CORRELATION OF BMI AND BLOOD PRESSURE WITH CAROTID ARTERY INTIMA MEDIA THICKNESS (CIMT) IN ADULTS

Dissertation submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600 032

In partial fulfillment of the requirement for the degree of
Doctor of Medicine in Physiology (Branch V)

M.D. (PHYSIOLOGY)
MAY – 2019

DEPARTMENT OF PHYSIOLOGY
TIRUNELVELI MEDICAL COLLEGE
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CERTIFICATE

This is to certify that the dissertation entitled, **"CORRELATION OF BMI AND BLOOD PRESSURE WITH CAROTID ARTERY INTIMA MEDIA THICKNESS (CIMT) IN ADULTS"** done by **Dr.S.MURUGANANTHAM** postgraduate in PHYSIOLOGY (2016-2019), is a bonafide research work carried out under our direct supervision and guidance and is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, for M.D. Degree Examination in Physiology (Branch V), to be held in May 2019.

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ENDORSEMENT BY THE GUIDE

This is to certify that the dissertation entitled, **"CORRELATION OF BMI AND BLOOD PRESSURE WITH CAROTID ARTERY INTIMA MEDIA THICKNESS (CIMT) IN ADULTS'** is a bonafide research work carried out by **Dr.S.MURUGANANTHAM,** in the Department of Physiology, Tirunelveli Medical College Hospital, Tirunelveli – 11 under my direct guidance and supervision in partial fulfillment of the requirement for the award of the degree of MD in PHYSIOLOGY (Branch – V) in May 2019.

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DECLARATION

I solemnly declare that the dissertation entitled **"CORRELATION OF BMI AND BLOOD PRESSURE WITH CAROTID ARTERY INTIMA MEDIA THICKNESS (CIMT) IN ADULTS''** is done by me at Tirunelveli Medical College Hospital, Tirunelveli.

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch V) in Physiology.

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PROTOCOL TITLE: CORRELATION OF BMI AND BLOOD PRESSURE WITH CAROTID ARTERY INTIMA MEDIA THICKNESS (cIMT) IN ADULTS
PRINCIPAL INVESTIGATOR: POST GRADUATE STUDENT
DESIGNATION OF PRINCIPAL INVESTIGATOR: DR.S.MURUGANANTHAM, MBBS.,
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear Dr.S.MURUGANANTHAM, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting Held on 01.09.2017.

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.
   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

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- I express my sincere gratitude to my guide **Dr. A. Jeya Jancy Selvi Ratnam DGO,MD,** Head of the Department of Physiology, Tirunelveli Medical College for she is not only my guide but also constantly extends her tremendous support and valuable guidance during these three years period.
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- Last, but **an important note of thanks to all participants of this study** without whom this could not be accomplished.

CERTIFICATE – II

This is certify that this dissertation work title **"CORRELATION OF BMI AND BLOOD PRESSURE WITH CAROTID ARTERY INTIMA MEDIA THICKNESS (CIMT) IN ADULTS"** of the candidate **Dr.S.MURUGANANTHAM** with registration Number **201615301** for the award of **M.D.** Degree in the branch of **PHYSIOLOGY (V).** 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 1**5 percentage** of plagiarism in the dissertation.

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http://care.diabetesjournals.org/content/30/10/2599

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CONTENTS

ABBREVIATION

AgRP – AGOUTI RELATED PEPTIDE

AT – ADIPOSE TISSUE

BMI – BODY MASS INDEX

BP – BLOOD PRESSURE

CCA – COMMON CAROTID ARTERY

CHD – CORONARY HEART DISEASE

CIMT – CAROTID ARTERY INTIMA MEDIA THICKNESS

CRP – C-REACTIVE PROTEIN

CVD – CARDIO VASCULAR DISEASE

EDC – ENDOCRINE DISRUPTING CHEMICAL

FTO – FAT MASS AND OBESITY ASSOCIATED

GI – GASTRO INTESTINAL

IAAT – INTRA ABDOMINAL ADIPOSE TISSUE

ICAVINTERNAL CAROTID ARTERY

IL-1 – INTER LEUKIN-1

IMT – INTIMA MEDIA THICKNESS

JNC – JOINT NATIONAL COMMITEE

LDL – LOW DENSITY LIPOPROTEIN

MAPK – MITOGEN ACTIVATED PROTEIN KINASE

MCH – MELANOCYTE CONCENTRATING HORMONE

MMP – MATRIX METALLO PROTEINASE

MSH – MELANOCYTE STIMULATING HORMONE

NO – NITRIC OXIDE

NPY – NEURO PEPTIDE Y

PI3K – PHOSPATIDYL INOSITOL TRI PHOSPHATE

POMC – PRO OPIO MELANO CORTIN

PVAT-PERI VASCULAR ADIPOSE TISSUE

PYY – PEPTIDE TYROSINE (3-36)

REE – RESTING ENERGY EXPENDITURE

TEE – TOTAL ENERGY EXPENDITURE

TEF – THERMIC EFFECT OF FOOD

TIMP – TISSUE INHIBITOR OF METALLOPROTEINASE

VCAM – VASCULAR CELL ADHESION MOLECULE

VEGF – VASCULAR ENDOTHELIAL GROWTH FACTOR

VLDL – VERY LOW DENSITY LIPOPROTEIN

VSMC – VASCULAR SMOOTH MUSCLE

WHO – WORLD HEALTH ORGANISATION

INTRODUCTION

Obesity is a major public health problem in developed countries and an emerging health problem in developing nations, such as India. According to WHO report in 2016, 650 million adults were obese[1]. India ranks 3 in the top 10 countries with obese people with a count of 40.4 million[2]. Obesity is well-recognized as a main risk factor for the development of metabolic disorders and cardiovascular disease (CVD), such as heart failure, myocardial infarction, and stroke. Obesity is also said to be one of the most ignored health problems[3]

Obesity isdefined as a state of excessive accumulation of adipose tissue mass[4]. It can be said as weight exceeding 10% of standard weight. Obesity is also a disease of caloric imbalance that results from an excess intake of calories that exceeds their consumption by the body. Excess energy is stored in the Adipose tissue as triglycerides and release the stored energy in the form of free fatty acids when the need arises for use at various sites[5].Hormones like Leptin play a key role by binding to receptors in the hypothalamus and increasing energy consumption.

Excess weight gain is best assessed by the body mass index, or BMI due to its suitability and non-invasiveness .The normal BMI range is 18.5 to 23.5 kg/m2 in Asian Indian population. Central, or visceral obesity

is associated with a much higher risk for several diseases than is subcutaneous fat.

Obesity, a part of the systemic inflammation, originates from Adipose tissue (AT), where inflammatory cells, mainly macrophages and T-lymphocytes accumulate creating local inflammation (6,7,8). Adipose tissue-derived inflammatory factors impinge on vascular cells to promote the development of atherosclerosis in obese people. This systemic pathologic process occurring in the vascular system is atherosclerosis.

Atherosclerosis in arterial wall is initiated by fat retention, oxidation, and modification resulting in intima-media thickening (IMT). This provokes chronic inflammation, which underlies the pathogenesis of coronary, cerebral and peripheral vascular disease. Various risk factors act in concert and cause vessel intimal lesions called atheromas (atheromatous or atherosclerotic plaques) that protrude into vessel lumens. Besides mechanically obstructing blood flow, plaques can also rupture leading to catastrophic thrombosis.[9]

Hypertension is also a risk factor for development of atherosclerosis, a systemic condition primarily affecting elastic arteries (carotid, aorta, and iliac arteries) as well as large and medium-sized muscular arteries. Arterial wall modifications represent an early involvement of the target organs in patients with hypertension[10,11].

