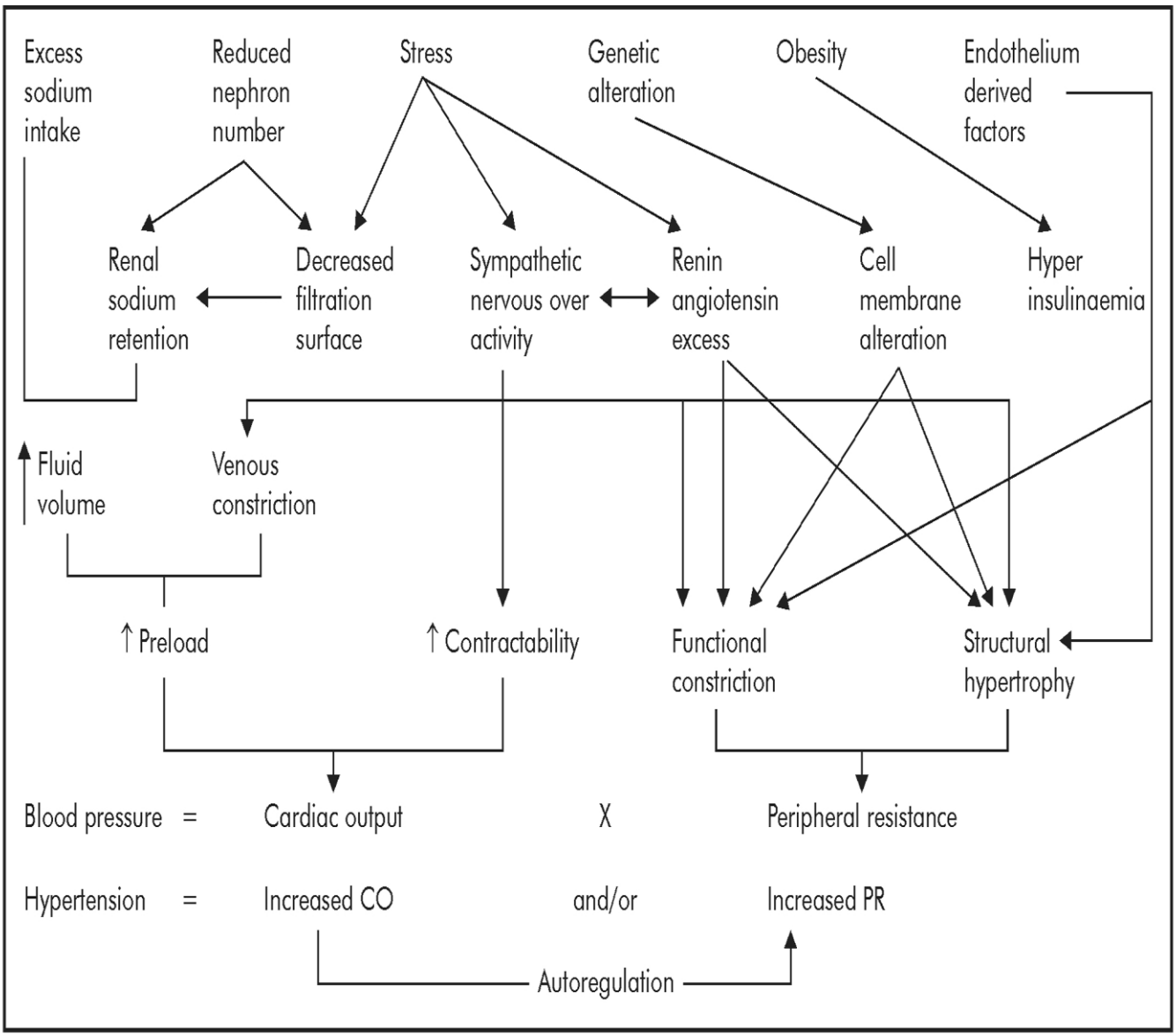
1. Primary Hypertension.
2. Secondary Hypertension.

PRIMARY (ESSENTIAL) HYPERTENSION

Primary hypertension, accounts for about 95% of all hypertension cases. This is defined as high blood pressure for which there is no obvious secondary cause like pheochromocytoma, renal vascular disease ,aldosteronism or gene mutations[6]. It is a heterogeneous disorder in which different patients will have different causal factors that can lead to high blood pressure which includes insulin resistance, obesity, high salt intake, high alcohol intake, sedentary lifestyle, low potassium intake ,stress and low calcium intake.

PATHOGENESIS OF PRIMARY(ESSENTIAL) HYPERTENSION[7]:

The pathogenesis of essential hypertension is multifactorial ,a multitude of renal,neuro hormonal ,vascular mechanisms and several other factors interacts with varying degrees and contributes to the development of hypertension.



Role of genetics[8]:

Genetically defined variation in blood pressure is termed as Inherited BP. Due to genetic variations or genes that are under-expressed or over-expressed as well as the intermediary phenotypes that they regulate can cause high blood pressure. Factors that increase blood pressure such as high alcohol intake, obesity and high salt intake are called as"hypertensinogenic factors". There are interactions between environmental factors and genetics that influence intermediary phenotypes like renin angiotensin aldosterone, sympathetic nerve activity and endothelial factors, which in turn influence other phenotypes such as vascular reactivity, sodium excretion and cardiac contractility.

Identification of genes that are responsible for development of hypertension is complicated due to the fact that the 2 phenotypes that determine blood pressure,i.e., Total peripheral resistance and cardiac output are controlled by intermediary phenotypes like vassopressor/vasodepresor hormones, autonomic nervous system, body fluid volume, structure of the cardiovascular system, renal function and many others. These phenotypes are controlled by complex mechanisms including blood pressure itself.

Association of blood pressure between parents and children and among siblings demonstrated by family studies suggesting the association of genes on blood pressure.Further more ,behavioural pattern has been also influenced by genetic factor might lead to elevation of blood pressure.

Mutations and polymorphism in genes such as angiotensin converting enzyme ,angiotensin gene, beta2 adrenergic receptor, angiotensinase c , adducin, G-Protein beta3 subunit and insulin receptor are linked to the development of essential hypertension.

In studies of twins and family members in which degree of familial aggregation of blood pressure is compared with the closeness of genetic sharing, genetic contributions have been estimated to range from 30% to 60%[9].Epidemiological data suggest that around 30 to 35% for hypertension is contributed by genetic factors, 10 to 15% by common household environmental factors and 50 to 55% by nonfamilial factors[10].

Many studies have been proposed for the genetic contribution of blood pressure. For example, Prat proposed that hypertension is due to autosomal dominant Inheritance. Pickering stated polygenic contribution for hypertension. Polymorphism of genes involving RAS system, aldosterone synthesis and adrenergic receptors have been noted to be more common in hypertensive patients than normotensive patients[11].

EXCESS SODIUM INTAKE AND SODIUM SENSITIVITY :

Excess sodium increase the blood pressure by increasing the fluid volume and preload[12]. In Western countries almost everyone ingest high sodium diet, but only half of them develop hypertension indicating a variable degree of sensitivity to sodium. Interactions between hereditary and other environmental factors may be involved .Many mechanisms for salt sensitivity has been proposed which

include increased activity of sodium hydrogen exchanger,defect in renal sodium excretion,impaired nitric oxide synthesis,increased sympathetic nervous system activity ,increased calcium entry into vascular smooth muscle.Fujiwora et al reported that modulation of nitric oxide synthesis by salt intake may be the mechanism for salt sensitivity in hypertension[13].

ALTERED RENAL PHYSIOLOGY:

Sodium is the predominant extracellular solute which retains water within extracellular compartment. The regulation of sodium and water excretion is the primary function of kidney which is done through two mechanisms:

Pressure natriuresis and pressure diuretics

Increase or decrease in urinary excretion of sodium and water in relation to change in renal perfusion pressure.

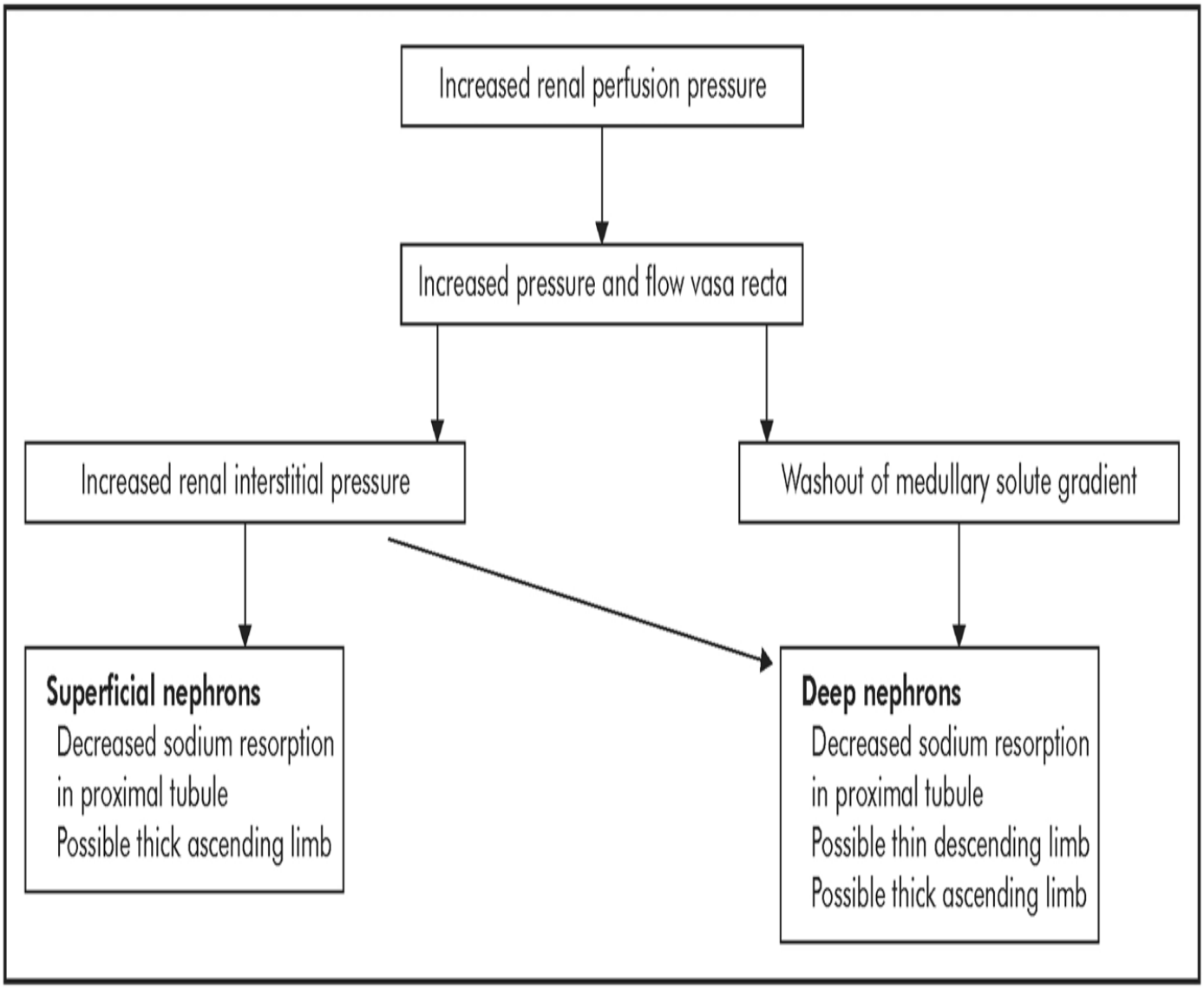
Renin angiotensin aldosterone system

It controls peripheral vascular artery resistance and re absorption of sodium and water.

Resetting of pressure natriuresis:

Regulation of body fluid volume by the kidney is the important mechanism for long term control of hypertension.Under normal conditions,sodium excretion is about 150mEq/day and perfusion pressure is about 100mmHg . The curve relating sodium excretion to arterial pressure is steep which can be shifted to right

or the slope can be depressed in renal insult[14]. Studies in animal model shows that alteration in renal function causing resetting of pressure natriuresis is inherited**.**



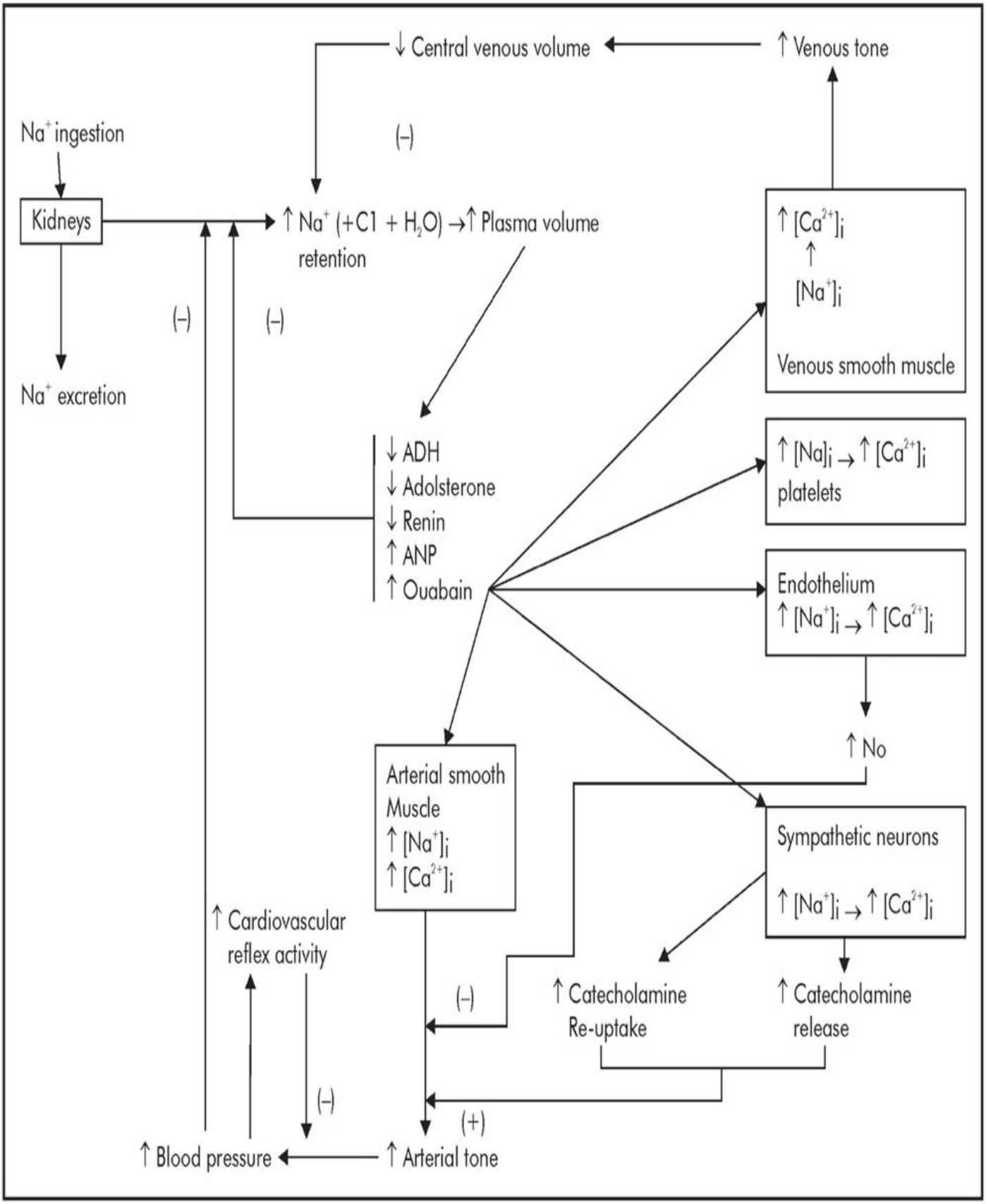
REDUCED NEPHRON NUMBER:

Brenner et al states the hypothesis that the nephron endowment at birth is inversely related to the risk of development of hypertension in later life[15]. Congenital decrease in number of nephrons or the filtration surface area(FSA) per glomerulus decrease the ability to excrete sodium,increases blood pressure.

This is contributed by the fetal environment and fetal under nutrition which leads to low birth weight and ultimately to hypertension in the future. It is estimated that a one kg decrease in birth weight is associated with 2-4 mm of Hg increase in systolic blood pressure in adulthood[16].

RENIN ANGIOTENSIN-ALDOSTERONE SYSTEM:

Renin angiotensin aldosterone system play a major role in the pathogenesis of hypertension .Renin,a protease produced by juxta glomerular cells convert angiotensinogen to angiotensin 1 which is then converted to angiotensin 2 by the Angiotensin-converting enzyme. Interaction of angiotensin 2 and G protein coupled receptors activate multiple cellular processes which contribute to hypertension and accelerated end organ damage . This includes vasoconstriction ,vascular inflammation,reactive oxygen species generation, vascular remodelling and aldosterone production.



There is more evidence that angiotensin 2 ,aldosterone ,renin and even

prorenin activates numerous signal pathways which causes vascular damage and can cause hypertension. In essential hypertension patients the plasma renin levels are expected to be low but in majority of patients having inappropriately normal or even elevated plasma renin angiotensin levels .Renin angiotensin aldosterone system is abnormally activated in patients with essential hypertension patients .

Three mechanisms have been proposed:

- ✓ **nephron heterogeneity**
- ✓ **non modulation**
- ✓ **increased sympathetic drive.**

NEPHRON HETEROGENEITY IN ESSENTIAL HYPERTENSION:[17]

1.There are ischaemic nephrons with impaired sodium excretion intermingled with adapting hyperfiltering hypernatriuretic nephrons .

2.renin secretion is high from ischaemic nephrons and low from the hyperfiltering nephrons.

3.the inappropriate circulating renin-angiotensin level impairs sodium excretion because:

A. In the adapting hypernatriuretic nephrons

- ✓ It increases tubular sodium reabsorption.
- ✓ It enhances tubuloglomerular feedback-mediated afferent constriction.

B. As the circulating renin level is diluted by non-participation of adapting nephrons ,it becomes inadequate to support efferent tone in hypoperfused nephrons.

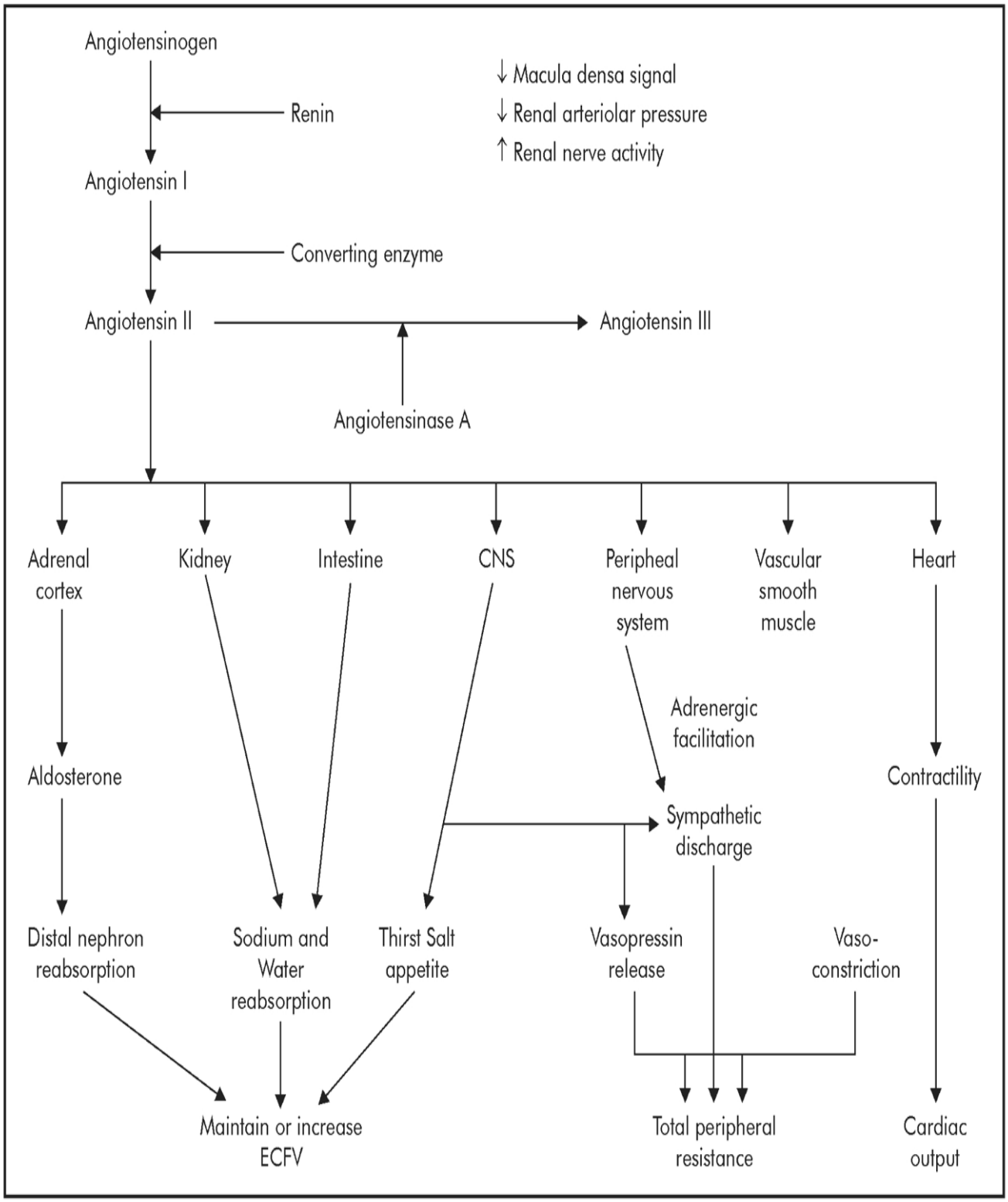
4.A loss of nephron number with age and from ischaemic further impairs sodium excretion.

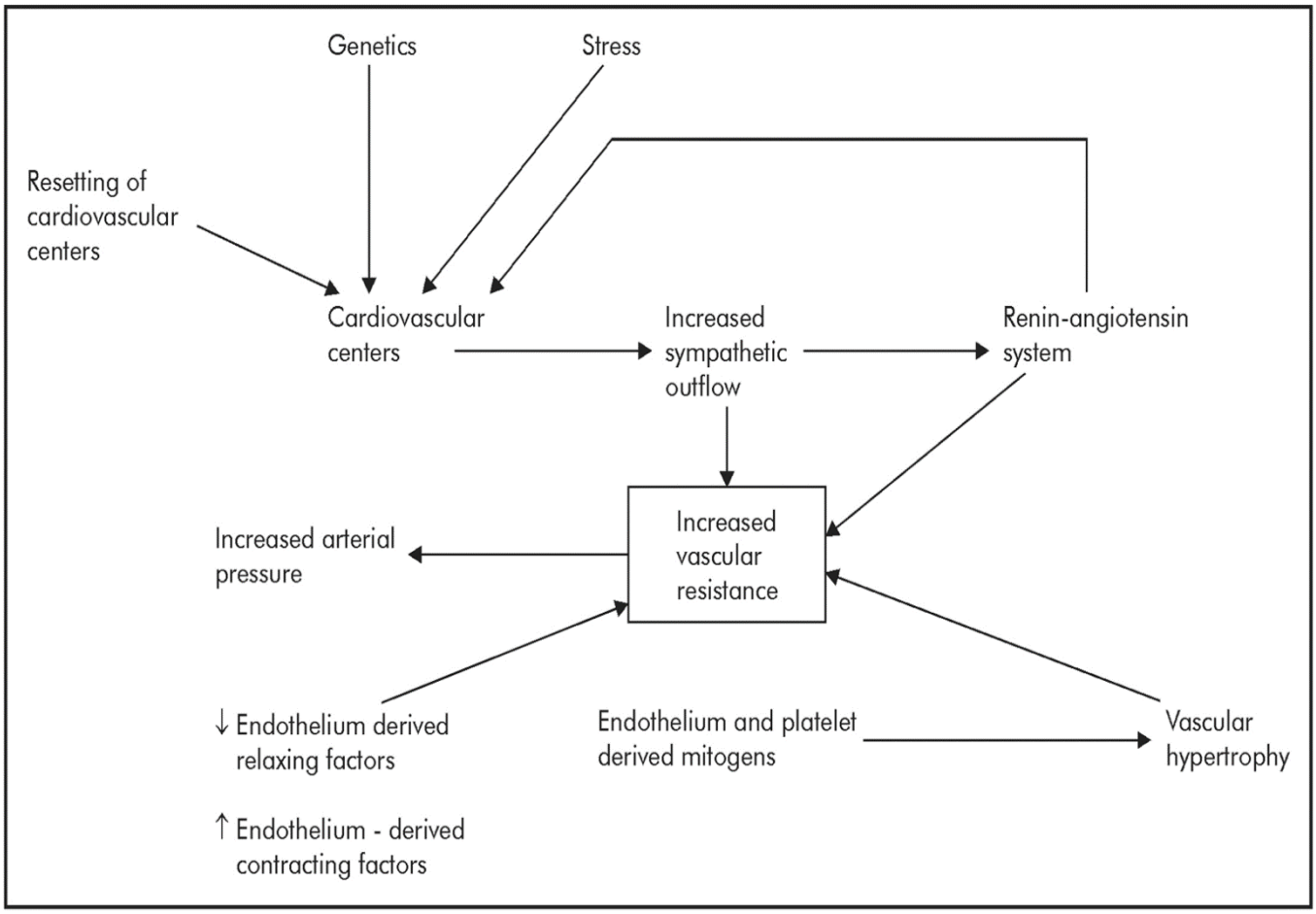
NON-MODULATION:

This is proposed by Williams and Hollenberg. Normal renin and high renin levels seen in nearly Half of the hypertensive patients is due to defective feedback regulation of the renin angiotensin system within the kidneys and the adrenal glands[18]. Non modulation is characterised by abnormal adrenal and renal responses to angiotensin 2 and salt load[19]. Non modulation in relation to high sodium intake will explain the mechanism of sodium sensitive hypertension.

STRESS AND SYMPATHETIC OVERACTIVITY:

Increased sympathetic activity maybe the important factor in essential hypertension .Excess renin-angiotensin activity interact with sympathetic nervous system. On other hand, stress can activate sympathetic nervous system which inturn may interact with renin angiotensin system,high salt intake and insulin resistance.


Angiotensinogen
Renin
↓ Macula densa signal
↓ Renal arteriolar pressure
↑ Renal nerve activity
Angiotensin I
Converting enzyme
Angiotensin II
Angiotensin III
Angiotensinase A
Adrenal cortex
Kidney
Intestine
CNS
Peripheal nervous system
Vascular smooth muscle
Heart
Adrenergic facilitation
Aldosterone
Contractility
Sympathetic discharge
Distal nephron reabsorption
Sodium and Water reabsorption
Thirst Salt appetite
Vasopressin release
Vaso-constriction
Maintain or increase ECFV
Total peripheral resistance
Cardiac output



BARORECEPTOR DYSFUNCTION:

Baroreceptors normally reduce blood pressure and heart rate through sympathetic stimulation and vagal stimulation when stimulated by rise in blood pressure or central venous pressure.Sustained Hypertension result in resetting of baroreceptor reflex through both structural and functional changes.The decreased inhibition over vasomotor center due to resetting of baroreflex may cause increased sympathetic outflow and in turn increases blood pressure.

PERIPHERAL RESISTANCE:

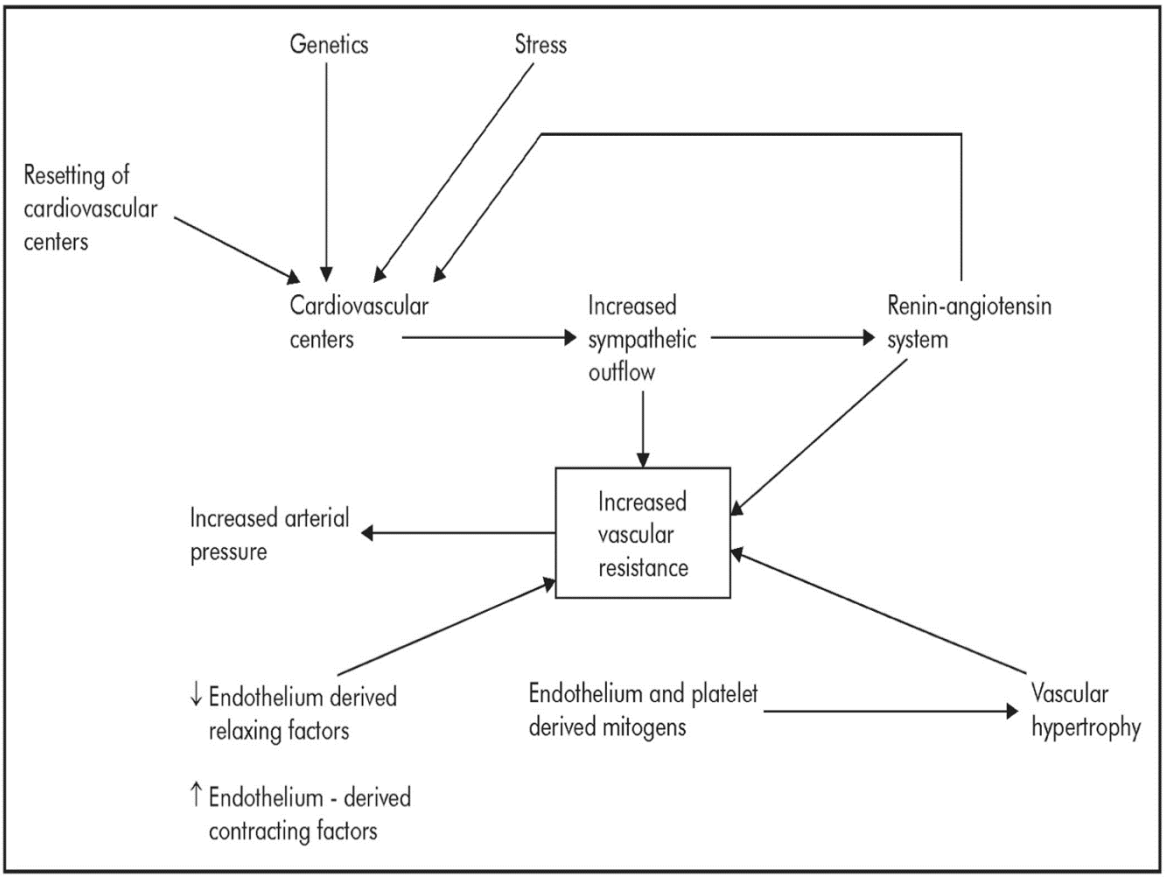
Increase in peripheral resistance particularly in precapillary vessel is the most important determinant in sustained rise in blood pressure .In experimental animal models structural changes in these vessels are observed including decrease in lumen diameter ,increased media to lumen ratio.Increased media to lumen ratio is the hallmark of hypertensive remodeling. Smooth muscle cells normally rearrange themselves in the smaller lumen diameter .This process is termed as inward eutrophic remodelling.Thus media to lumen ratio is increased but cross sectional area is unchanged. Lumen diameter is decreased and inward eutrophic remodeling is increased thus causing systemic vascular resistance to increase. This is the hallmark of diastolic hypertension

In contrast remodeling of large arteries is caused by hypertrophic gene expression causing increase in medial thickness and increase in media to lumen ratio.this type of remodelling causes increase in the vascular smooth muscle cell size and also accumulation of extracellular matrix proteins (collagen,fibronectin)due to activation of TGF-beta .This leads to large artery stiffness which is the hallmark of isolated systolic hypertension.

Hence antihypertensive therapy will not provide adequate cardiovascular protection unless vascular remodelling is prevented or reversed by normalising endothelial function and eliminating underlying neurohormonal activation.[20]

CELL MEMBRANE ALTERATION:

Alterations in the physical properties of the cell membrane and multiple transport system play a role in the pathogenesis of hypertension[21].Evidence suggesting that there is stimulation of sodium potassium exchanger in hypertension is due to either by enhanced calcium entry or by an increased intracellular calcium load.Increased sodium potassium exchanger stimulates cell growth , vascular tone and increases sodium reabsorption in renal proximal tubule[22].

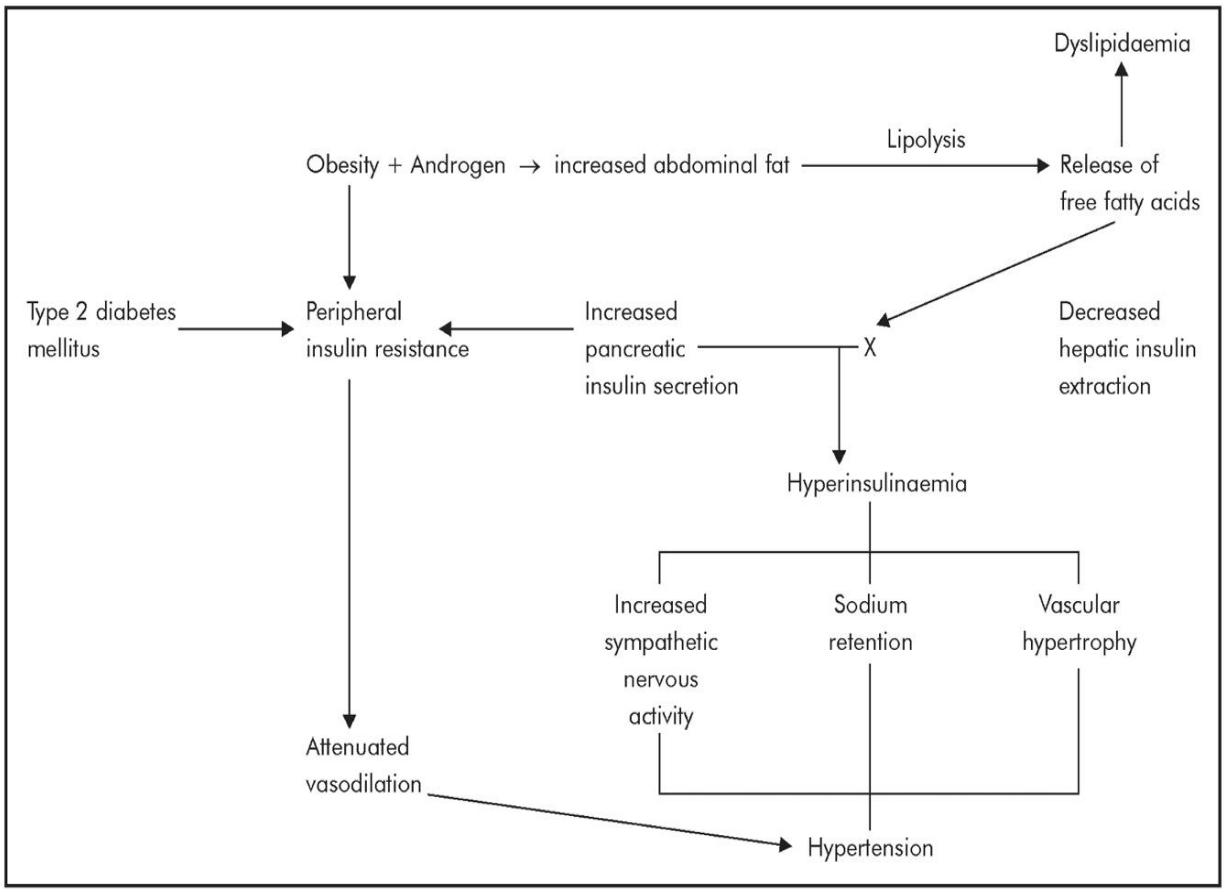


ENDOTHELIAL DYSFUNCTION :

Nitric oxide (NO) is the major endogenous vasodilator but its role in regulation of blood pressure is uncertain[23].Many studies have shown that nitric oxide has influence over renal hemodynamics and blood pressure[24]. Nitric oxide is more active in medullary circulation. When there is decreased nitric oxide synthesis or vascular responsiveness,pressure natriuresis response increases followed by reduction in renal papillary blood flow ,sodium excretion and renal interstitial hydrostatic pressure,without changes in renal blood flow or glomerular filtration rate[25]. Endothelial 1 causes prolonged vasoconstriction and hence endothelial receptor blockage improves vasodilatation in hypertensive patients.

OBESITY:

Obesity is one of the most important risk factor for hypertension. Obesity causes increased cardiac output,stroke volume ,low peripheral resistance and increased total blood volume[26]. The prevalence of hypertension increases in relation to the increase in BMI ,fasting blood glucose level and degree of upper body obesity[27].



INSULIN RESISTANCE AND HYPERINSULINEMIA :

Hyperinsulinemia is associated with rise in blood pressure. Many mechanisms explaining the association has been proposed which include[28]

- Enhanced renal sodium and water reabsorption

  Increased blood pressure sensitivity to dietary salt intake .

  Augmentation of the pressure and aldosterone response to angiotensin2

  Changes in transmembrane electrolyte transport

- Increased intracellular calcium accumulation

  Stimulation of growth factor,especially in vascular smooth muscle.

Stimulation of sympathetic nervous activity

Reduced synthesis of vasodilatory prostaglandins

Impaired vasodilation

Increased secretion of endothelin

Hyperinsulinemia in hypertension is due to consequence of resistance of insulin on peripheral utilisation of glucose. This is especially seen in patients with obesity. This association is seen in Asian black as well as Whites. Impairment of peripheral action of insulin results from defect in the vasodilatory effect of insulin mediated through increase in synthesis of nitric oxide, which normally counter regulates the pressor effect of insulin[29].The pressor effect of insulin includes increased renal sodium reabsorption , increase in sympathetic activity and tropic action on vascular hypertrophy.