Ultrasound measurements of IMT and plaque occurrence in the carotid arteries are important as the extent of arteriosclerosis and atherosclerosis in these vessels reflects the severity of arterial damage in other vascular territories[12,13].

High resolution ultrasonography is a non invasive, simple, safe (non ionising) inexpensive, precise, and reproducible method of examining and evaluating the walls of carotid arteries. Extra cranial carotid arteries are chosen for IMT assessment because of their superficial location, easy accessibility, adequate size, and limited movement[14]. Even though obesity prevalence is increasing at an alarming rate in India, few Indian studies are available to study the atherosclerotic changes occurring in the vascular system with the body mass index and blood pressure in a simple, universal and non invasive manner. Hence this study is undertaken to throw light on this aspect.

AIM

The aim of this study is

1) To correlate BMI with the carotid IMT values in adults

2)To correlate Blood pressure measurements with the carotid IMT values in adults

MATERIALS AND METHODS

STUDY DESIGN: Cross-sectional type of study.

STUDY CENTRE AND PERIOD: Tirunelveli Medical College Hospital

Period -October 2017 to August 2018

SAMPLE SIZE: 100 subjects

ETHICAL CONSIDERATIONS:

Institutional ethical committee clearance was obtained prior to the commencement of the study. The patients who were attending the non-communicable disease OPD were recruited for this study. All the subjects were clearly explained about the study in their own language. Informed consent was obtained from those who were willing to participate in this study.

INCLUSION CRITERIA:

- Patients of both the sex
- Age group of 30-60 years
- Hypertensive cases

EXCLUSION CRITERIA:

- Known diabetic patients
- Known Ischemic heart disease

- Known cerebro vascular accidents
- Bronchial Asthma
- Vasculitis disorders
- Thyroid and other Endocrine disorders
- History of Chronic steroid therapy
- Body builders
- Pregnancy

METHODOLOGY:

After getting informed consent, the information about personal details, brief medical history was noted in a separate proforma sheet.

Height and weight measurements were taken following a standard protocol.

WHO STEPS Surveillance- Training & Practical Guides-Guide to Physical Measurements

Measurement of Height:

1.Ask the participant to remove their:

- Footwear (shoes, slippers, sandals etc)
- Head gear (hat, cap, hair bows, comb, ribbons, etc).

2.Ask the participant to stand on the board facing you

3 Ask the participant to stand with:

• Feet together • Heels against the back board • Knees straight

4 Ask the participant to look straight ahead and not look up.

5 Make sure eyes are the same level as the ears.

6 Move the measure arm gently down onto the head of the participant and ask the participant to breathe in and stand tall.

7 Read the height in centimetres at the exact point.

8 Ask the participant to step away from the measuring board

Measurement of weight:

1.Ask the participant to remove their footwear (shoes, slippers, sandals etc) and socks.

2. Ask the participant to step onto scale with one foot on each side of the scale.

3. Ask the participant to:

• stand still • face forward • place arms on the side and • wait until asked to step off

4.Record the weight in kilograms on the participant's Instrument

Measurement of BMI:

BMI was calculated using Quetlet's formula: weight (kg)/ height (m^2).

BMI(kg/m2)	Classification
18.5-22.9	Normal
23.0-24.9	Overweight
≥25	Obese

Measurement of Blood pressure of a participant using the sphygmomanometer.

Ask the participant to sit quietly and rest for 15 minutes with their legs uncrossed.

1.Place the right arm* of the participant on the table with the palm facing upward.

2. Remove or roll up clothing on the arm.

3. Select the appropriate cuff size for the participant using the following table:

Arm Circumference (cms)	Cuff Size
22-32	Medium (M)
> 32	Large (L)

4. Position the cuff above the elbow aligning the mark ART on the cuff with the brachial artery.

5. Wrap the cuff snugly onto the arm and securely fasten with the Velcro.

Note: The lower edge of the cuff should be placed 1.2 to 2.5 cm above the inner side of the elbow joint.

6. Keep the level of the cuff at the same level as the heart during measurement

7. Put stethoscope earpieces in ear and set to bell.

8.Palpate pulse at either brachial or radial artery. Take a pulse count for one full minute.

9. Pump up pressure and inflate cuff until unable to feel pulse.

10. Continue to inflate cuff 30 mmHg beyond this point.

11. Apply the bell of the stethoscope to the right antecubital fossa.

12.Listen for pulse sounds while deflating the cuff slowly.

13.Record the systolic blood pressure (SBP) when a pulse is first audible.

14. Record the diastolic blood pressure (DBP) when the pulse sound disappears.

15. Deflate the cuff fully and let the arm rest for three minutes (between each of the readings).

16. Repeat Steps 2-7 twice to obtain three readings (and take the mean of the second and third readings for analysis purposes).

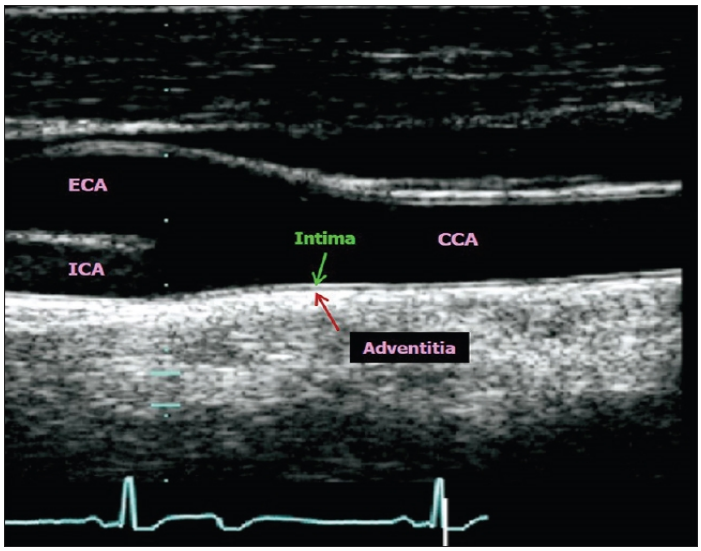
Classification of hypertension for adults aged >18yrs according JNC

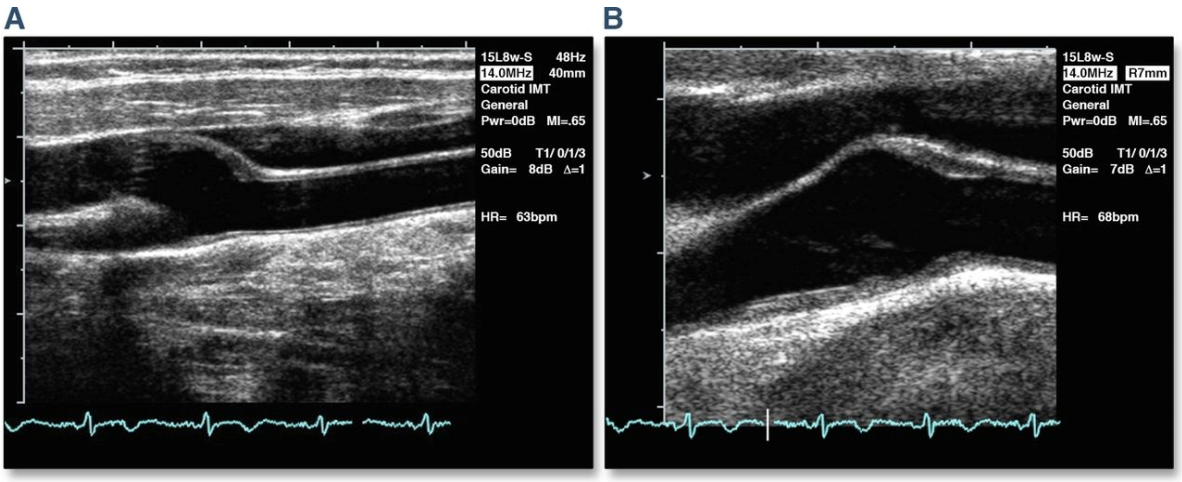
Category	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	90-119	60-79
Prehypertension	120-139	80-89
stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	>160	>100
Isolated systolic Hypertension	>/=140	<90

Measurement of carotid artery intima media thickness (CIMT)

Examination of carotid artery was performed in Radiology department with a high-resolution ultrasound doppler scanner SCONOSCAPE, equipped with a 7 MHz linear array transducer. The patient being in supine position and chest being elevated with a pillow and the head being turned to the opposite side of the carotids to be examined. The probe will be placed on the medial side of the sternocleidomastoid muscle to identify the carotid vessel and the carotid bulb will be traced. The carotid wall will show parallel echogenic lines separated by a hypoechoic region (media). The inner line is the lumen – intima interface and the outer is the media – adventitia interface.

Carotid IMT was measured on both sides and the average value is taken as the mean CIMT. Multiple projections were used to acquire images of the left and right common carotid, bulb and internal carotid arteries. Measurements were taken in the carotid bulb and 1cm proximal and distal to the bulb including CCA and ICA respectivelly. The average of three measurements of each carotid artery will be taken as mean thickness (CIMT)





The intimal plus medial thickness (IMT) was measured as the distance from the leading edge of the first echogenic line to the second echogenic line. The first echogenic line represents the lumen intimal interface and the second line is produced by media-adventitia interface.

IMT values above 0.9mm are regarded as abnormal. Focal thickening of the luminal surface >1.5 mm is called as plaque.

REVIEW OF LITERATURE

BODY MASS AND OBESITY

Definition of Obesity

Obesity is broadly defined as a state of excess adipose tissue mass. Growing evidence suggests that obesity is a disorder of the energy homeostasis system, rather than simply arising from the passive accumulation of excess weight.Reliable fat-mass quantitation requires sophisticated tools that are not widely available (e.g., magnetic resonance imaging or dual energy X-ray absorptiometry)[15].

PREVALENCE OF OBESITY

GLOBAL SCENARIO

According to WHO report in 2016, 650 million adults were obese.39% of adults aged 18 years and over (39% of men and 40% of women) were overweight. Overall, about 13% of the world's adult population (11% of men and 15% of women) were obese in 2016. Over 340 million children and adolescents aged 5-19 years were overweight or obese in 2016.Obesity is now on the rise in low- and middle-income countries, particularly in urban settings. Overweight is linked to more deaths worldwide than underweight[16].

INDIAN SCENARIO

There were 20 million obese women and 9.8 million obese men in India in 2014 according a study published in the British medical journal, Lancet. Severe obesity was observed in an additional 4 million Indian women. The study, comparing body-mass index from 1975 to 2014 from adults in 186 countries showed a more significant rise in obesity in India from its 19th position for both men and women in 1975 to rankings 5th and 3rd respectively in 2014(17).

OBESITY AND ANTHROPOMETRY

Anthro pometry literally means "Human Measure".

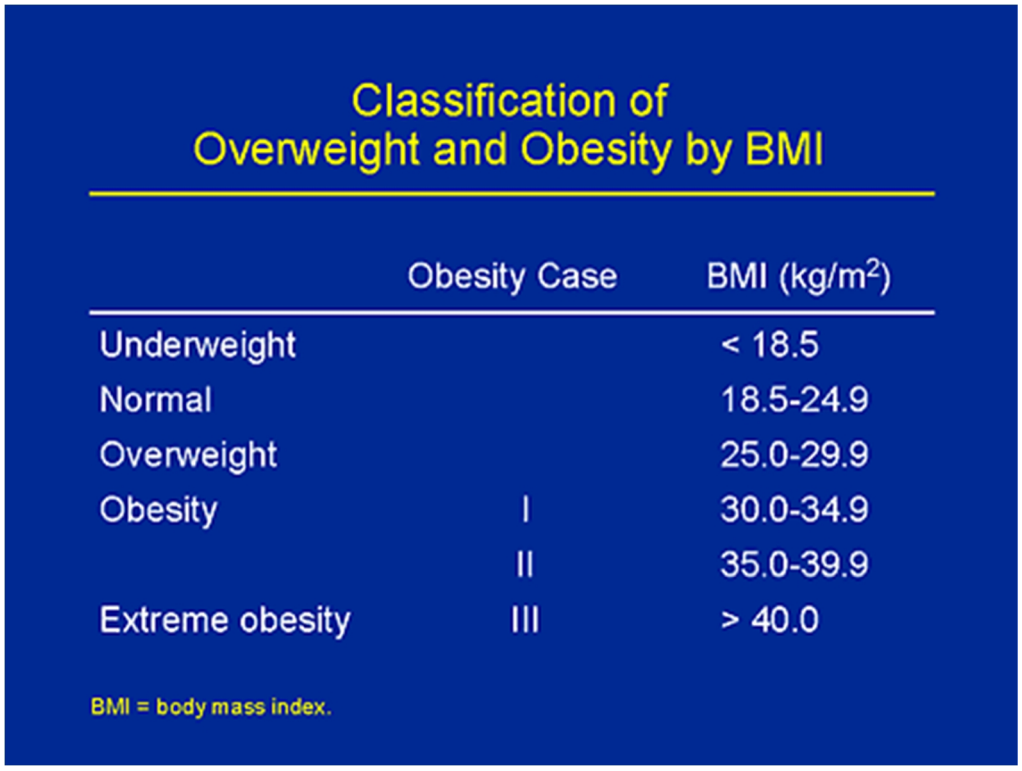
Anthropometry is the study of measurement of human body in terms of dimensions of bone, adipose tissue and muscle. It is a key component of nutrition status assessment both in children and adults[18].

Overweight and obesity classification are done by Body Mass Index (BMI).

Body Mass Index(BMI):

It is the value obtained by dividing the actual body weight in kilograms by the height of the body in square meters. It acts as a surrogate measure of body fatness and is the most widely accepted definition of obesity. BMI satisfies our need to estimate body-fat mass at a population level and thus gauge a group's susceptibility to complications of obesity.

BMI is not used for body builders, pregnant women, elderly, long distance athletes and young children.



WHO GUIDE LINES-OVER WEIGHT AND OBESITY-

- WHO Expert consultation concluded that Asian populations have a higher risk even at lower BMI. The cut-off point for observed risk varies from 22 to 25kg/m^2 and for higher risk starts from 26 to 31 kg/m^2. BMI greater than 23kg/m^2 are said to be overweight and greater than 25kg/m^2 are said to be obese for Asian Indians[19].