SECONDARY HYPERTENSION[30]:

The cause for hypertension is identified in around 5 to 10% of the patient and some of them are curable. This is known as secondary hypertension.

CAUSES OF SECONDARY HYPERTENSION[30,31]

Renal disorders:

1.Renal parenchymal disorders:

- ✓ Acute and chronic glomerulonephritis, polycystic kidney disease, interstitial nephritis , Hereditary nephritis, radiation nephritis
- ✓ Chronic reflex nephropathy
- ✓ Obstructive uropathy.

- ✓ Liddle syndrome
- ✓ Renin secreting tumours

2. Reno vascular disorders:

- ✓ Fibromuscular dysplasia.
- ✓ Coarctation of aorta
- ✓ Arteriosclerosis
- ✓ Renal artery stenosis

Endocrine disorders:

- Cushing syndrome
- Conn syndrome
- Bilateral adrenocortical hyperplasia
- Adrenal carcinoma
- Primary aldosteronism
- Ectopic corticotropin secreting tumour
- Acromegaly
- Pheochromocytoma
- Metabolic syndrome
- Hyperthyroidism
- Hypothyroidism
- Hyperparathyroidism
- Carcinoid

Toxemia of pregnancy

Neurogenic factors:

- Raised intracranial pressure
- Acute porphyria
- Poliomyelitis
- Spinal cord injuries
- Denervation
- Familial dysautonomia
- Psychogenic

Other causes:

- Sympathomimetic drugs
- Oral contraceptives
- Erythropoietin
- Estrogen therapy
- Glucocorticoid or mineralocorticoid therapy
- Antidepressants
- Mono amino oxidase inhibitors
- Lead toxicity
- Excessive salt appetite
- Alcohol abuse
- Amphetamines

CALCIUM:

Calcium is a mineral found in teeth and bone. Dietary sources include milk, egg yolk, Nuts, lentils, cheese, figs, cabbage, etc.

The total body calcium its around 100 to 170 grams. 99% of calcium is found in bones. 0.1% is found in extracellular fluid and 0.5% is found in soft tissues. It is found as calcium carbonate or phosphate. Normal plasma level of calcium is 9 to 11 milligram per deciliter. Calcium exists in 3 types namely

Ionised calcium

Protein bound calcium

Complex calcium

Physiologically active form of calcium is ionised calcium, approximately 40% of total calcium is ionised form. Albumin is major protein to bind calcium.

CALCIUM AND ESSENTIAL HYPERTENSION: PATHOGENESIS:

Many hypothesis have been postulated that calcium homeostatic abnormalities at cellular and organ level acts as a primary factor in pathogenesis of hypertension in experimental studies. A low calcium diet is implicated in causing hypertension in several studies. Exaggerated natriuresis leading to excessive secretion of phosphorus and calcium may lead to hypertension.

Leukocyte calcium levels have been increased in some hypertensives. Natriuretic hormone alters membrane permeability leading to increased intracellular sodium and sodium calcium exchange inhibition thereby causing calcium accumulation in smooth muscle cells of the vessel. Increased calcium

leads to increased vascular tone and contractility leading to increased peripheral vascular resistance and causes increase in blood pressure.

This increase in calcium in vascular smooth muscle cells due to raised intracellular sodium levels would be explained by the following:

1. Inhibition of sodium potassium exchange pump causes depolarization of muscle fibre causing increase in calcium entry through calcium channels (voltage gated).
2. Increased intracellular sodium results in smaller sodium gradient between external medium and sarcoplasm, causing decrease in calcium extrusion from cell via sodium calcium exchange, which is dependent on this gradient.
3. A very small increase in intracellular sodium can cause rise in intracellular calcium enough to increase the vascular smooth muscle resting tone to increase by about 50 percentage.
4. Increase in intracellular sodium at the presynaptic terminal of the sympathetic neuron promotes calcium dependent noradrenaline release which causes release of calcium from intracellular stores.

Moreover, natriuretic factor inhibits Ouabain sensitive sodium potassium ATPase pump causing increased intracellular calcium accumulation and increased vascular smooth muscle tone.

In patients with essential hypertension defects in calcium concentration, membrane binding and transport are identified in RBCs ,platelet and adipocytes.

Sodium calcium exchange is impaired and there is reduced calcium buffering. In RBCs of hypertensive patients the amount of calcium bound to the inner surface is reduced by 25-30%[33,34]. This leads to increased cellular permeability to sodium and inhibition of sodium potassium ATPase activity partially.

The calmodulin concentration in RBC in hypertension patients is found to be normal but the ability of calmodulin in activating calcium ATPase is impaired. This is because the affinity of calcium pump is reduced and the activity of the pump is also low[35] . It was also demonstrated that basal calcium ATPase activity is reduced in RBC membranes of hypertensive patients when compared with their controls[36]. These collective evidence suggest that basic alteration in the hypertensive subjects inner membrane calcium calmodulin binding and subsequent activation of energy dependent cation pumps such as calcium ATPase[37.]

In patients with hypertension,Intracellular calcium concentration is increased in the platelets.This is associated with decrease in extracellular calcium levels. This calcium homeostasis in platelets depends on stimulating efflux,limiting membrane fluxes and increase in sarcoplasmic reticulum sequestration[38]. All of these process are calcium calmodulin dependent only.

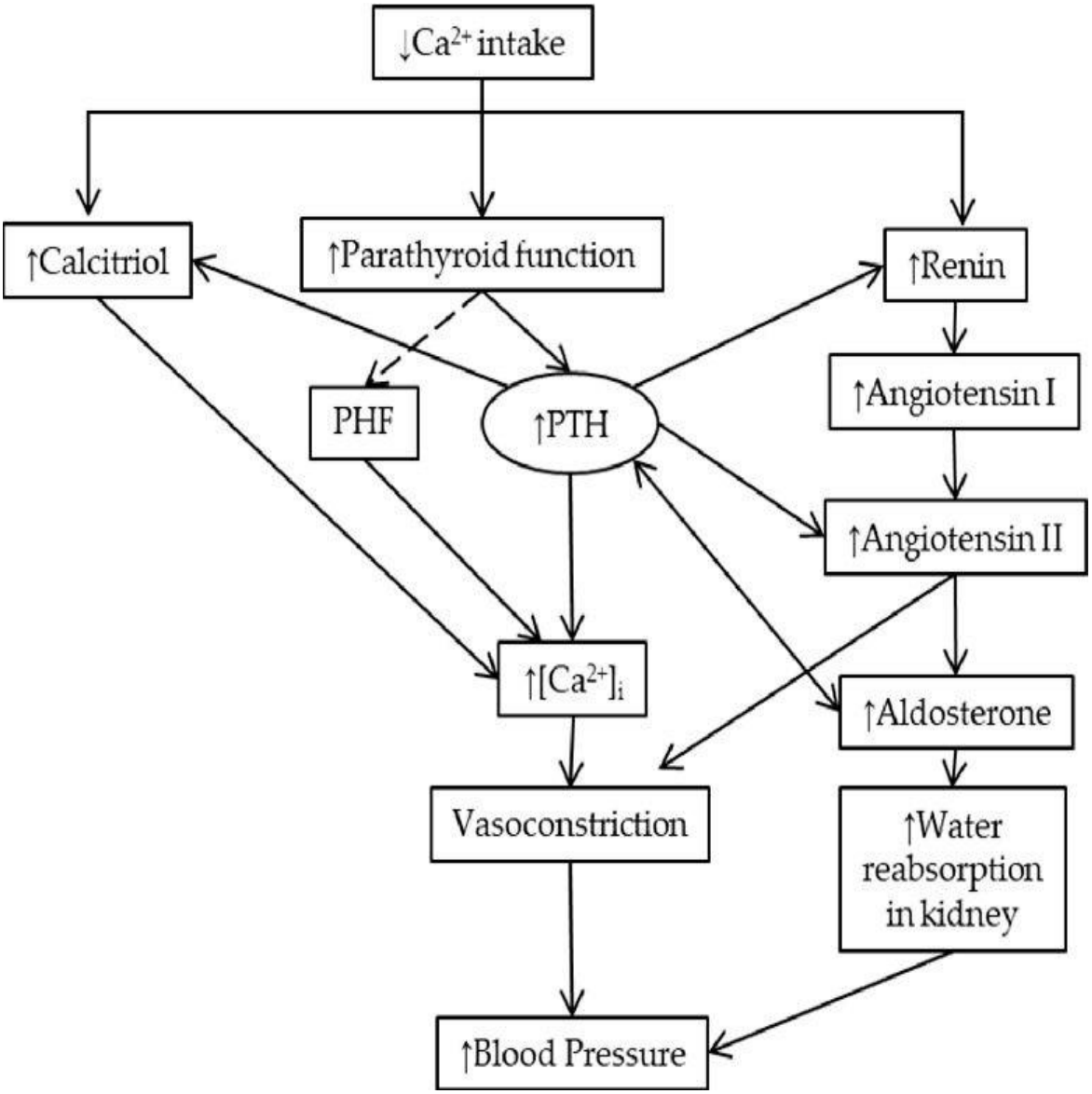
Regulation of normal calcium content in the cytosol is dependent on calcium ATPase and defects in calcium binding in RBCs.There is the possibility

of generalised membrane associated defect which is supported by the following observations: Intracellular calcium concentration is increased in red blood cells and adipocytes of hypertensive patients[39].

CALCIUM AND DIET:

Many studies show association between dietary calcium and blood pressure. But increased intake of dietary calcium in the benefit of treating hypertension remains controversial. Previous analysis of the NHANES 1 and 2 have yielded conflicting findings regarding the influence of various dietary variables on blood pressure particularly calcium[40].

Many cross sectional studies have shown relation between dietary calcium intake and blood pressure[41,42].Recent report from a large cohort study of women showed that dietary calcium intake was inversely related to hypertension among women[43].A study known as Western Electric Heart Study showed that calcium intake was inversely proportional to the incidence of increased diastolic BP but not of increased systolic blood pressure[44].



URINARY CALCIUM EXCRETION:

In patients with essential hypertension, there is increase in total and fractional urinary calcium excretion[45].There is a population survey that demonstrated positive correlation between the urinary calcium excretion and blood pressure among 9321 men[46]. This greater calcium excretion might be due

to greater dietary calcium intake.But the limitation of the study is that dietary calcium intake was not estimated in the study.But this cause and effect relationship is inconsistent with epidemiological data Since there is decreased intake of calcium in hypertensive patients.

In addition, in an interventional trial,which assessed urinary calcium excretion and dietary calcium intake in hypertensive subjects have observed that lower calcium intakes were associated with higher excretion rates[47]. But whether this excessive calcium excretion is the result of decreased ability to reabsorb calcium by the kidney or due to enhanced intestinal absorption as a result of decreased oral intake of calcium is controversial.

CALCIUM SUPPLEMENTATION:

Many short term studies of dietary intervention or either calcium supplementation in non pregnant adults show a decrease in blood pressure by 1.44/0.84 mmHg[48].But calcium supplementation can rarely causes increase in blood pressure and increase in renal stones,excessive calcium intake is not recommended but it is best to ensure that intake of calcium is not reduced by reduction in milk and cheese intake in order to reduce saturated fat consumption.

AIM AND OBJECTIVES

- To study the serum calcium levels in patients with primary hypertension.
- To correlate serum calcium levels and blood pressure.

METHODOLOGY

Study design:

Analytical study

Duration of study:

1 year(June 2021 to June 2022)

Sample size:

100 cases and 100 controls

Place of study:

out patient department and medical wards of tirunelveli medical college and hospital.

Inclusion criteria:

- ✓ Newly detected essential hypertensive patients
- ✓ Patients above 18 years of age
- ✓ Both sexes

Exclusion criteria:

- ✓ Known cases of hypertension on antihypertensives
- ✓ Chronic renal failure
- ✓ Patients with secondary hypertension
- ✓ Peripheral vascular disease
- ✓ Diabetes mellitus
- ✓ Cerebrovascular accident
- ✓ Ischemic heart disease

- ✓ Pregnancy
- ✓ Patients with malignant hypertension
- ✓ Adolescent and young adults
- ✓ Patients with acute illness
- ✓ Females on oral contraceptives
- ✓ Patients with any other medical or surgical complications

After applying these criteria ,100 cases with essential hypertension were included after getting informed consent from them. Similarly 100 normotensive controls were selected and included in the study after getting informed consent. History and clinical examination was conducted in patients with hypertension. Relevant blood and urine investigations were done to rule out secondary hypertension. Patients weight and height were measured body mass index was calculated using the formula BMI=weight in kg/(height in meter)^2. All peripheral pulses were checked to rule out early atherosclerotic changes. Fundus examination was done to rule out hypertensive retinopathy. Patients were asked to refrain from smoking ,drinking coffee or tea at least 30 mins before blood pressure measurement.

BMI values are 18.5 to 24.9 kg/m^2 was taken as normal weight.25-29.9 kg/m^2 was taken as overweight, more than 30 kg/m^2 was taken as obese.

Family history was considered in father ,mother and siblings. Life is considered sedentary with physical activity was less than 3 METS .

Alcoholism was defined as more than 2 drinks per day. Smoker was defined as more than 5 cigarettes per day.

Guidelines for measurement of blood pressure:

Condition for patients:

- Patient must sit quietly with back supported and arm at the level of heart for 5 mins.
- Sitting position was taken for routine measurements.
- For patients more than 65 years postural changes were checked by taking readings immediately and after 2 mins of standing.
- No smoking 30 mins prior to measurement
- No caffeine intake 30 mins prior to measurement.
- A warm silent setting.
- No exogenous stimulants like nasal decongestant or eye drops like phenylephrine.

Equipments:

Mercury manometer calibrated every 6 months was used to measure the blood pressure. The cuff should cover two third of the arm length.

Technique:

Two readings were taken on each occasion. For diagnosis 3 sets of readings 1 week apart was obtained. Blood pressure was taken in both arms . If the arm

pressure is elevated blood pressure was taken in lower limb. If there is pressure difference between both arms the arm with higher blood pressure is considered.

Blood pressure is recorded by inflating the bladder to a pressure of 20 mmhg above the systolic pressure which is identified by disappearance of radial pulse. If the bladder deflated at the rate of 3mmHg per second. Korotkoff sound phase 1 was considered as systolic blood pressure and phase 5 (disappearance) was considered as diastolic blood pressure.

Urine routine analysis was done in all those subjects. Over night fasting blood sugar and renal function test was done by using DAM technique(Diacetyl mono amine).

Serum calcium levels were estimated by using cresolphthalein complexone method. Serum albumin was measured by BCG method.

Corrected serum calcium levels were obtained by using the formula :

corrected serum calcium = serum calcium+0.8(4.0-serum albumin).

Hypertension was defined as per JNC 8 guidelines ,systolic pressure more than 140mmhg and diastolic pressure more than 90mmhg were considered as hypertensives.

Statistical analysis:

All the collected data were entered in Microsoft excel spreadsheet and statistically analysed using SPSS software. Results were considered significant if p value was <0.05.

The tests used for statistical analysis includes the following:

- ✓ Chi square test
- ✓ Pearson's correlation.

OBSERVATION AND RESULTS

200 SUBJECTS were included in this study among them 100 were hypertensive(cases) and 100 were normotensive(controls).

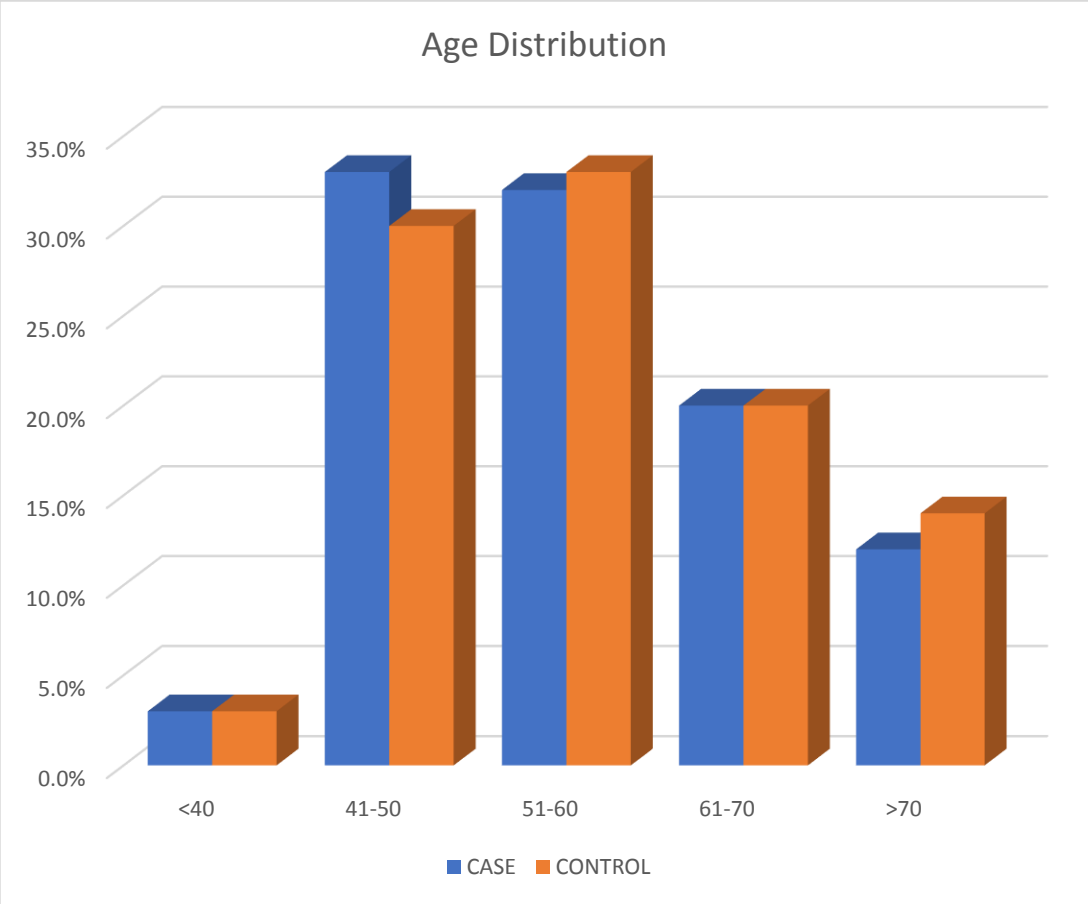
Newly detected hypertensive patients were included in cases.

1.AGE DISTRIBUTION:

Age group * Group Crosstabulation						
			Group		Total	P value
			Case	Control		
Age group	<40	Count	3	3	6	0.989
		% within Group	3.0%	3.0%	3.0%	
	41-50	Count	33	30	63	
		% within Group	33.0%	30.0%	31.5%	
	51-60	Count	32	33	65	
		% within Group	32.0%	33.0%	32.5%	
	61-70	Count	20	20	40	
		% within Group	20.0%	20.0%	20.0%	
	>71	Count	12	14	26	
		% within Group	12.0%	14.0%	13.0%	
Total		Count	100	100	200	
		% within Group	100.0%	100.0%	100.0%	

P value= 0.989

Among the cases ,age distribution were less than 40 years (3%),41-50 years(33%),51-60years(32%),61-70years(20%) and above 70years (12%). Among the controls age distribution were less than 40 years (3%),41-50 years(30%),51-60years(33%),61-70years(20%) and above 70years (14%). Most of the patients in both study group and control group were of similar age.there was no statistically significant difference in the age distribution of cases and controls.(p>0.05)

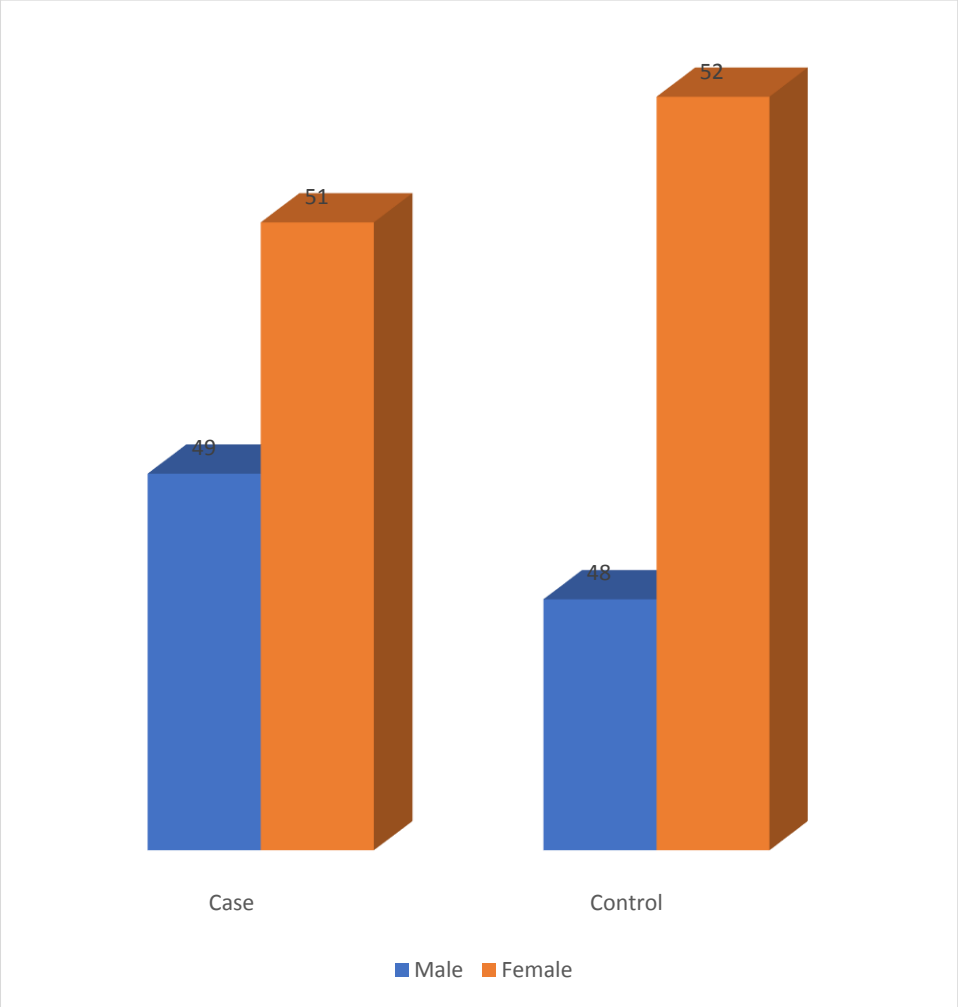


2.SEX DISTRIBUTION:

			Group		Total	P value
			Case	Control		
Sex	F	Count	49	48	97	0.887
		% within Group	49.0%	48.0%	48.5%	
	M	Count	51	52	103	
		% within Group	51.0%	52.0%	51.5%	
Total		Count	100	100	200	
		% within Group	100.0%	100.0%	100.0%	

P value=0.887

Among the cases,49% were males and 51% were females.Among the controls,48% were male and 52% were females.p value was >0.05.Hence there was no statistical difference in the sex distribution of cases and controls.

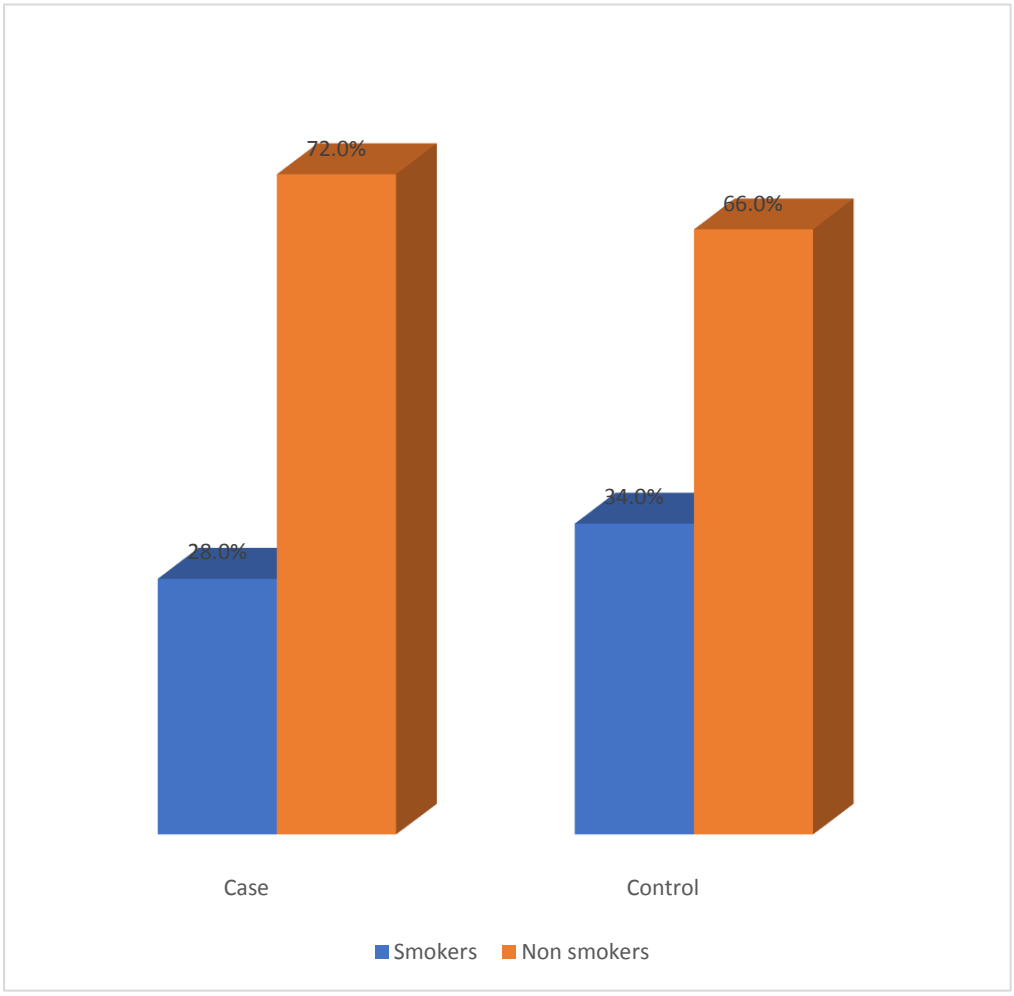

52
51
49
48
Case
Control
Male
Female

3.DISTRIBUTION OF SMOKERS AMONG CASES AND CONTROLS:

			Group		Total	P value
			Case	Control		
Smoking	No	Count	72	66	138	0.359
		% within Group	72.0%	66.0%	69.0%	
	Yes	Count	28	34	62	
		% within Group	28.0%	34.0%	31.0%	
Total		Count	100	100	200	
		% within Group	100.0%	100.0%	100.0%	

P value =0.359

In cases,28%were smokers and 72% were non smokers .In controls,34% were smokers and 66% were non smokers.p>0.05. Hence there was no statistical difference regarding smoking among cases and controls.

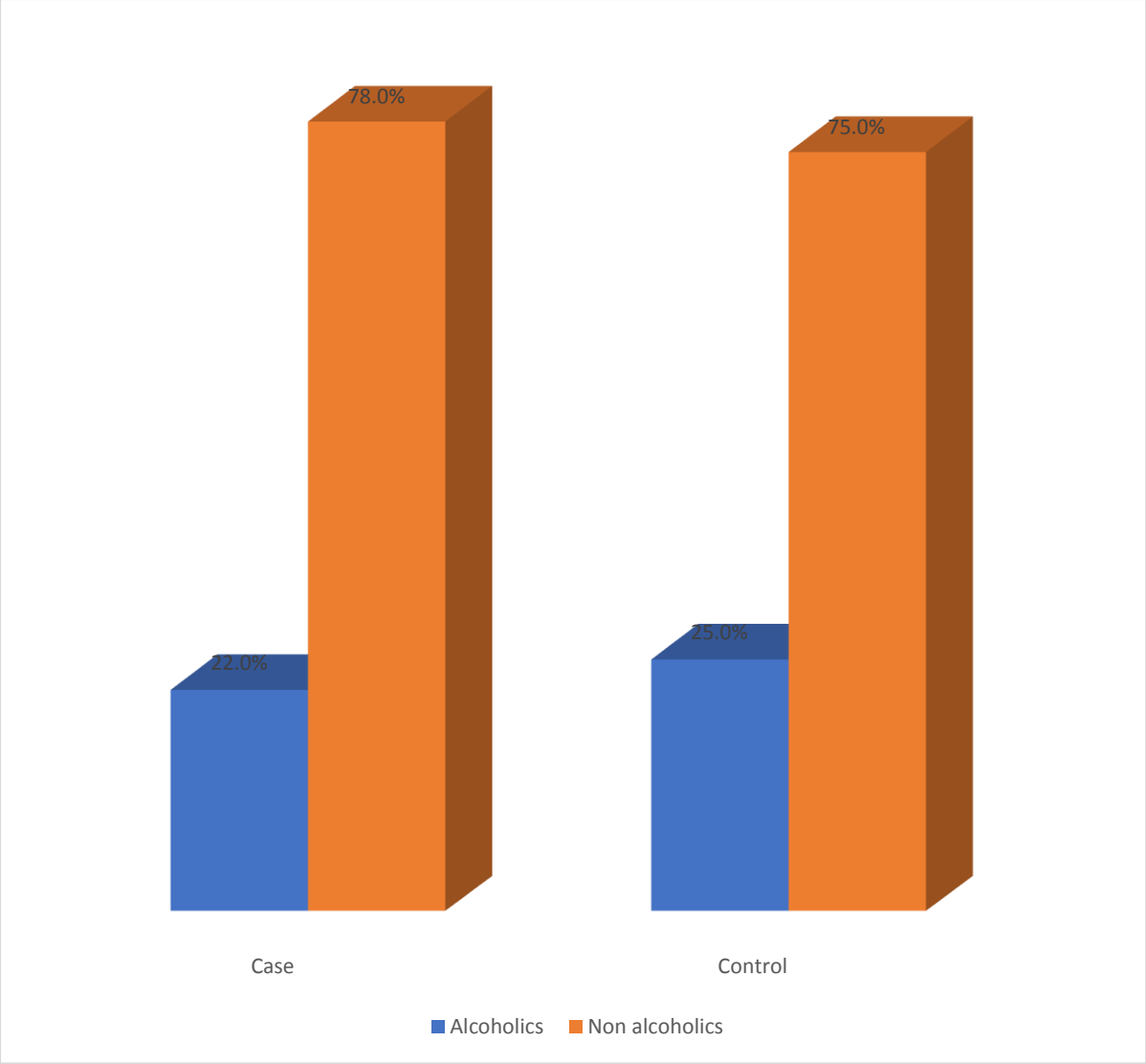

72.0%
66.0%
34.0%
28.0%
Case
Control
Smokers
Non smokers

4.DISTRIBUTION OF ALCOHOLICS AMONG CASES AND CONTROLS:

			Group		Total	P value
			Case	Control		
Alcohol	No	Count	78	75	153	0.617
		% within Group	78.0%	75.0%	76.5%	
	Yes	Count	22	25	47	
		% within Group	22.0%	25.0%	23.5%	
Total		Count	100	100	200	
		% within Group	100.0%	100.0%	100.0%	

P value=0.617

In cases,22%were alcoholics and 78% were non alcoholics .In controls,25% were alcoholics and 75% were non alcoholics .p>0.05. Hence there was no statistical difference regarding alcohol consumptions among cases and controls.

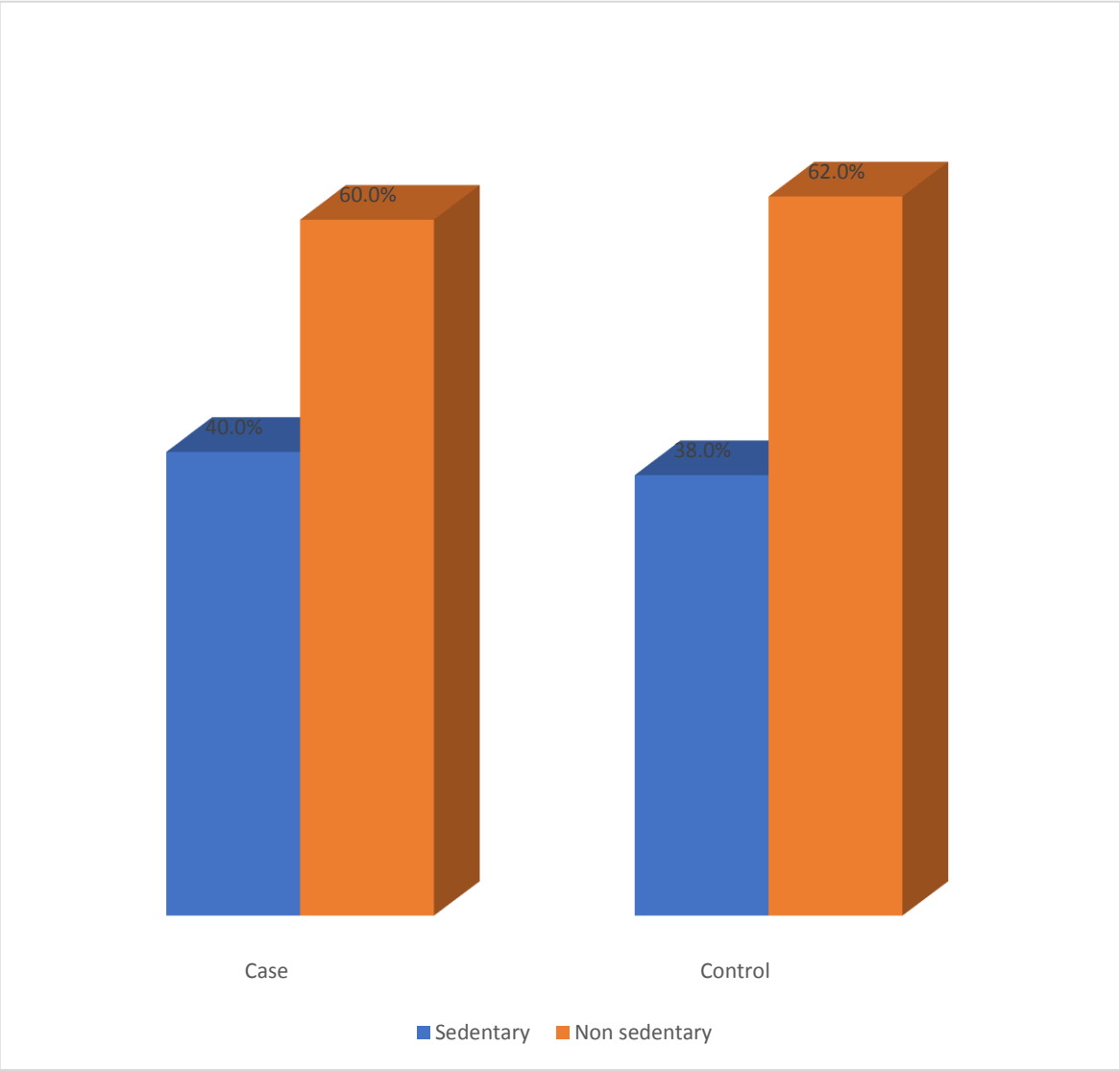

78.0%
75.0%
22.0%
25.0%
Case
Control
Alcoholics
Non alcoholics

5. DISTRIBUTION OF LIFESTYLE AMONG CASES AND CONTROLS:

			Group		Total	P value
			Case	Control		
Life style	NS	Count	60	62	122	0.772
		% within Group	60.0%	62.0%	61.0%	
	S	Count	40	38	78	
		% within Group	40.0%	38.0%	39.0%	
Total		Count	100	100	200	
		% within Group	100.0%	100.0%	100.0%	

P value=0.772

In cases,40% had sedentary habits and 60% had non sedentary habits..In controls,38% had sedentary habits and 62% had non sedentary habits .p>0.05. Hence there was no statistically significant difference noted in the lifestyle among cases and controls.