The BMI for native Asian Indians [24]

Classification	Obesity Class	BMI(kg/m^2)
Under weight		<18.5
Normal		18.5-22.9
Overweight		23.0-27.9
Obesity	I	28.0-32.9
	II	33.0-37.9
Extreme obesity	III	≥38

WHO GUIDELINES

Percent ideal body weight:

- Overweight: 10 to 20% above the reasonable body weight
- Obese: more than 20% above the reasonable body weight

The obese persons can be classified further as

- Mildly obese: 20-40% overweight
- Moderately obese: 41 to 100% overweight
- Severe (extremely): greater than 100% overweight

As the BMI value is same for all ages and sexes of adults, it gives more information about the population level measure of obese and also overweight[25,26,27]. BMI was considered a superior tool in correlating the effect of weight with morbidity and mortality. At the same BMI values,

Asians of Indian origin tend to have 7-8% of higher percentage body fat than Europoids[28]with increased prevalence of cardiovascular risk and diabetes. Weight gain of about 5 kg during 18-20 years of life, increases the risk of developing hypertension, diabetes and CHD.[29]

VARIOUS PATTERNS OF OBESITY

Central obesity or android obesity or upper body obesity is the type of obesity which is most likely to be associated with an altered risk factor profile contributing to an increased CVD and type 2 diabetes risk.

Gynoid obesity or, lower body obesity with fat located around the hips and buttocks) is seldom associated with such metabolic complications

"Normal Weight Obesity" is defined as a condition of having normal BMI but the percentage of body fat is high[30].

TOFI (Thin on the outside, fat on the Inside) are those people with BMI within normal limits with high intra-abdominal fat and thus more susceptible to DM. Fat fit phenotype have greater BMI but metabolically normal[31].

Thus obesity consequences are linked to the amount of intra abdominal fat rather than fat at other areas like buttocks and hip[32].This central abdominal obesity is associated with increased incidence of hypertension and atherogenic lipid profile both of which can increase the chance of cardiovascular disease[33,34].

ENERGY BALANCE:

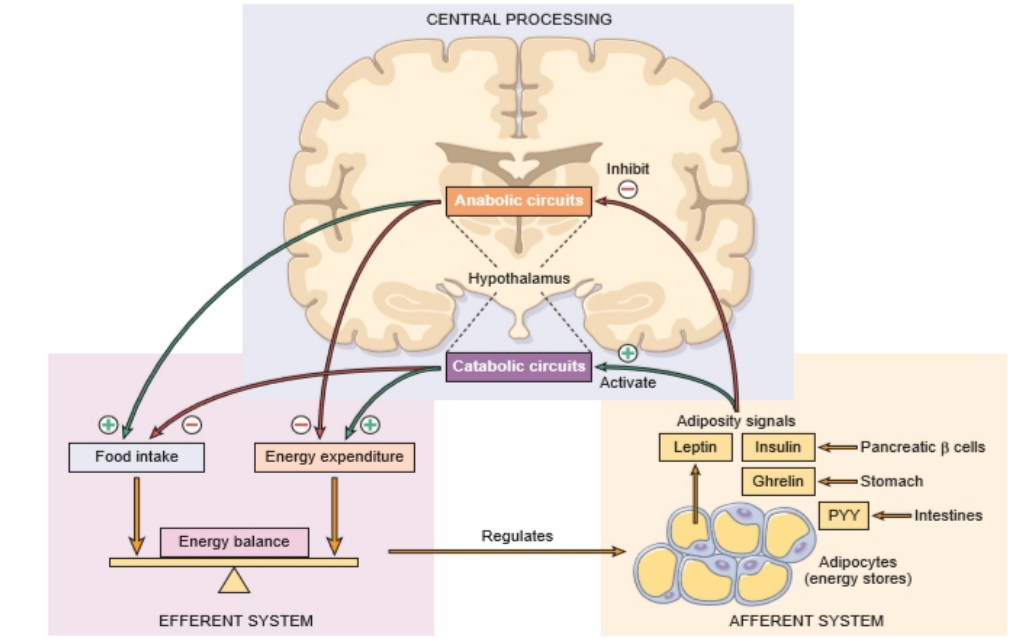


Figure 9-30 Regulation of energy balance. Adipose tissues generate afferent signals that influence the activity of the hypothalamus, which is the central regulator of appetite and satiety. These signals decrease food intake by inhibiting anabolic circuits, and enhance energy expenditure through the activation of catabolic circuits. PYY, Peptide YY. See text for details.

The major fundamental cause of obesity and overweight is an imbalance between calories consumed and calories expended. Gastrointestinal tract has the capacity to absorb large quantity of nutrients. In 1 year, only 5% increase in caloric intake than energy expenditure will lead on to 5kg increase in weight in adipose tissue. Total daily energy expenditure (TEE) includes resting energy expenditure (REE) (70%), thermic effect of food (10%) and energy expended during physical activity (20%). REE denotes the energy expended for normal organ and cellular function during post absorptive resting state[35]. Thermic effect of food (TEF) denotes the energy expended after ingestion of a meal. Obese persons usually have higher REE than lean persons of same height.

DIETARY LIPIDS / LIPO PROTEINS

The major constituents of dietary lipids are chiefly long chain triglycerides with lesser amounts of phospholipids, cholesterol, cholesterol esters and fat soluble vitamins[36]. The major route of normal intestinal absorption of lipids is through lymphatics. Many types of lipoprotein are exist each having characteristic lipid and protein compositions. The various classes are 1) Chylomicrons 2) VLDL 3) LDL 4) HDL

1. Chylomicrons transport lipids absorbed from the intestine to adipose, cardiac, and skeletal muscle tissue, where their triglyceride components are hydrolyzed by the activity of the lipoprotein lipase, allowing the released free fatty acids to be absorbed by the tissues.
2. VLDL and LDL transfer triacylglycerols (TAG) and cholesterol from liver to other tissues by endogenous lipid transport.
3. HDL transport cholesterol from extra hepatic tissues to liver by reverse cholesterol transport.

   Another subclass, Lipoprotein(a) [Lp(a)] consists of an LDL-like particle and the specific apolipoprotein(a) [apo(a)], which is bound covalently to the apoB of the LDL-like particle and its plasma concentrationare highly heritable and mainly controlled by the apolipoprotein(a) gene located on chromosome 6q[37].

STORAGE OF LIPIDS AS TRIGLYCERIDES

Triglycerides are stored in the adipose tissue as body's major energy reserve. Triglycerides are a much more compact fuel than glycogen, yielding 9.3kcal/g upon oxidation.Most of the triglyceride are derived from chylomicrons and very-low-density lipoprotein (VLDL) triglycerides that originate,respectively, from dietary and hepatic sources[40].

ROLE OF HORMONES:

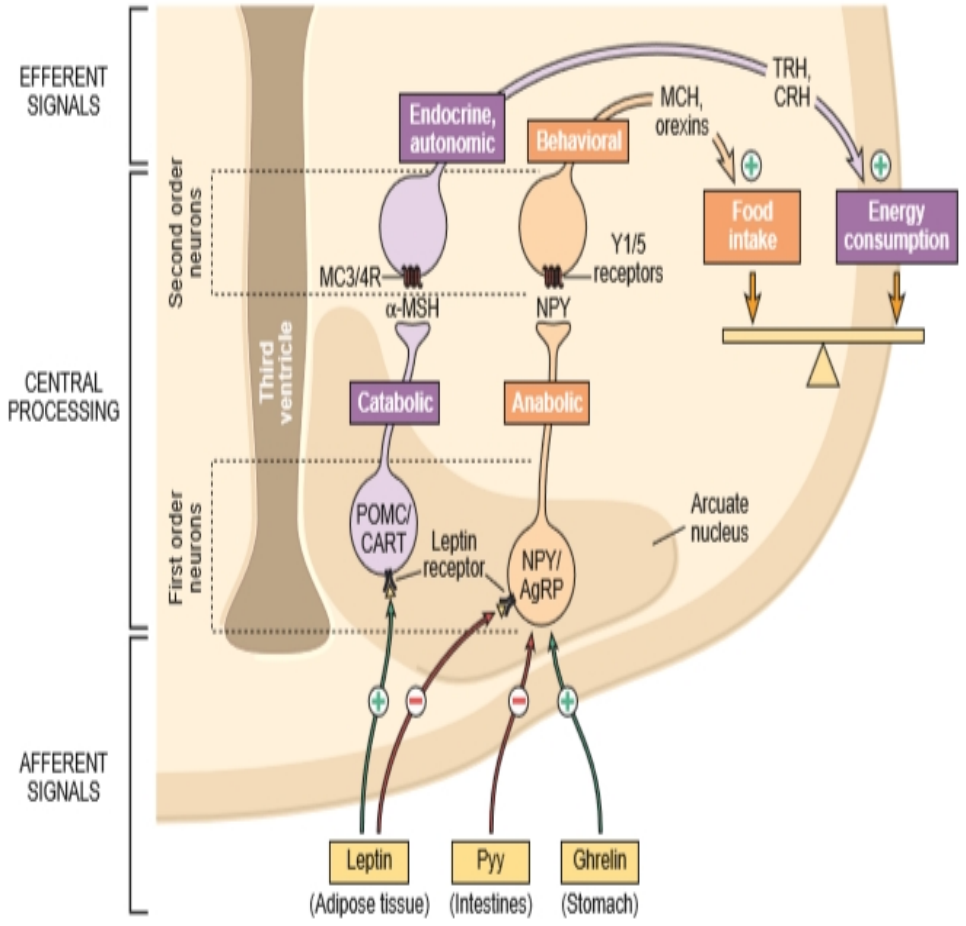
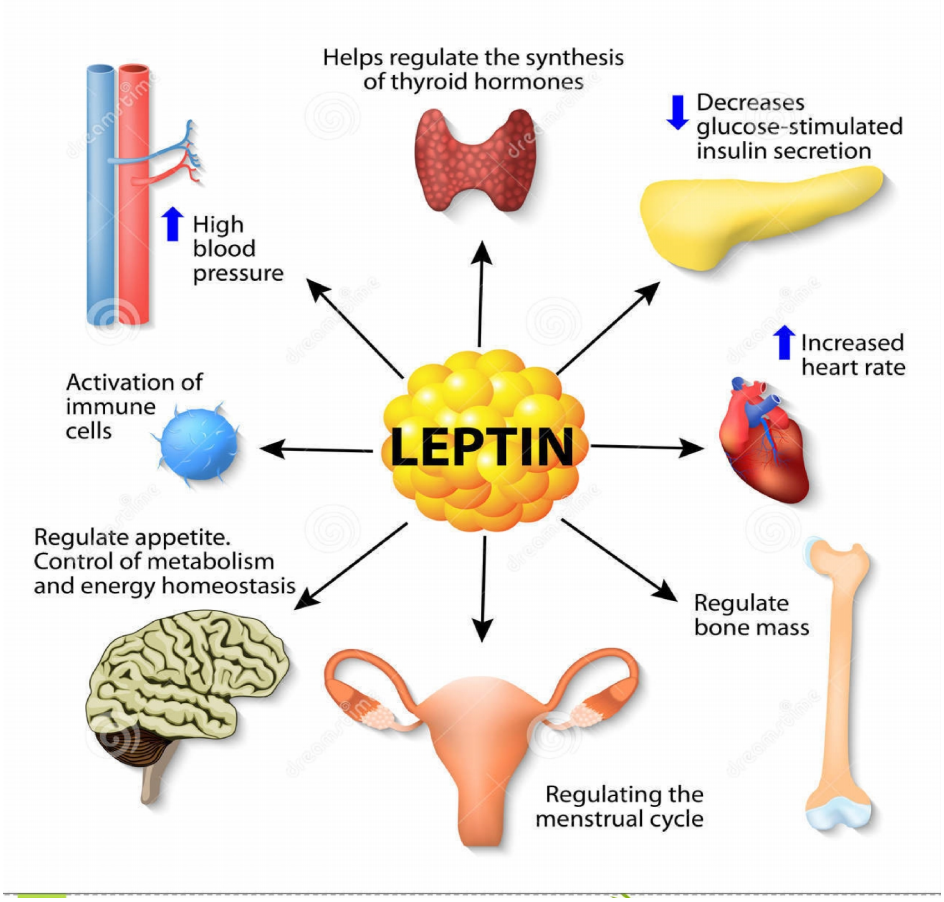


Figure 9-31 Neurohumoral circuits in the hypothalamus that regulate energy balance. Shown are POMC/CART anorexigenic neurons and NPY/AgRP orexigenic neurons in the arcuate nucleus of the hypothalamus, and their pathways. See text for details.

Body weight regulation is coordinated by hormones and neuronal circuit. A major hormone regulating these adaptations is LEPTIN, an adipocyte derived hormone which circulates at concentrations proportional to body-fat mass, plays a significant role in the relationship between obesity and energy homeostasis. Other major hormonal signals are insulin, gut peptides and cortisol. Hormones like Neuropeptide YY (NPY), Agouti related peptide (AgRP), Melanocyte concentrating hormone(MCH), cortisol and Ghrelin stimulate appetite. Melanocyte stimulating hormone MSH and Leptin, decrease appetite. Peptide tyrosine(PYY3-36) is produced in the gut cells and their production is proportional to the kcal intake. This hormone is particularly produced after a meal and signals the brain, that the body is no longer hungry.

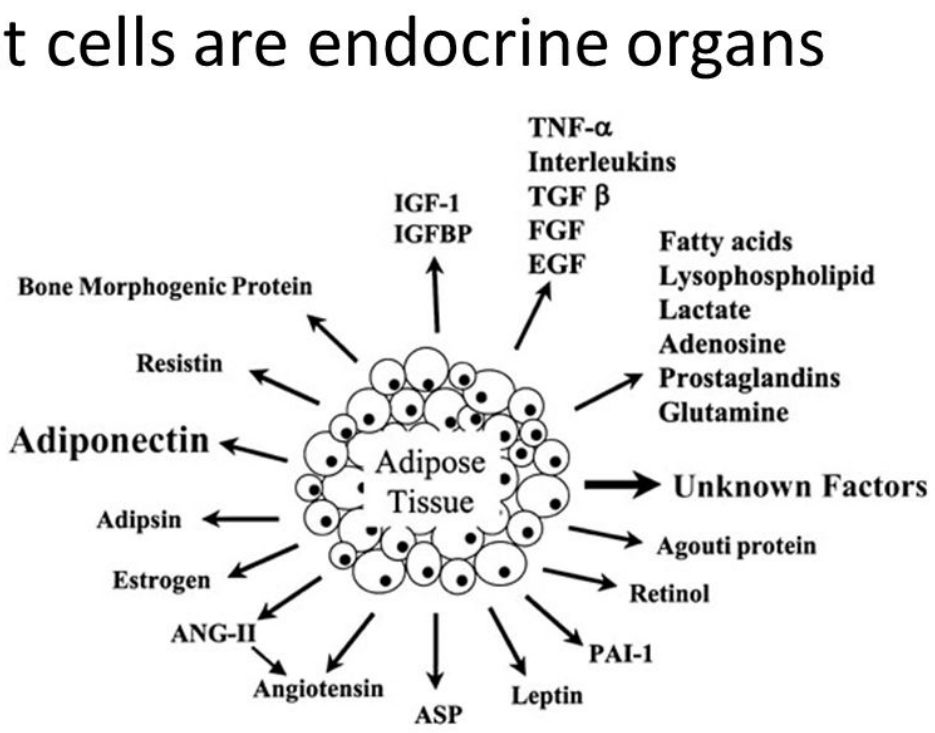


FAT AS AN ORGAN

➢ Adipose tissue is collection of connective tissue in which adipocytes or fat cells are predominating and constitutes 15-20% of the body weight in men while in women a little higher[41]. Adipose tissue as an endocrine tissue respond to both neural and hormonal stimuli. Adipose tissue helps in thermal insulation, cushioning and keeping the organs in its place. 85% of total adipose tissue mass is found under the skin called subcutaneous fat. Very smaller amount is seen within the abdomen called intra-abdominal fat or visceral fat. This includes both retroperitoneal fat (drains into systemic circulation) and intraperitoneal

fat (drains into portal circulation). Mesenteric and omental fat comes under intraperitoneal category[42].