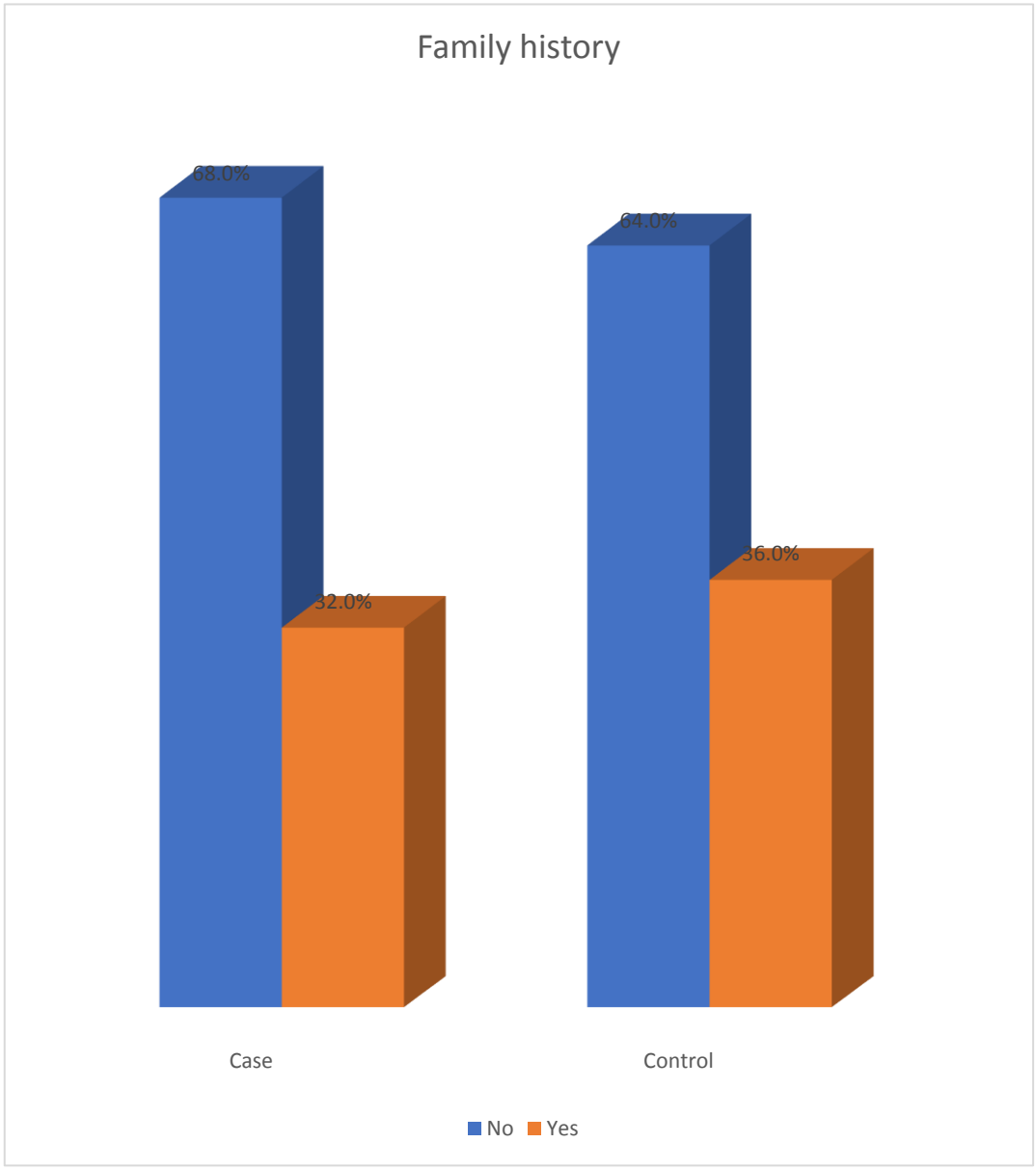

60.0%
62.0%
40.0%
38.0%
Case
Control
Sedentary
Non sedentary

6.DISTRIBUTION OF FAMILY HISTORY OF HYPERTENSION AMONG CASES AND CONTROLS:

			Group		Total	P value
			Case	Control		
Family history	No	Count	68	64	132	0.55
		% within Group	68.0%	64.0%	66.0%	
	Yes	Count	32	36	68	
		% within Group	32.0%	36.0%	34.0%	
Total		Count	100	100	200	
		% within Group	100.0%	100.0%	100.0%	

P value=0.55

Among the cases,32% had positive family history and 68% had no significant family history. Among controls,36% had a positive family history and 64% had no family history of hypertension.p value was >0.05. There was no statistically significant difference in the family history of cases and controls.

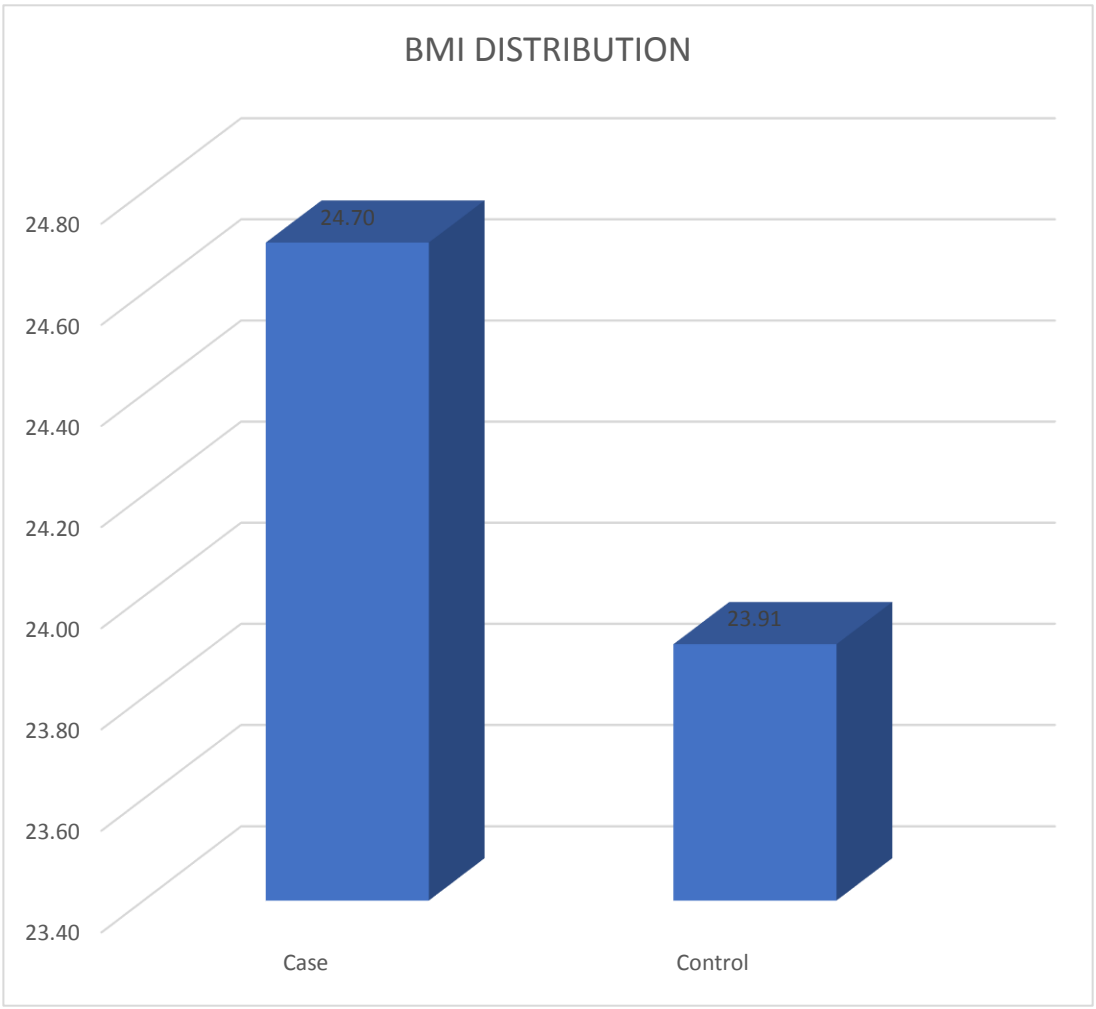

Family history
68.0%
32.0%
64.0%
36.0%
Case
Control
No
Yes

7.DISTRIBUTION OF BMI BETWEEN CASES AND CONTROLS:

Group		Mean	Standard .Deviation
BMI	Case	24.70	3.87
	Control	23.91	3.72

P value=0.141

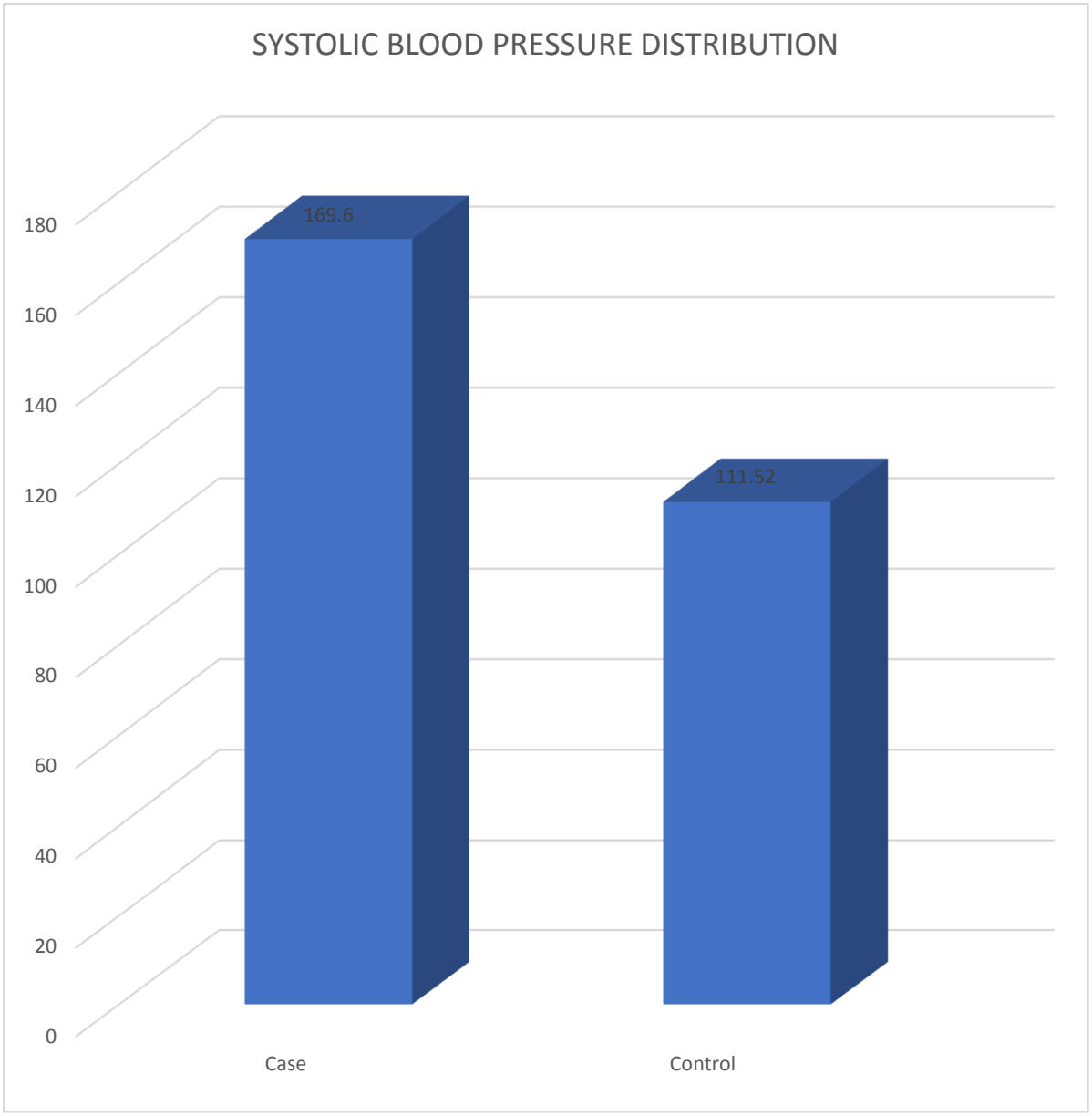
The mean BMI among cases was 24.70 and among controls was 23.91.P value was more than 0.05.Hence there was no statistically significant difference in the distribution of Body Mass Index(BMI) among cases and controls.


BMI DISTRIBUTION
24.80
24.60
24.40
24.20
24.00
23.80
23.60
23.40
24.70
23.91
Case
Control

8. DISTRIBUTION OF SYSTOLIC BLOOD PRESSURE AMONG CASES AND CONTROLS:

Group		Mean	Standard Deviation
SYSTOLIC BP	Case	169.60	18.00
	Control	111.52	6.96

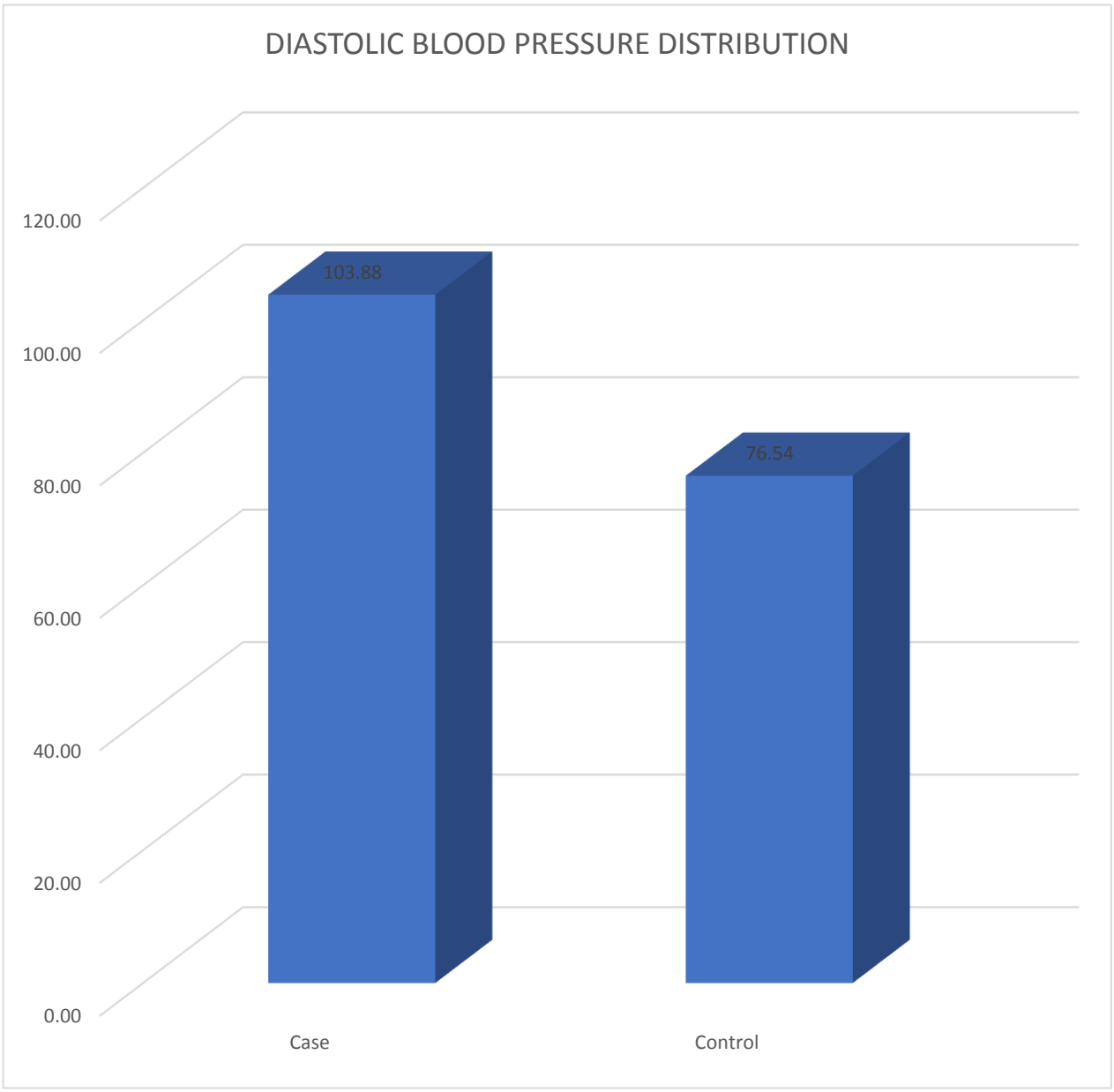
The mean systolic blood pressure among the cases was 169.6±18.00 mmHg.Among the controls the mean distribution of systolic blood pressure was 111.52±6.96 mmHg. The systolic blood pressure was elevated in cases but this is due to the inclusion criteria of the study and hence statistical analysis was not done about its significance.


SYSTOLIC BLOOD PRESSURE DISTRIBUTION
180
160
140
120
100
80
60
40
20
0
169.6
111.52
Case
Control

9. DISTRIBUTION OF DIASTOLIC BLOOD PRESSURE AMONG CASES AND CONTROLS:

Group		Mean	Standard Deviation
DIASTOLIC BP	Case	103.88	8.74
	Control	76.54	6.89

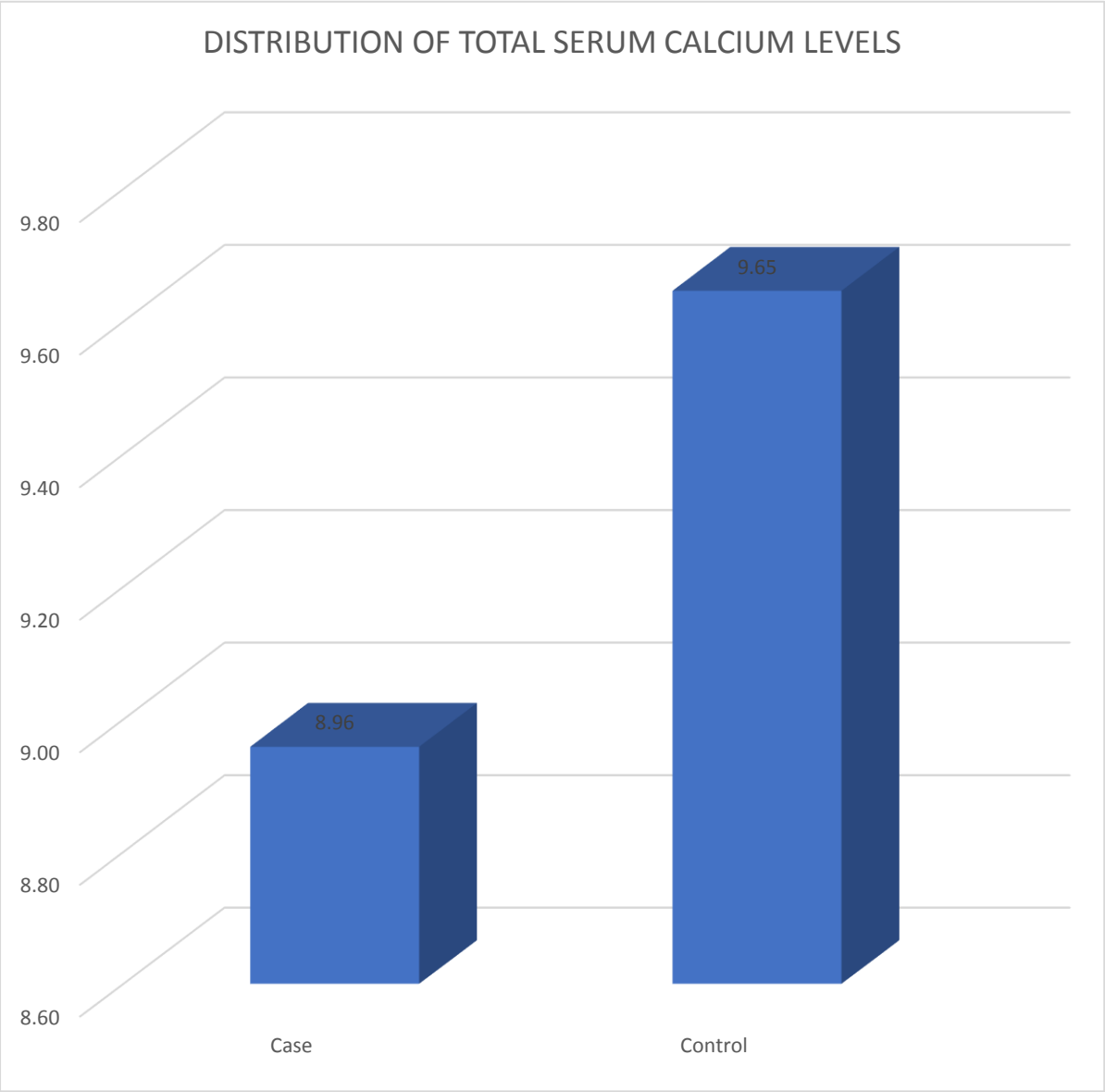
The mean diastolic blood pressure among the cases was 103.88±8.74 mmHg.Among the controls the mean distribution of diastolic blood pressure was 76.54±6.89 mmHg. The diastolic blood pressure was elevated in cases but this is due to the inclusion criteria of the study and hence statistical analysis was not done about its significance.