➢ Excess energy stored in subcutaneous tissue will overflow to IAAT and skeletal muscle and liver producing metabolic dysfunction. Metabolic products of omental and mesenteric fat tissue are released into portal vein PI in abdominal areas.



The size of the adipocytes can increase up to 10 times called as hypertrophy. When the upper limit of fat storage is reached by hypertrophy then the fat cells now undergo hyperplasia. New adipocytes are developed from immature precursor cells. Once created, the number of fat cells cannot be

reduced naturally. This is the reason why obese persons have a greater difficulty in losing weight once it has been achieved[43]

PATHOGENESIS OF OBESITY

GENES AND ENVIRONMENT:

Our body size depends on the complex interaction between environmental factors and genetic background. Only 40% variance in body mass is explained by genetic background in humans [44]. Persons with genetic predisposition are more prone for weight gain and develop obesity related diseases when they are exposed to a modern lifestyle during their life time.

INFLUENCES OF CHILDHOOD AND PARENTAL OBESITY

The risk of getting obesity in adulthood also depends on being obese as a child or having at least one obese parent. This risk increases with increasing age and with degree of childhood obesity.

MONOGENIC CAUSES OF OBESITY

Leptin gene mutation:

In Leptin gene mutated obese individuals, deficiency of leptin causes severe hyperphagia and obesity in both humans and animals, with physiological leptin replacement ameliorating both the hyperphagia and obesity.

Serum leptin levels increase exponentially with fat mass, which shows that in obesity there is insensitivity to leptin resulting in body fat deregulation[45]

Leptin receptor mutation:

Mutation in leptin receptor gene resulted in hypogonadotropic hypogonadism, failure of pubertal development, secondary hypothyroidism, and delay in growth. These findings confirm the importance of leptin in endocrine regulation of energy balance and hypothalamic functions in humans

Certain other mutations leading to obesity are pro-opiomelanocortin gene mutation(POMC), melanocortin 4 receptor mutations, prohormone convertase 1 gene mutation and mutation of Neurotrophin receptor TrkB.

POLYGENIC CAUSES OF OBESITY

Obesity may result from gene –environment interactions or due to gene-gene interactions. The major breakthrough given by genome-wide association studies was the discovery of fat mass and obesity associated gene (FTO)[46]. Many studies have shown that a strong association between single nucleotide polymorphism in FTO gene and fat mass (BMI) in both adult and childhood obesity.

ROLE OF EDC

Numerous studies link exposure to EDCs to a variety of outcomes of potential relevance to obesity, including stimulation of adipogenesis and changes of insulin secretion, insulin sensitivity, and liver metabolism[47].That the increase of human exposure to EDCs parallels the rise

in obesity rates in the United States (raises the possibility of a causal link between the two).

Modern lifestyle has had a major influence on body energy use vs. storage. With all kinds of foods becoming readily available at any times while humans are sedentary, the combination of higher energy intake and less energy expenditure is at the heart of the obesity problem. Some factors are shown to be involved in abdominal obesity include age, gender, ethnic, inherited genes, stress, sex steroid hormones, nutrition, and physical activity/exercise

Interactions between genes, development, and environment

Environmental factors includes changes of diet composition and lifestyle, environmental toxins, infections, changes in the microbiome[48]along with maternal obesity and diabetes. Vertical transmission of phenotype could exacerbate (or mitigate) shared genetic predispositions between mother and o□spring while also a□ecting the phenotypes of progeny in the absence of primary genetic predisposition. Genes that contribute to obesity susceptibility through direct e□ects on energy intake and expenditure may also influence the response to developmental/ environmental factors, such as intrauterine and perinatal exposures to “obesogenic” diets, toxins, and others.

Role of epigenetic modifications

Epigenetic modification of genes typically involves changes in how transcriptional complexes access regulatory elements in the genome and can occur during development and throughout life.

GI factors, bariatric surgery, and the microbiome

Bariatric surgical procedures can produce profound and long-lasting e□ects on body weight. Chief among these procedures are Roux-en-Y gastric bypass and vertical sleeve gastrectomy, each of which can produce profound and sustained weight loss that cannot be reliably achieved by other means because these procedures alter communication between the GI tract and energy homeostasis neurocircuits (referred to as the "gut–brain axis")[49].

The gut microbiome and other GI factors

The composition of the gut bacteria in humans has also been linked to obesity risk[50]. Alterations in diet can profoundly a□ect the composition of gut bacteria at multiple levels of the GI tract, and obesity itself may also a□ect the composition of gut bacteria.

Social and economic factors

Low-cost foods with high energy density and high reward value, are readily available in underserved areas, and tend to be preferentially selected by lower income groups[51]. Excess consumption of such foods is linked to rising obesity rates. The concept of a "food desert," defined as a low-income area in which the nearest supermarket is atleast 1 mile away, has become a

focus of public health policies aimed at improving both diet and health. Studies suggest that BMI tends to be lower in areas where the consumption of vegetables and fruits is higher [52]

Roles of sedentary behavior, lack of exercise, and nonexercise activity thermogenesis also plays a major role.

Smoking cessation is reliably associated with weight gain[53], presumably owing to withdrawal of the pharmacological e□ect of nicotine to suppress food intake and weight gain.

Fuel partitioning, insulin, and obesity

More recent brain-centric models, in which the brain, by virtue of its operational control of food intake and energy expenditure, imposes excess calories on passive adipocytes sometimes referred to as "pull" and "push" models, respectively[54].Embedded within this debate is the extent to which adipocyte autonomous processes can pull substrate molecules preferentially into adipocytes, and by "partitioning" calories in this way cause higher fractional deposition of calories as fat.

COMMON HEALTH CONSEQUENCES OF OVERWEIGHT AND OBESITY

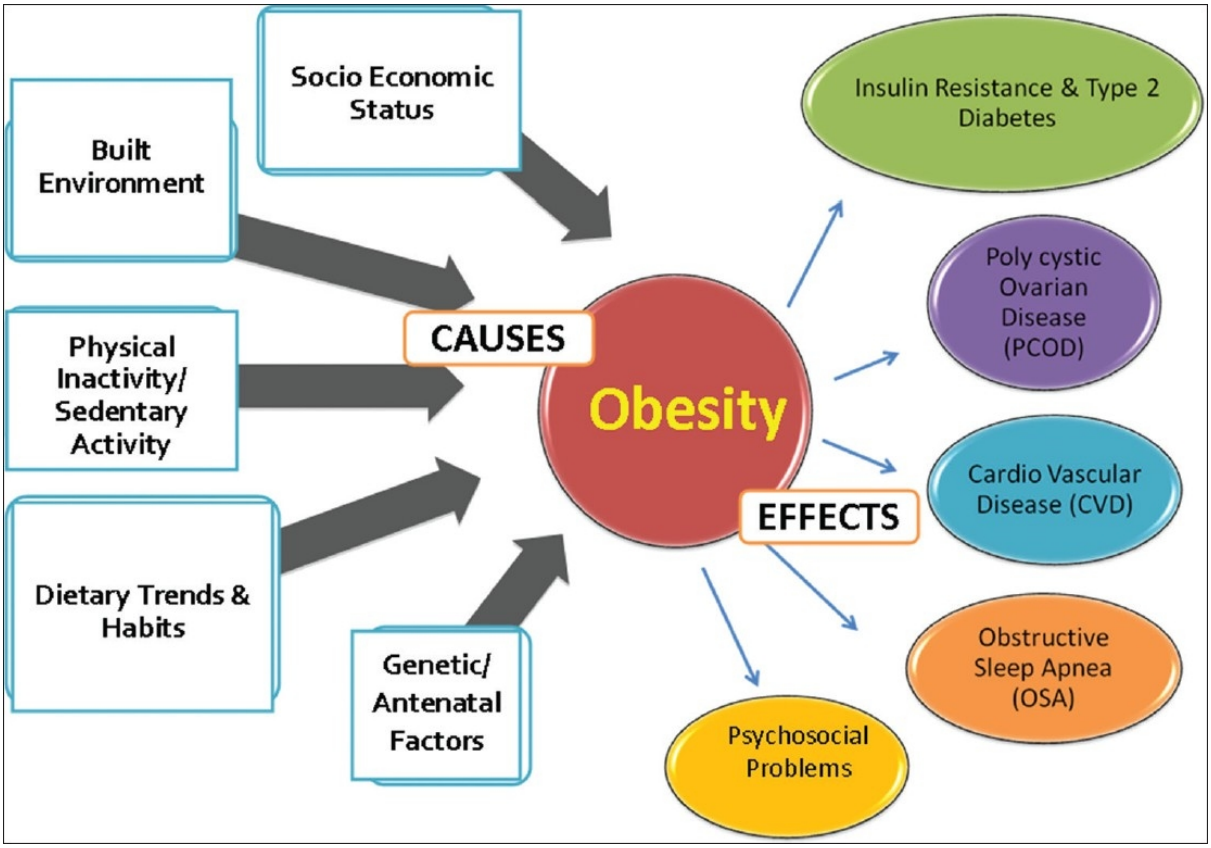
Increased BMI is one of the major risk factor for noncommunicable diseases,

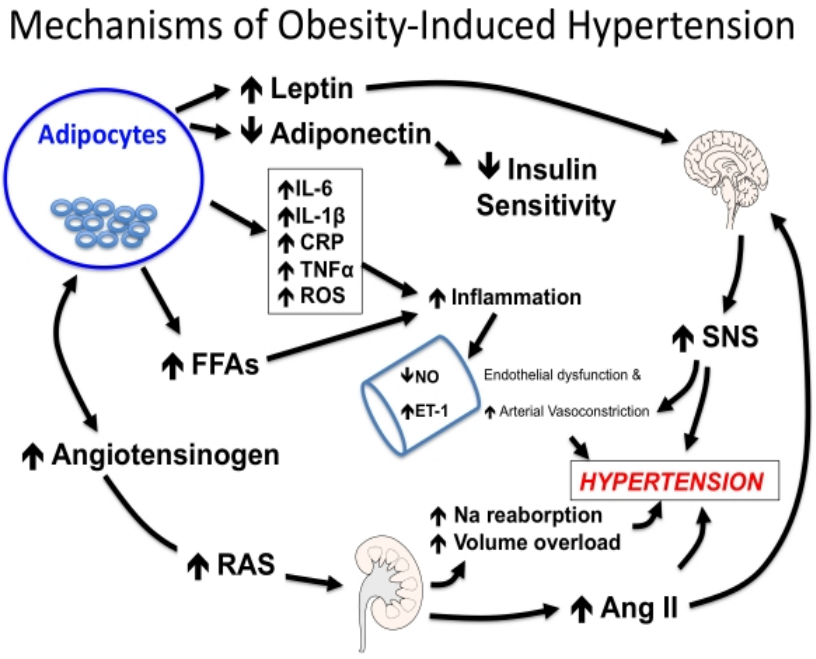
- Cardiovascular diseases mainly stroke and heart disease- leading cause of death in 2012 as per WHO report

- Diabetes
- Musculoskeletal disorders like osteoarthritis
- Cancer - In 2007, the National Cancer Institute estimated that 4% of cancers in men and 7% of cancers in women were attributable to obesity, numbers that can be expected to rise as obesity increases.

  The clearest associations with increased risk were for cancers of the esophagus, pancreas, colon and rectum, breast, endometrium, kidney, thyroid, and gallbladder. The mechanisms by which obesity promotes cancer development are unknown.

The risk for these diseases increases with increasing BMI. Childhood obesity has a higher chance of obesity in adult, disability in adulthood and premature death.


Socio Economic Status
Built Environment
Physical Inactivity/ Sedentary Activity
Dietary Trends & Habits
Genetic/ Antenatal Factors
CAUSES
Obesity
EFFECTS
Insulin Resistance & Type 2 Diabetes
Poly cystic Ovarian Disease (PCOD)
Cardio Vascular Disease (CVD)
Obstructive Sleep Apnea (OSA)
Psychosocial Problems


Mechanisms of Obesity-Induced Hypertension
Adipocytes
↑ Leptin
↓ Adiponectin
↓ Insulin Sensitivity
↑IL-6
↑IL-1β
↑ CRP
↑ TNFα
↑ ROS
↑ Inflammation
↑ FFAs
↓NO
↑ET-1
Endothelial dysfunction &
↑ Arterial Vasoconstriction
↑ SNS
↑ Angiotensinogen
HYPERTENSION
↑ Na reaborption
↑ Volume overload
↑ RAS
↑ Ang II