DIASTOLIC BLOOD PRESSURE DISTRIBUTION
120.00
100.00
80.00
60.00
40.00
20.00
0.00
103.88
76.54
Case
Control

10. DISTRIBUTION OF TOTAL SERUM CALCIUM LEVELS AMONG CASES AND CONTROLS:

Group		Mean	Standard Deviation	P value
TOTAL SERUM CALCIUM	Case	8.96	0.65	<0.0001
	Control	9.65	0.81	

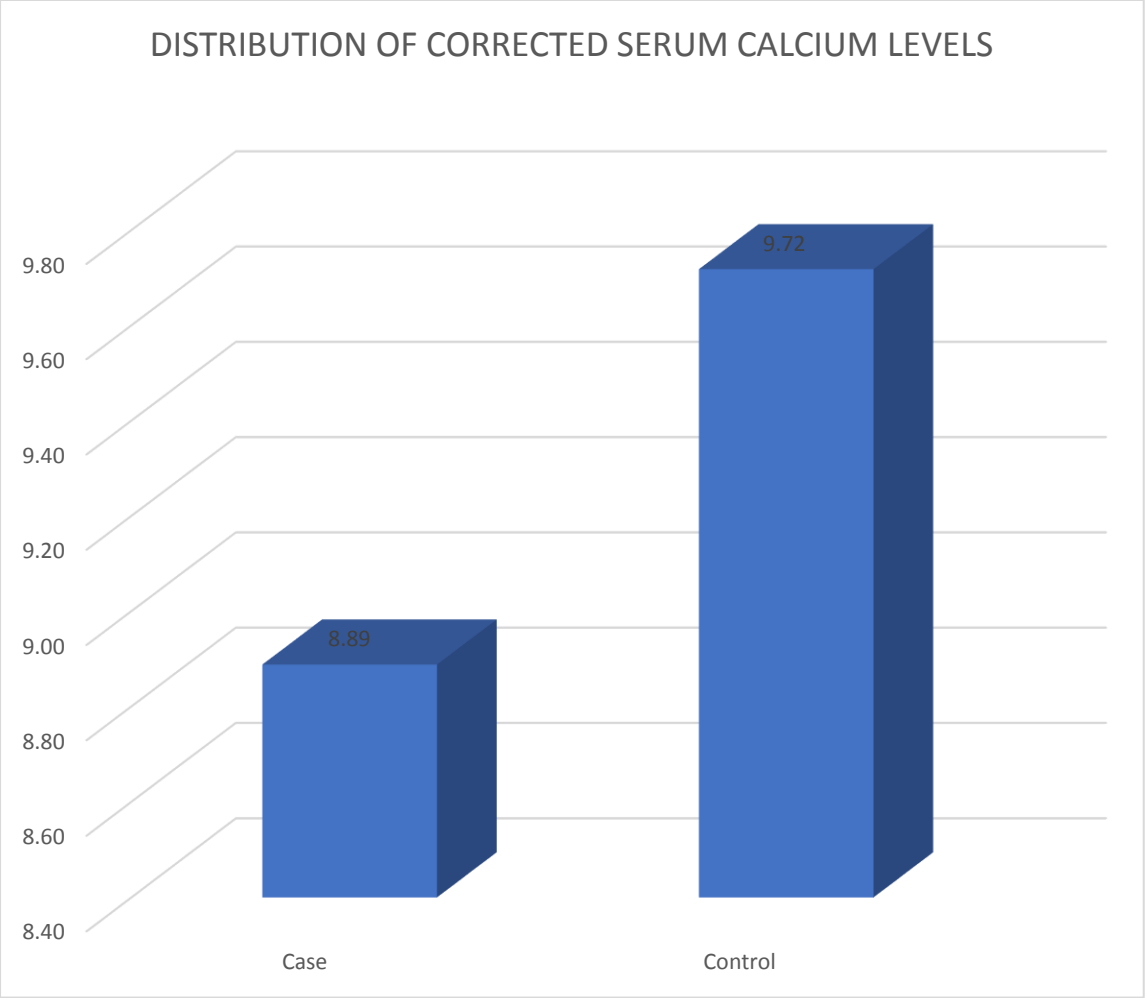
The mean Serum calcium level among the cases was 8.96±0.65 while in the controls ,the mean was 9.65±0.81 .p value was <0.0001. Hence there was statistically significant difference in calcium levels among cases and controls. This shows that serum calcium levels was significantly lower in the hypertensive population.


DISTRIBUTION OF TOTAL SERUM CALCIUM LEVELS
9.80
9.60
9.40
9.20
9.00
8.80
8.60
8.96
9.65
Case
Control

11. DISTRIBUTION OF CORRECTED SERUM CALCIUM LEVELS AMONG CASES AND CONTROLS:

Group		Mean	Standard Deviation	P value
CORRECTED CALCIUM	Case	8.89	0.72	<0.0001
	Control	9.72	0.86	

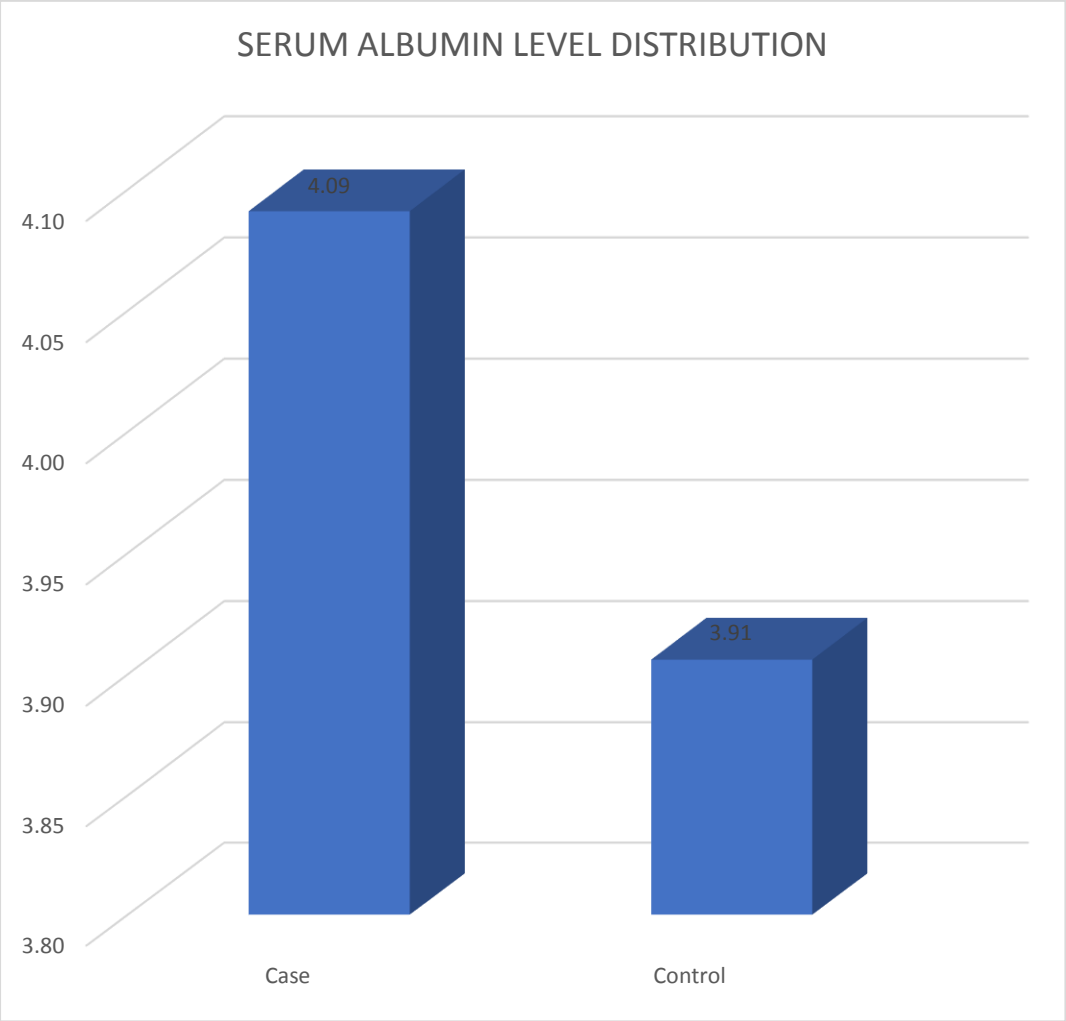
The mean Serum corrected calcium level among the cases was 8.89±0.72 while in the controls ,the mean was 9.72±0.86 .p value was <0.0001. Hence there was statistically significant difference in corrected calcium levels among cases and controls. This shows that serum corrected calcium levels was significantly lower in the hypertensive population.


DISTRIBUTION OF CORRECTED SERUM CALCIUM LEVELS
9.80
9.60
9.40
9.20
9.00
8.80
8.60
8.40
8.89
9.72
Case
Control

12. DISTRIBUTION OF SERUM ALBUMIN BETWEEN CASES AND CONTROLS:

Group		Mean	Standard Deviation	P value
SERUM ALBUMIN	Case	4.09	0.37	0.052
	Control	4.01	0.41	

The mean serum albumin levels among cases was 4.09±0.37 and among controls was 4.01±0.41.p value was more than 0.05.Hence there was no statistically significant difference in the distribution of serum albumin among cases and controls.


SERUM ALBUMIN LEVEL DISTRIBUTION
4.10
4.05
4.00
3.95
3.90
3.85
3.80
4.09
3.91
Case
Control

13.CORRELATION BETWEEN SYSTOLIC BLOOD PRESSURE AND SERUM TOTAL CALCIUM LEVELS AMONG CASES:

		Systolic blood pressure	Total calcium
SYSTOLIC BP	Pearson correlation	1	-419**
	Sig.(2-tailed)		.000
	N	200	200
TOTAL CALCIUM	Pearson correlation	-419**	1
	Sig.(2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlation between systolic bp and total calcium level :

	Pearson's Correlation	
Systolic BP & Total calcium level	Correlation co-efficient	Sig.(2-tailed)
	-.419	.00

Significant negative correlation was found between total serum calcium levels and systolic bp

14.CORRELATION BETWEEN DIASTOLIC BLOOD PRESSURE AND SERUM TOTAL CALCIUM LEVELS IN CASES:

		TOTAL CALCIUM	DIASTOLIC BP
TOTAL CALCIUM	Pearson Correlation	1	-.392**
	Sig. (2-tailed)		.000
	N	200	200
DIASTOLIC BP	Pearson Correlation	-.392**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

Correlation between diastolic bp and total calcium level :

	Pearson's Correlation	
Diastolic BP & total calcium level	Correlation co-efficient	Sig.(2-tailed)
	-.392	.00

Significant negative correlation was found between total serum calcium levels and diastolic bp

15.CORRELATION BETWEEN SYSTOLIC BLOOD PRESSURE AND SERUM CORRECTED CALCIUM LEVELS IN CASES:

		SYSTOLIC BP	CORRECTED CALCIUM
SYSTOLIC BP	Pearson Correlation	1	-.433**
	Sig. (2-tailed)		.000
	N	200	200
CORRECTED CALCIUM	Pearson Correlation	-.433**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

CORRELATION BETWEEN SYSTOLIC BP AND CORRECTED CALCIUM LEVEL :

Systolic BP & corrected calcium level	Pearson's Correlation	
	Correlation co-efficient	Sig.(2-tailed)
	-.433	.00

Significant negative correlation was found between corrected serum calcium levels and systolic bp

16.CORRELATION BETWEEN DIASTOLIC BLOOD PRESSURE AND SERUM CORRECTED CALCIUM LEVELS IN CASES:

		CORRECTED CALCIUM	DIASTOLIC BP
CORRECTED CALCIUM	Pearson Correlation	1	-.398**
	Sig. (2-tailed)		.000
	N	200	200
DIASTOLIC BP	Pearson Correlation	-.398**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

CORRELATION BETWEEN DIASTOLIC BP AND CORRECTED CALCIUM LEVEL :

	Pearson's Correlation	
	Correlation co-efficient	Sig.(2-tailed)
Diastolic BP & corrected calcium level	-.398	.00

Significant negative correlation was found between corrected serum calcium levels and diastolic bp.

17.CORRELATION OF CALCIUM LEVELS WITH AGE GROUPS AMONG CASES:

		TOTAL SR.CALCIUM		P value
		Mean	Standard Deviation	
Age group	<40	8.78	1.01	0.924
	41-50	8.97	0.64	
	51-60	8.90	0.54	
	61-70	8.99	0.85	
	>71	9.08	0.64	

		CORRECTED CALCIUM		P value
		Mean	Standard Deviation	
Age group	<40	8.87	0.85	0.937
	41-50	8.88	0.78	
	51-60	8.88	0.54	
	61-70	8.83	0.84	
	>71	9.06	0.81	

P value was more than 0.05 . Hence there is no statistically significant difference between total and corrected calcium levels among different age groups in this study.

18.CORRELATION OF THE CALCIUM LEVELS WITH SEX AMONG CASES:

Sex		Mean	Standard Deviation	P Value
TOTAL SERUM CALCIUM	F	8.94	0.71	0.821
	M	8.97	0.61	
CORRECTED CALCIUM	F	8.91	0.70	0.782
	M	8.87	0.74	

There was no statistically significant difference in total and corrected calcium levels with relation to sex among cases.P value >0.05.

19.CORRELATION OF CALCIUM LEVELS WITH SMOKING AMONG CASES:

Smoking		Mean	Standard Deviation	P value
Total serum calcium	No	8.94	0.66	0.633
	Yes	9.01	0.65	
Corrected serum calcium	No	8.88	0.70	0.804
	Yes	8.92	0.78	

There was no statistically significant difference in total and corrected calcium levels with relation to smoking among cases.P value >0.05.

20.CORRELATION OF SERUM CALCIUM LEVELS WITH ALCOHOL AMONG CASES:

Alcohol		Mean	Standard Deviation	P value
Total serum calcium	No	8.96	0.67	0.903
	Yes	8.94	0.62	
Corrected serum calcium	No	8.89	0.72	0.863
	Yes	8.86	0.73	

There was no statistically significant difference in total and corrected calcium levels with relation to alcoholism among cases.P value >0.05.

21.CORRELATION OF SERUM CALCIUM LEVELS WITH LIFESTYLE AMONG CASES:

Life style		Mean	Standard Deviation	P value
Total serum calcium	NS	8.99	0.61	0.554
	S	8.91	0.73	
Corrected serum calcium	NS	8.95	0.68	0.308
	S	8.80	0.77	

There was no statistically significant difference in total and corrected calcium levels with relation to lifestyle among cases.P value >0.05.

22.CORRELATION OF SERUM CALCIUM LEVELS WITH FAMILY HISTORY OF HYPERTENSION AMONG CASES:

Family history		Mean	Standard Deviation	P value
Total serum calcium	No	8.93	0.64	0.525
	Yes	9.02	0.70	
Corrected serum calcium	No	8.86	0.71	0.561
	Yes	8.95	0.74	

There was no statistically significant difference in total and corrected calcium levels with relation to family history of hypertension among cases.P value >0.05.

DISCUSSION

Systemic hypertension is a leading cause of death and disability all over the world. It is readily identifiable and a reversible risk factor for stroke, myocardial infarction, heart failure, peripheral arterial disease, atrial fibrillation and aortic dissection. Essential hypertension constitutes more than 90% of the hypertension. Evidences shows that calcium metabolism is altered in hypertension but whether it is causal relationship or a secondary association is unresolved.

Various epidemiological studies states that the calcium status of humans with essential hypertension and genetic animal models of hypertension is characterised by low serum total and ionised calcium levels, increased intracellular calcium, increased urinary calcium, excretion and increased parathyroid hormone excretion[3-6,78.]

In this study serum total calcium and corrected calcium levels were used. Corrected serum calcium is an alternative to serum ionised calcium but not a substitute.

In this study, a total of 100 persons are enrolled as cases. Age and sex matched controls were included. In the case group 3% of the cases were less than 40 years of age, 33 % were from 41 to 50 years, 32% were among 51 to 60 years,20% were between 61 to 70 years ,12% were among more than 70 years.

Among the controls ,3% were less than 40 years, 30% were between 41 to 50 years,33% were between 51 to 60 years,20% were between 61 to 70 years and 14% were from more than 70 year.

Among the cases,49% were males and 51% were females.Among the controls,48% were male and 52% were females. 28 % of the cases and 34% of the controls were smokers.similarly,22% of cases and 25% of the controls were alcoholics.40% of the cases have sedentary life style and 38% of the controls have sedentary lifestyle.32% of cases have positive family history of hypertension and 36% of controls have positive family history of hypertension.

The mean BMI among the cases was 24.70% and among the controls was 23.91%. The mean systolic blood pressure among the cases was 169.6±18 mm Hg. Among the controls the mean systolic blood pressure was 111.52± 6.96 mmHg. The mean diastolic blood pressure among the cases was 103.88±8.74 mmHg.Among the controls the mean distribution of diastolic blood pressure was 76.54±6.89 mmHg.

The mean Serum calcium level among the cases was 8.96±0.65 while in the controls ,the mean was 9.65±0.81 . The mean Serum corrected calcium level among the cases was 8.89±0.72 while in the controls ,the mean was 9.72±0.86.

Statistical analysis showed that total and corrected serum calcium levels were lowered significantly in cases when compared to normotensive controls.P value was <.001. This result is similar to some of the following studies.

The study conducted by K.Sudhakar et al showed that the mean total serum calcium levels were decreased significantly in hypertensive groups as compared to normotensive controls.

Sturzzullo P et al studied biochemical abnormalities of calcium metabolism and detected the significant reduction in total serum calcium levels in hypertensive subjects, although unable to detect significant reduction in serum ionised calcium levels. This study also showed there was increase in total and fractional urinary calcium excretion in hypertensive subjects.

McCaroon Da and Resnick Lm, Larigh Jh et al also noted that essential hypertensive subjects had lower serum ionised calcium levels compared to normotensive subjects even when the total calcium levels were similar.

Another study done by AR Folsom et al showed that hypertensive subjects have lower mean serum levels of ultra filtrable calcium,ionised calcium,complexed calcium and high levels of protein bound calcium.

In Lindl study there was a pattern of negative calcium with lowered levels of serum ionised calcium and increased urinary calcium excretion was reported in hypertensive people. Salt loading was done to untreated hypertensive subjects for 1 week and salt sensitivity was analysed. It was found that salt loading

increased urinary calcium excretion by 95% . These findings support that calcium metabolism is involved in the regulation of blood pressure.

Touyz et al reported a decrease in serum total calcium in essential hypertensive patients. Bolli P et al conducted a study on correlation of platelet calcium with blood pressure-effect of anti hypertensive therapy. This showed that essential hypertensive patients had decrease in serum total calcium concentration.

LIMITATIONS OF THE STUDY

- ✓ Only serum calcium levels were measured.
- ✓ Serum ionised calcium,urinary calcium, serum parathormone levels and arterial blood gas analysis were not measured due to financial limitations.
- ✓ Follow up was not done in this study
- ✓ Sample size was also small

CONCLUSION

Serum total calcium levels and corrected calcium levels were reduced significantly in essential hypertensive patients as compared to their normotensive controls.

There is a significant negative correlation between blood pressure and serum calcium levels in essential hypertensive patients.

There was no significant difference between the serum calcium levels and age, sex, life style, BMI, smoking, alcohol and family history of hypertension in essential hypertensive patients.

Since significant changes in serum calcium was seen among hypertensive people, this study recommends consuming calcium rich foods as a primary prevention for hypertension. But calcium supplements may increase the risk of renal stones and rarely increase the blood pressure, larger studies with RCT trials are needed to recommend calcium supplementation as a primary prevention of hypertension.

BIBLIOGRAPHY

1. Stamler J, Stamler R, Neaton JD. Blood pressure systolic and diastolic, and cardiovascular risks. US population data. Arch Intern Med 1993; 153: 598-615.
2. Vanden, Hooten PCW, Feskens EJM et al, for the seven countries study research group. The relation between blood pressure and mortality due to coronary heart disease among men in different parts of the world. N Engl J Med 2000; 342: 1-8.
3. C Guyton., John E Hall., Overview of circulation; Textbook of medical physiology,11 th edition; Pages 160 – 167.
4. R L Bijlani.,Understanding medical physiology,A textbook for medical students;3 rd edition,Pages219-224.
5. 2017 ACC/AHA and JNC 8 hypertension guidelines.
6. ohn E Hall.,Joey P Granger.,Michael E Hall.,Daniel W Jones., Pathophysiology of Hypertension ; Hurst's The Heart, Volume II; 12 th edition,Pages1570 – 1605.
7. Ronald G. Victor and Norman M. Kaplan , Systemic Hypertension: Mechanisms and Diagnosis ; Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 8th ed. Pages1027-1046.

8. Essential Hypertension – Pathogenesis and Pathophysiology Sanjay Vikrant, SC Tiwari.Journal, Indian Academy of Clinical Medicine Vol. 2, No. 3 september 2001.
9. Illiadou A, Lichtenstein P, Morgenstein R. Repeated blood pressure measurements in a sample of Swedish twins: Heritability and associations with polymorphisms in the renin – angiotensin – aldosterone system. J Hypertens 20: 1453, 2002.
10. Samani NJ; Genetics of hypertension: Oxford Textbook of Medicine, 4 th edition, 2003: 1160-1164.
11. Kuznetsova T, Wars J. m 2357 Angiotensin gene polymorphism and cardiovascular renal risks. J Hypertens. 1999; 17: 9.
12. Campese VM, Tawadrous M, Bigazzi R et al. Salt intake and plasma arterial natriuretic peptide and nitric oxide in hypertension. Hypertension 1996; 28: 335-40.
13. Fujiwara N, Osanai T, Kamada T et al. Study of the relationship between plasma nitrite and nitrate level and salt sensitivity in human hypertension : Meditation of NO synthesis by salt intake. Circulation 2000; 101:856-61.
14. Guyton AC. Kidneys and fluid in pressure regulation. Small volume but large pressure changes. Hypertension 1992; 19 (Suppl I): 12-8.
15. Brenner BM, Gracia DL, Anderson S. Glomeruli and blood pressure. Less of one, more of other. Am J Hypertens 1988; 1: 335-47.

16. Law CM, Sheil AW, Newsone LA. Fetal, infant, and childhood growth and adult blood pressure. A longitudinal study from birth to 22 years of age. Circulation 2002; 105: 1088.
17. Sealey JE, Blumenfeld JD, Bell GM et al. On the renal basis of essential hypertension : nephron heterogeneity with discordant renin secretion and sodium excretion causing a hypertensive vasocenstriction volume relation. J Hypertens 1988; 6: 763-77.
18. Williams GH, Hollenberg NK. Non-modulation hypertension. A subset of sodium-sensitive hypertension. Hypertension 1991; 17 (Suppl I): I81-I85.
19. Williams GH. Essential hypertension as an endocrine disease. Endocr Metab Clin North Am 1994; 23: 429-44.
20. Duprez DA: Role of the renin-angiotensin-aldosterone system in vascular remodeling and inflammation:A clinical review. J Hypertens 2006; 24:983.
21. Russo C, Oliveri O, Girelli D et al. Increased membrane ratios of metabolite to precursor fatty acid in essential hypertension. Hypertension 1997; 29: 1058-63.
22. Soleimani M, Singh G. Physiologic and molecular aspects of the Na + /H + exchanges in health and disease processes. J Invest Med 1995; 43: 419-30.
23. Lowenstein CJ, Dinerman JL, Snyder SH. Nitric oxide a physiologic messenger. Ann Intern Med 1994; 120:227-37.

24. Haynes WG, Noon JP, Walker BR, Webb DJ. Inhibition of nitric oxide synthesis increases blood pressure in healthy humans. J Hypertens 1993; 11: 1375-80.

25. Cowley AW, Roman RJ. The role of the kidney in hypertension. JAMA 1996; 275: 1581-9.

26. Oren S, Grossman E, Frohlich ED. Arterial and venous compliance in obese and non obese subjects. Am J Cardiol 1996; 77: 665-776.

27. Schmidt MI, Watson RL, Duncan BB et al. Clustering of dyslipidemia, hyperuricemia, diabetes and hypertension and its association with fasting insulin and central and overall obesity in a general population. Metabolism 1996; 45: 699-706.

28. Donnelly R, Connell JMC. Insulin resistance : possible role in the aetiology and clinical cause of hypertension. Clin Sci 1992; 83: 265-75.

29. Cardillo C, Killcoyne CM, Mambi S. Vasodilator response to systemic but not to total hyperinsulinemia in the human fore arm. Hypertension. 1998; 32: 740.

30. Jon D. Blumenfeld John H. Laragh., Chapter on Primary and Secondary Hypertension; Brenner: Brenner and Rector's The Kidney, 8th ed.Pages 1465 – 1516.

31. Laragh JH, Brenner BM (eds): Hypertension Pathophysiology, Diagnosis, and Management, 2nd ed. New York, Raven Press, 1995, pp 1897–191.

32. European Society of Hypertension-European Society of Cardiology Guidelines Committee : 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003; 21:1011
33. Postnov YV, Orlov SN, Pokudin NI. Decrease of calcium binding by the red blood cell membrane in spontaneously hypertensive rats and in essential hypertension. Pflugers Arch 1979;379:191-195.
34. Orlov SN, Postnov YV. Ca 2+ binding and membrane fluidity in essential and renal hypertension. Clin Sci 1982;63:281- 284.
35. Postnov YV, Orlov SN, Reznikova MB, Rjazhsky GG, Pokudin NI. Calmodulin distribution and Ca transport in the erythrocytes of patients with essential hypertension. Clin Sci 1984;66:459-463.
36. Morris CD, Vincenzi F, McCarron DA. Ca 2+ ATPase activity in human hypertension. Kidney Int 1985; 27:197.
37. Cox JA, Comte M, Stein EA. Activation of human erythrocyte Ca 2+ dependent Mg 2+ -activated ATPase by calmodulin and calcium: quantitative analysis. Proc Natl Acad Sci USA 1982;79:4265-4269.
38. Bass LF. Ca 2+ homeostasis in unstimulated platelets. J Biol Chem 1984,259:1263-1270.
39. Zidek W, Vetter H, Dorst KG, Zumkley H, Losse H. Intracellular Na + and Ca 2+ activities in essential hypertension. Clin Sci 1982;63:413-435.

40. Sempos C, Cooper R, Kovar MG, et al: Dietary calcium and blood pressure in National Health and Nutrition Examination Surveys I and II. Hypertension 1986;8:1067-1074
41. Kok FJ, Vandenbrouke JP, van der Heide-Wessel C, van der Heide R: Dietary sodium, calcium, potassium, and blood pressure. Am J Epidemiol 1986;123:1043-1048.
42. Kromhout D, Bosschieter EB, Coulander C: Potassium, calcium, alcohol intake and blood pressure: The Zutphen Study. Am J Clin Nutr 1985;41:1299-1304.
43. Witteman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, Rosner B, Hennekens CH: A prospective study of nutritional factors and hypertension among US women. Circulation 1989;80:1320-1327.
44. Zhang HY, Liu K, Shekelle R, Dyer A, Stamler J: The impact of calcium intake on incidence of elevated blood pressure: The Western Electric Study (abstract). Am J Epidemiol 1988;128: 916-917.
45. Strazzullo , et al.. The renal calcium leak in primary hypertension; Pathophysiological aspects and clinical implications. Nut Metabolism of cardiovascular diseases 1991;1:98 – 103.
46. Kesteloot H, Geboers J. Calcium and blood pressure. Lancet 1982;1:813-815.
47. McCarron DA, Morris CD. Oral Ca 2+ in mild to moderate hypertension: a randomized, placebo-controlled trial [Abstract]. Clin Res 1984;32:335.

48. Griffith LE, Guyatt GH, Cook RJ, et al: The influence of dietary and nondietary calcium supplementation on blood pressure: An updated meta-analysis of randomized controlled trials. Am J Hypertens 1999; 12:84.

49. K.Park., Epidemiology of chronic non – communicable diseases and conditions, Park's Textbook of Preventive and Social medicine. Pages 323 – 327.

PROFORMA

Name:

Age:

Address:

Sex: M / F

Diet: V / NV

Occupation:

SYMPTOMS:

- Headache
- Oliguria
- Giddiness
- Puffiness of face
- Blurring of vision
- Epistaxis
- Swelling of legs
- Anorexia
- Chest pain
- Vomiting / Hiccups
- Palpitation
- Easy fatiguability
- Dyspnoea

- Polydipsia
- Polyuria
- Bony pain

PAST HISTORY

- DM
- Angina / MI
- Heart Failure
- Renal Disorders
- PVD
- Stroke
- Thyroid Surgery
- Radiation
- Bony fracture
- abnormality

PERSONAL HISTORY

- Smoking
- Alcohol
- Dietary milk quantity – ML

FAMILY HISTORY

- Hypertension
- Diabetes Mellitus
- Drug abuse

ANTHRPOMETRY

- Ht cm
- Wt kg
- Hip cm waist cm
- BMI
- WHR

GENERAL EXAMINATION

- Fundus
- Blood pressure
- Pedal edema
- Supine
- Pulse Rate
- Grading of Hypertension

SYSTEMIC EXAMINATION

- CVS
- RS
- ABDOMEN
- CNS

INVESTIGATIONS

- Urine Albumin
- Sugar

- Deposits
- Blood Glucose
- Urea
- Serum Creatinine
- ECG
- CXR PA VIEW
- Serum Calcium
- Corrected calcium
- Total protein
- Albumin
- Globulin

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் எண்ணம்:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	இந்த ஆய்வு பக்கவாத நோயினால் பாதிக்கப்படுபவர்களுக்கு நடத்தப்படுகிறது என்பதை மருத்துவர் மூலம் புரிந்துகொண்டேன். இந்த ஆய்வில் எனக்கு மூளைக்கு ஸ்கேன், கழுத்துப்பகுதிக்கு மற்றும் எடுக்கப்படுகிறது என்பதை மருத்துவர் மூலம் அறிந்து கொண்டேன். மேலும்	☐
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.	☐
6	என் குழந்தை இந்த ஆய்வில் பங்குக் கொள்ள நான் முழுமனதுடன் சம்மதம் தெரிவிக்கிறேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் /..... இடம் .....

ஆய்வாளரின் பெயர் .....

மையம் .....

சாட்சியின் கையொப்பம் /..... இடம் .....

பெயர் மற்றும் விலாசம் ....

S.no	Name	Age	Sex	Smoking	Alcohol	Life style	Family history	BMI	SYSTOLIC BP	DIASTOLIC BP	BLOOD UREA	SERUM CREATININ	USG ABDOMEN	TOTAL SR.CALCIUM	SR.ALBUMIN	CORRECTED CALCIUM
1	Parthasarathy	65	M	Y	N	NS	N	19.6	184	98	26	0.8	N	8.44	4.3	8.2
2	Shanthi	58	F	N	N	S	N	21.5	160	106	28	0.5	N	8.5	4.2	8.3
3	Manohari	45	F	N	N	NS	N	20.2	190	120	26	0.7	N	10	4.6	9.5
4	Rajammal	75	F	N	N	NS	Y	26.7	146	96	23	1	N	8.52	4	8.5
5	Lenin	55	M	Y	Y	S	N	23.2	158	92	24	1.1	N	9.26	3.9	9.3
6	Geetha	41	F	N	N	NS	N	20.8	152	96	32	0.9	N	9.52	3.5	9.9
7	Pandurangan	76	M	N	N	S	N	19.06	166	108	31	0.6	N	8.32	4.4	8.0
8	Rajan	52	M	Y	Y	NS	N	20.5	184	106	30	0.9	N	9.98	4.2	9.8
9	Nagammal	56	F	N	N	NS	Y	27.12	194	116	25	1	N	9	3.5	9.4
10	Essakiammal	45	F	N	N	NS	N	28.3	162	112	28	0.8	N	8.36	4.5	8.0
11	Jakkammal	62	F	N	N	S	N	30.1	142	96	33	0.6	N	9.76	4.4	9.4
12	Ramalingam	53	M	Y	Y	NS	N	19.6	156	104	32	0.7	F	8.17	3.7	8.4
13	Mohamed safi	54	M	Y	N	NS	Y	23.1	174	112	24	1	N	8.52	4.5	8.1
14	Susila	56	F	N	N	NS	N	20.5	160	102	22	0.9	N	8.87	4	8.9
15	Kaliammal	56	F	N	N	S	Y	20.3	152	96	20	1.1	N	8.96	4.1	8.9
16	Devaki	55	F	N	N	NS	N	27.9	146	98	22	0.8	N	8.30	3.9	8.4
17	Narasimman	74	M	Y	Y	NS	N	21.9	168	90	32	0.7	N	9.50	3.5	9.9
18	Pattammal	65	F	N	N	S	N	27.5	194	106	26	0.5	N	8.53	3.8	8.7
19	Lakshmi	48	F	N	N	NS	N	20.7	184	110	28	0.9	N	8.04	4.2	7.9
20	Ramakrishnan	43	M	N	N	NS	N	20.3	186	102	26	1	N	8.25	4.1	8.2
21	Thilagavathi	54	F	N	N	NS	N	21.09	154	98	32	0.8	N	9	3.9	9.1
22	Navaneethan	45	M	Y	Y	S	Y	22.7	148	110	26	0.9	N	9.68	3.5	10.1
23	Purushothaman	45	M	N	N	S	N	21.8	156	112	32	0.7	N	8.72	4.5	8.3
24	Regina	46	F	N	N	NS	N	27.9	142	102	35	0.9	N	9.41	4.4	9.1
25	Essakiraja	52	M	Y	N	S	N	26.8	162	104	28	0.6	N	10	4	10
26	Mala	48	F	N	N	NS	Y	20.9	174	98	36	1	N	8.65	4.4	8.3
27	Lingam	51	M	Y	Y	NS	N	21.2	194	108	22	1	N	8.58	3.8	8.7
28	Saroja	72	F	N	N	S	N	20.3	166	92	27	0.8	N	8.63	4.2	8.5
29	Ravi	48	M	N	Y	NS	Y	21.8	184	106	21	0.8	N	8.44	4.5	8.0
30	Masilamani	45	M	Y	Y	NS	N	26.8	186	112	35	0.9	F	8.90	3.2	9.6
31	Loganathan	65	M	N	Y	NS	N	30.4	174	98	37	0.7	N	8.15	4.5	7.8
32	Baby	65	F	N	N	S	Y	27.6	144	92	27	1	N	8.23	3.8	8.4
33	Madhavan	58	M	N	N	NS	N	28.6	176	104	22	0.8	N	9.20	4.4	8.9
34	Alamelu	65	F	N	N	S	N	27.3	190	102	26	0.7	N	8.27	4	8.3
35	Ajay	57	M	Y	Y	NS	Y	26.2	186	94	32	0.5	N	9	4.5	8.6
36	Parimala	55	F	N	N	S	N	19.3	160	96	28	0.9	N	8.38	4.2	8.2
37	Sriram	73	M	Y	N	S	Y	26.1	164	102	24	0.6	N	8.42	4.8	7.8
38	Meeran	49	M	N	Y	NS	N	28.01	156	98	21	0.9	F	8.67	4.4	8.3
39	Jamuna	45	F	N	N	NS	Y	21.12	148	106	32	1	N	9.32	4.2	9.2

S.no	Name	Age	Sex	Smoking	Alcohol	Life style	Family history	BMI	SYSTOLIC BP	DIASTOLIC BP	BLOOD UREA	SERUM CREATININ	USG ABDOMEN	TOTAL SR.CALCIUM	SR.ALBUMIN	CORRECTED CALCIUM
40	Annammal	64	F	N	N	S	N	27.8	186	100	36	0.8	N	9.92	3.8	10.1
41	Mumtaj	62	F	N	N	NS	Y	32.1	166	98	24	0.9	N	8.76	4.3	8.5
42	Ramanujam	55	M	Y	N	NS	N	26.9	194	124	28	0.6	N	8.62	4.5	8.2
43	Suguna	52	F	N	N	S	Y	21.3	198	116	32	0.6	N	8.25	4.1	8.2
44	Malini	48	F	N	N	NS	N	26.7	178	112	31	0.8	N	8.54	3.8	8.7
45	Murugesh	76	M	Y	N	NS	N	26.8	162	98	28	0.9	N	9.21	4	9.2
46	Manjunathan	43	M	Y	Y	NS	N	28.1	158	92	26	1	N	8.96	4.4	8.6
47	Terasa	58	F	N	N	S	Y	27.9	142	94	25	0.8	N	8.84	3.5	9.2
48	Kumutha	64	F	N	N	NS	N	28.2	150	116	39	1.1	N	9	4.2	8.8
49	Kathiresan	58	M	Y	N	S	Y	25.3	188	90	28	0.7	F	8.60	4.4	8.3
50	Mariyammal	53	F	N	N	S	N	21.7	146	100	23	0.9	N	8.42	3.6	8.7
51	Babu	43	F	N	N	NS	Y	22.9	170	98	26	0.6	N	8.32	4.2	8.2
52	Saratha	70	F	N	N	S	N	20.3	194	96	32	0.9	N	7.28	4.5	6.9
53	Palanivel	67	M	N	N	NS	N	20.2	152	100	26	0.6	N	8.51	4.2	8.3
54	Yuvaraj	39	M	N	N	NS	Y	28.9	158	102	31	0.5	N	9.27	4.1	9.2
55	Arockiyamary	76	F	N	N	NS	N	20.8	150	110	36	0.8	N	8.60	3.9	8.7
56	Selvam	54	M	Y	Y	S	Y	26.7	190	120	34	1	N	9.91	4.5	9.5
57	Fathima	55	F	N	N	NS	N	21.8	152	106	27	0.8	N	8.15	3.7	8.4
58	Johnson	54	M	N	N	S	N	29.2	208	126	29	1	N	9.38	4.2	9.2
59	Kala	52	F	N	N	NS	Y	26.3	178	110	36	0.9	N	8.69	3.5	9.1
60	Renuga	36	F	N	N	NS	N	21.1	162	104	38	0.7	N	9.46	4	9.5
61	Visalatchi	72	F	N	N	S	N	28.6	164	110	27	0.6	N	9.80	4	9.8
62	Jeyakumar	45	M	Y	N	NS	Y	27.1	170	106	26	0.9	N	10.43	3.8	10.6
63	Theivasigamani	68	M	N	N	NS	N	30.2	184	108	23	0.6	N	8.26	4.5	7.9
64	Kuppu	45	F	N	N	NS	N	24.3	152	100	28	0.8	N	9.37	4.1	9.3
65	Dharmaraj	73	M	N	N	S	Y	21.5	196	102	27	0.9	N	8.48	3.8	8.6
66	Vembu	68	M	Y	Y	NS	N	27.6	150	98	35	0.8	N	8.81	3.5	9.2
67	Chandran	47	M	N	N	NS	N	28.4	146	92	23	0.8	N	8.24	3.7	8.5
68	Rajendran	45	M	N	N	S	Y	24.9	170	96	32	0.6	N	9.30	4.2	9.1
69	Kasturi	43	F	N	N	NS	N	25.9	204	118	30	0.9	N	8.24	4.1	8.2
70	Murugammal	42	F	N	N	NS	Y	28.7	174	98	26	0.8	N	9.26	3.7	9.5
71	Sambath	45	M	Y	Y	S	N	28.6	198	104	29	0.7	N	8.19	3.2	8.8
72	Mageswari	52	F	N	N	NS	Y	27.5	152	102	31	1	N	9.37	4.2	9.2
73	Abraham	42	M	N	N	NS	N	19.8	144	96	36	1.1	N	10.05	3.6	10.4
74	Rajendran	46	M	N	N	S	N	20.3	188	98	28	0.5	N	8.69	4.5	8.3
75	Panjali	61	F	N	N	S	Y	21.7	152	94	29	0.8	N	10.84	4.8	10.2
76	Padmavati	65	F	N	N	NS	N	19.8	198	116	31	0.6	N	10.32	4.2	10.2
77	Amutha	50	F	N	N	S	Y	20.4	158	104	24	0.7	N	9.76	4	9.8
78	Mahadevan	44	M	Y	Y	NS	N	22.6	162	110	37	0.9	N	9.80	4.3	9.6

S.no	Name	Age	Sex	Smoking	Alcohol	Life style	Family history	BMI	SYSTOLIC BP	DIASTOLIC BP	BLOOD UREA	SERUM CREATININ	USG ABDOMEN	TOTAL SR.CALCIUM	SR.ALBUMIN	CORRECTED CALCIUM
79	Raju	65	M	N	N	S	N	25.1	148	98	33	0.8	N	9.25	4.4	8.9
80	Angammal	55	F	N	N	NS	Y	23.6	166	96	31	1	N	8.89	4.6	8.4
81	Kannan	41	M	Y	Y	S	N	21.6	184	112	28	0.7	N	8.27	4.8	7.6
82	Santhanam	55	M	N	N	NS	N	20.7	194	116	32	0.6	N	9.8	4.3	9.6
83	Devi	36	F	N	N	S	Y	29	178	108	28	0.9	N	7.62	3.6	7.9
84	Koteeswari	42	F	N	N	S	N	28	172	112	32	0.5	N	8.84	4.1	8.8
85	Durai	55	M	N	N	S	N	28	192	122	34	0.8	N	8.59	3.5	9.0
86	Sankar	55	M	Y	Y	NS	Y	22.3	158	102	28	0.7	N	8.3	3.8	8.5
87	Raja	54	M	Y	N	S	N	27.9	176	110	31	0.7	N	8.61	4.2	8.4
88	Srinivasan	85	M	N	N	NS	N	26.4	188	106	27	1	N	9.71	4	9.7
89	Jayashree	60	F	N	N	NS	Y	24.2	172	98	32	0.8	N	9.10	3.9	9.2
90	Narayanan	61	M	Y	Y	S	N	21.7	148	92	34	0.7	N	9.65	4.8	9
91	Veerasamy	50	M	N	Y	S	N	22.6	152	94	32	0.6	N	9.40	4.3	9.2
92	Jayalakshmi	75	F	N	N	NS	Y	28.9	166	96	28	0.9	N	9.91	4	9.9
93	Karunagaran	65	M	Y	N	NS	N	25.2	148	92	29	1	N	9.32	4.2	9.2
94	Munusamy	63	M	N	N	NS	N	17.6	182	110	31	0.7	N	9.17	3.9	9.3
95	Kannaiya	56	M	N	N	S	N	19.5	198	122	37	0.5	N	9.58	3.6	9.9
96	Ramani	80	F	N	N	NS	Y	36	172	108	26	0.9	N	9.84	3.7	10.1
97	Manohar	45	M	Y	Y	S	N	23.9	146	94	25	0.7	N	8.32	4.8	7.7
98	Radika	49	F	N	N	NS	N	32.1	158	96	32	0.6	N	9.16	4.4	8.8
99	Durai	42	M	Y	Y	S	N	34.3	194	116	29	0.9	N	8.75	4.0	8.8
100	Aandal	65	F	N	N	NS	N	27.7	202	124	30	0.8	N	9.42	4.1	9.3

S.no	Name	Age	Sex	Smoking	Alcohol	Life style	Family history	BMI	SYSTOLIC BP	DIASTOLIC BP	BLOOD UREA	SERUM CREATININE	USG ABDOMEN	TOTAL SR.CALCIUM	SR.ALBUMIN	CORRECTED CALCIUM
1	Gurusamy	66	M	Y	N	NS	N	30.45	110	70	30	0.8	N	8.34	4.4	8.0
2	Durai	58	M	Y	Y	NS	Y	27.82	108	74	32	0.7	F	9.7	3.5	10.1
3	Muthammal	46	F	N	N	NS	N	19.36	116	80	28	0.6	N	9.18	3.8	9.3
4	Mahadevi	74	F	N	N	S	N	29.62	100	64	19	0.8	N	10.20	4.1	10.1
5	Maharajan	56	M	Y	N	NS	N	20.64	110	76	27	0.5	N	9.3	4	9.3
6	Selvi	42	F	N	N	NS	Y	20.21	120	82	22	0.8	N	8.7	4.5	8.3
7	Sheik	78	M	N	Y	S	N	27.82	110	80	36	1.0	N	11	3.5	11.4
8	Muthulakshmi	51	F	N	N	S	N	29.76	100	70	31	0.9	N	9.8	3.9	9.9
9	Ganapathy	54	M	Y	Y	NS	Y	28.13	116	84	29	0.8	N	8.12	4.4	7.8
10	Gnanam	46	F	N	N	NS	N	21.76	114	70	28	0.9	N	9.6	3.8	9.8
11	Manikandan	66	M	N	N	S	N	28.12	120	90	32	0.8	N	9.19	3.6	9.5
12	Krishnammal	52	F	N	N	NS	Y	22.76	122	82	34	0.8	N	10.4	4.3	10.2
13	Sundaram	55	M	Y	Y	S	Y	27.55	110	70	26	0.6	N	9.7	3.8	9.9
14	Madhiyalagan	57	M	Y	N	S	N	23.18	106	62	18	0.7	F	10.3	3.5	10.7
15	Selvi	57	F	N	N	NS	N	20.79	118	82	34	0.9	N	8.36	4.6	7.9
16	Paldurai	52	M	N	N	NS	Y	27.98	104	74	38	1.1	N	9.7	4.2	9.5
17	Esakkiammal	75	F	N	N	NS	N	28.88	116	88	36	1.0	N	8.1	3.9	8.2
18	Muthukumar	66	M	Y	Y	S	N	20.08	100	80	28	0.9	N	10	3.1	10.7
19	Chinnathai	42	F	N	N	NS	Y	27.67	118	88	22	0.7	N	9.6	4	9.6
20	Mariappan	45	M	Y	Y	NS	N	20.96	120	70	28	0.7	N	10.1	4.3	9.9
21	Mohanraj	55	M	N	N	S	N	28.33	114	84	26	0.8	N	10.4	3.9	10.5
22	Rabiya	46	F	N	N	NS	N	19.38	108	76	20	0.6	N	10.8	4.1	10.7
23	Lakshmi	44	F	N	N	S	N	26.77	112	92	31	0.9	N	9.3	4.5	8.9
24	Murugan	47	M	Y	N	NS	Y	28.67	100	70	38	1.1	N	9.7	3.8	9.9
25	Subathra	51	F	N	N	NS	N	21.80	104	76	34	1.0	N	9.4	3.6	9.7
26	Divya	49	F	N	N	NS	N	19.60	108	88	32	0.9	N	9	3.3	9.6
27	Perumal	52	M	Y	N	S	Y	30.14	112	72	28	0.7	N	11.3	4.2	11.1
28	Balamurugan	76	M	N	Y	NS	Y	27.33	120	80	22	0.8	N	9.9	4	9.9
29	Paapathi	47	F	N	N	NS	N	22.41	118	88	21	0.7	N	8.52	3.8	8.7
30	Maharajan	43	M	N	Y	S	N	19.38	122	76	26	0.8	N	7.9	3.7	8.6
31	Oorvasi	61	F	N	N	NS	N	21.99	108	74	32	0.9	N	9.12	3.7	9.4
32	Pattammal	62	F	N	N	S	Y	28.12	110	78	34	0.9	N	10.3	3.4	10.8
33	Krishnasamy	59	M	Y	Y	S	Y	22.65	100	68	36	0.8	N	9.7	3.1	10.4
34	Babu	63	M	N	N	NS	Y	26.04	118	80	38	1.0	N	10	4.0	10
35	Suriya	59	F	N	N	NS	N	31.25	116	76	21	0.6	N	9.8	3.3	10.4
36	Chinnathai	55	F	N	N	S	N	21.12	120	84	19	0.7	N	9.2	3.4	9.7
37	Suresh	74	M	Y	Y	NS	N	27.94	120	82	39	0.9	N	9.7	4.1	9.6
38	Eshwari	50	F	N	N	S	Y	21.45	110	78	35	0.8	N	9.3	3.5	9.7
39	Subramanian	44	M	Y	Y	NS	N	20.95	122	84	31	0.7	N	9.46	3.3	10
40	Ponmani	65	F	N	N	NS	N	21.27	100	72	27	0.6	N	10.9	4.1	10.8
41	Sumathy	63	F	N	N	S	Y	24.52	108	68	26	0.6	N	10.60	4.5	10.2

S.no	Name	Age	Sex	Smoking	Alcohol	Life style	Family history	BMI	SYSTOLIC BP	DIASTOLIC BP	BLOOD UREA	SERUM CREATININE	USG ABDOMEN	TOTAL SR.CALCIUM	SR.ALBUMIN	CORRECTED CALCIUM
42	Sudhakar	57	M	N	Y	NS	N	20.80	110	74	22	0.7	N	8.01	3.4	8.5
43	Perarasu	51	M	Y	N	NS	N	23.76	122	86	20	0.6	F	9.45	4.0	9.4
44	Lakshmi	49	F	N	N	S	N	20.42	110	74	33	0.9	N	9.6	3.8	9.8
45	Karpagam	77	F	N	N	NS	Y	21.12	120	82	31	0.9	N	9.8	4.5	9.4
46	Thangammal	44	F	N	N	NS	N	19.38	102	68	30	0.7	N	9.2	4.1	9.1
47	Jeyaraj	58	M	Y	Y	S	Y	20.99	100	66	38	0.8	N	8.47	5.2	7.5
48	Poomari	64	F	N	N	NS	Y	27.20	108	74	32	0.9	N	9.89	4.4	9.6
49	Ranjith	59	M	Y	N	NS	N	20.07	118	74	34	0.8	N	10.9	3.9	11
50	Malliga	51	F	N	N	NS	N	19.14	120	84	36	0.9	N	10.02	4	10
51	Abdhul	55	M	N	Y	S	N	21.12	108	68	26	0.7	N	11.7	3.7	11.9
52	Subramanian	41	M	Y	Y	NS	Y	26.88	110	74	28	0.8	N	10.8	3.8	11
53	Durga	74	F	N	N	NS	Y	21.45	116	78	23	0.6	N	9.86	4.3	9.6
54	Shanmugasundara	69	M	Y	N	NS	N	25.95	106	66	25	0.6	N	9.16	4	9.1
55	Muthammal	40	F	N	N	S	N	19.66	102	64	20	0.7	N	9.57	3.9	9.6
56	Palraj	78	M	N	Y	NS	Y	26.11	104	68	19	0.6	N	10.5	4.3	10.3
57	Mariammal	51	F	N	N	NS	N	23.62	100	68	19	0.7	N	8.3	4.1	8.2
58	Krishnan	56	M	N	N	S	N	26.99	110	78	22	0.9	N	9.64	3.7	9.9
59	Prakash	55	M	Y	Y	S	Y	20.43	122	86	26	0.9	N	9.02	3.6	9.3
60	Saraswathi	51	F	N	N	NS	N	23.66	120	80	28	0.8	N	9.8	4	9.9
61	Bala	38	M	Y	N	NS	N	20.76	122	82	37	1.0	N	9.10	3.4	9.6
62	Shivan	74	M	Y	Y	NS	N	27.48	118	78	36	0.8	N	9.9	4.1	9.8
63	Premalatha	48	F	N	N	NS	N	23.89	106	68	39	1.1	N	10.13	4.2	10
64	Jebasingh	69	M	N	Y	S	Y	23.99	108	66	37	1.0	N	9.25	3.2	9.9
65	Devakani	42	F	N	N	NS	N	21.65	110	72	38	1.1	N	9.6	3.5	10
66	Muthukunar	71	M	N	N	NS	Y	19.62	100	70	36	1.0	N	8.62	4	8.6
67	Punitha	69	F	N	N	NS	N	23.48	120	76	27	0.8	N	8.2	3.8	8.4
68	Pandi	47	M	Y	Y	S	Y	21.05	108	72	21	0.6	N	9.3	2.6	10.4
69	Amaravathy	43	F	N	N	S	Y	25.36	120	86	25	0.7	N	10.8	4.2	10.6
70	Ramakrishnan	41	M	Y	N	S	N	26.24	106	68	24	0.6	N	9.7	3.9	9.8
71	Murugeshwari	44	F	N	N	NS	N	28.13	110	74	26	0.8	N	10.4	4	10
72	Ramesh	48	M	Y	N	NS	N	20.31	100	70	28	0.9	N	11	4.8	10.4
73	Subathra	56	F	N	N	NS	Y	21.08	120	82	38	1.0	N	11.3	4.7	10.7
74	Kumar	42	M	Y	Y	NS	Y	27.57	122	86	34	0.8	N	9.73	3.7	10
75	Chellammal	45	F	N	N	S	Y	23.16	104	72	32	0.6	N	9.20	3.6	9.5
76	Miuthuvel	63	M	N	N	NS	N	20.92	116	82	20	0.7	N	8.2	4.2	8
77	Raj	65	M	Y	Y	S	N	21.01	108	72	30	0.9	N	9.06	3.8	9.2
78	Vadivel	52	M	Y	N	NS	Y	21.87	104	66	31	0.6	N	8.79	3.2	9.4
79	Elizabeth	48	F	N	N	NS	N	30.45	102	70	36	0.8	N	9.20	4.5	8.8
80	Rasammal	66	F	N	N	NS	N	28.12	110	78	34	0.9	N	10.42	3.6	10.7
81	Noor mohamed	56	M	Y	Y	S	Y	24.95	120	82	24	0.7	N	9.77	3.8	9.9
82	Chitra	42	F	N	N	S	N	22.22	118	82	26	0.9	N	9.48	3.8	9.6

S.no	Name	Age	Sex	Smoking	Alcohol	Life style	Family history	BMI	SYSTOLIC BP	DIASTOLIC BP	BLOOD UREA	SERUM CREATININE	USG ABDOMEN	TOTAL SR.CALCIUM	SR.ALBUMIN	CORRECTED CALCIUM
83	Muthammal	56	F	N	N	NS	Y	20.30	116	84	22	0.6	N	9.19	4.1	9
84	Balamurugan	38	M	Y	N	NS	N	26.77	120	86	28	0.8	N	8.45	4	8.4
85	Padma	41	F	N	N	S	N	20.56	110	78	21	0.7	N	9.27	3.9	9.3
86	Pandi	53	M	Y	N	NS	Y	27.95	120	84	30	0.7	N	9.79	3.8	9.9
87	Vasantha	56	F	N	N	S	N	20.57	110	78	35	1.0	N	9.95	4.2	9.8
88	Sekar	59	M	Y	N	NS	N	27.94	118	88	36	1.0	N	9.7	4.1	9.6
89	Vijaya	81	F	N	N	NS	Y	36.88	102	76	38	1.1	N	9.9	3.5	10.3
90	Karthick	63	M	N	Y	S	N	19.06	106	72	34	0.9	N	10.42	4.1	10.3
91	Petchiammal	64	F	N	N	NS	N	20.21	108	70	36	0.8	N	11	3.4	11.5
92	Shanmugam	51	M	Y	N	NS	Y	19.62	112	82	22	0.6	N	9.18	3.9	9.2
93	Sudalai	76	M	N	N	S	N	20.35	106	76	26	0.8	N	9.25	4.5	8.8
94	Kumaraselvi	66	F	N	N	S	N	21.86	112	84	28	0.9	N	9.37	3.5	9.8
95	Hariharan	63	M	Y	N	NS	N	28.12	108	74	32	0.9	N	9.68	4	9.7
96	Leelavathi	72	F	N	N	S	Y	21.22	120	82	38	1.0	N	10.7	3.9	10.8
97	Ibrahim	80	M	N	N	S	N	24.56	112	76	31	0.9	N	11.3	3.5	11.7
98	Suresh	49	M	Y	Y	NS	N	26.21	110	74	26	0.7	N	10.17	4.1	10
99	Sundaravalli	45	F	N	N	S	N	19.56	108	74	25	0.6	N	9.42	3.8	9.6
100	Shakthi	65	M	N	N	NS	N	22.11	106	68	20	0.7	N	9.37	4.5	9

MASTER CHART KEY

S.No: Serial number

Sex:

- M-Male
- F-Female

Smoking:

- Y-Yes
- N-No

Alcohol:

- Y-Yes
- N-No

Lifestyle:

- S-Sedentary
- NS-Non sedentary

Family history:

- Y-Yes
- N-No

BMI:Body Mass Index

USG abdomen:

- N-Normal study
- F-Fatty liver