Oxidative Stress and Endothelial Dysfunction

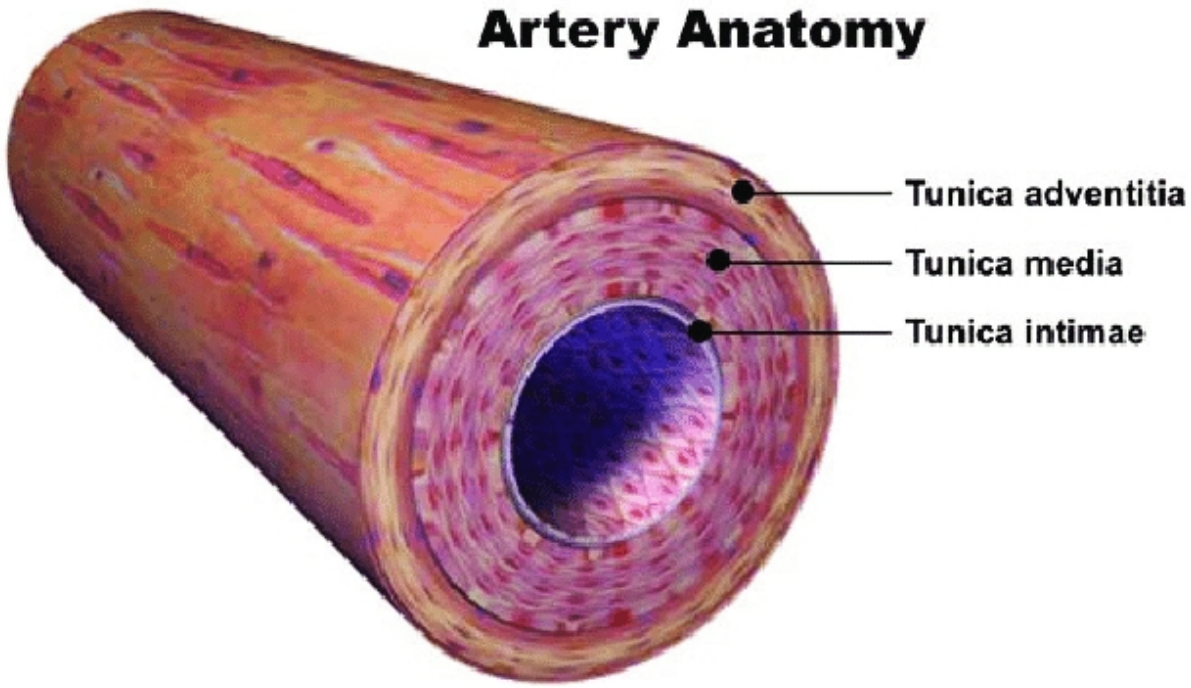
In non diabetic humans, fat accumulation is correlated with oxidative stress[55]. Insulin exerts pro- and anti-atherogenic actions on the vasculature. The balance between nitric oxide (NO)-dependent vasodilator actions and endothelin-1- dependent vasoconstrictor actions of insulin is regulated by phosphatidyl inositol3kinase-dependent (PI3K) - and mitogen-activated protein kinase (MAPK)-dependent signaling in vascular endothelium, respectively. During insulin-resistant conditions, pathway-specific impairment in PI3K-dependent signaling may cause imbalance between production of NO and secretion of endothelin-1 and lead to endothelial dysfunction. Insulin resistance produces impairment in PI3kinase dependent signaling pathway. Hence Endothelial dysfunction causes an imbalance between nitric oxide production and endothelin 1 secretion[56].

Weight of The Heart in Obesity

Hearts of obese individuals have extensive subepicardial fat depots. Study also reported the presence of fat deposits up to 50% of the heart weight without any sign of abnormal heart function[57].

VASCULAR SYSTEM AND ATHEROSCLEROSIS

Structure of Vascular Wall



Arteries have a trilaminar structure. The inner “intima” layer consists of a monolayer of endothelial cells. The middle layer or the “tunica media”, consists of layers of smooth-muscle cells. The outer layer “the adventitia”, consists of looser extracellular matrix which may have occasional fibroblasts, nerve terminals and mast cells. The medium-sized muscular arteries contain a “prominent tunica media” and atherosclerosis commonly affects this type of muscular artery[57].

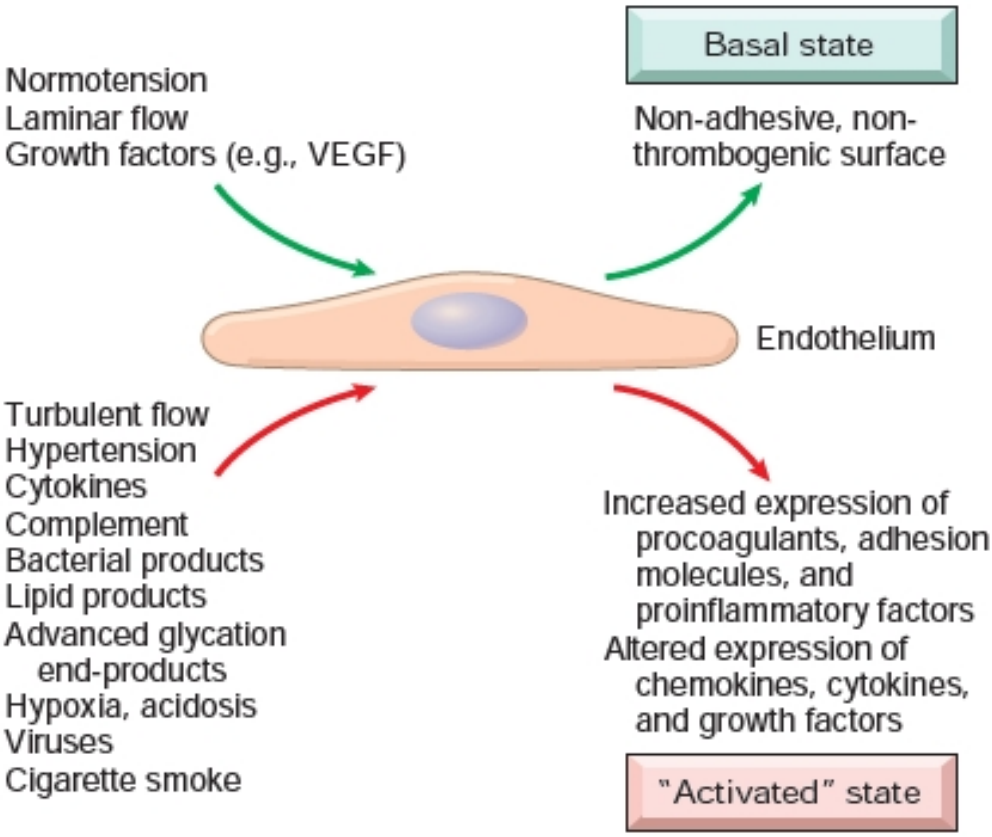
Endothelial Cell

It forms the interface between blood compartment and the tissues. The ability of endothelial cells to serve as a selectively permeable barrier fails in:

- Atherosclerosis
- Hypertension
- Renal disease and
- Other situations of "capillary leak"(pulmonary oedema)

The endogenous substances produced by endothelial cells are

- Prostacyclins
- endothelium-derived hyperpolarizing Factor
- nitric oxide (NO) and
- hydrogen peroxide



Basal and activated endothelial cell states

Under physiologic condition they provide a tonic vasodilatory stimuli in vivo. Impaired production or excess catabolism of NO impairs this endothelium-dependent vasodilator function and may contribute to excessive vasoconstriction in various pathologic situations.

Under pathologic conditions the excessive production of reactive Oxygen Species (e.g superoxide anion) by endothelial or smooth muscle cells can promote the local oxidative stress and also inactivates the NO[58].

Endothelial cell Injury

Endothelial cell injury is the cornerstone of the response-to-injury hypothesis. The two most important causes are hemodynamic disturbances and hypercholesterolemia.

Hemodynamic Disturbances

Plaques occur at ostia of exiting vessels, branch points, and along the posterior wall of the abdominal aorta, where there are disturbed flow patterns. Nonturbulent laminar flow leads to the induction of endothelial genes whose products (e.g., the antioxidant superoxide dismutase) actually protect against atherosclerosis and vice versa.

Dyslipoproteinemias include (1) increased LDL cholesterol (2) decreased HDL cholesterol, and (3) increased levels of the abnormal lipoprotein (a) which are associated with an increased risk of atherosclerosis. The dominant lipids in atheromatous plaques are cholesterol and cholesterol esters.

Hypercholesterolemia cause endothelial cell membrane and mitochondrial damage, increased local reactive oxygen species production, and accelerates nitric oxide decay, damping its vasodilator activity[59].

Vascular Wall Response to Injury

Endothelial Junctions are largely impermeable but in inflammationeven leukocytes can slip between adjacent endothelial cells. Endothelial cells can respond to various stimuli by a process termed endothelial activation. Activated endothelial cells express adhesion molecules(VCAM-1) and produce cytokines and chemokines, growth factors, vasoactive molecules that result either in vasoconstriction or vasodilation. Major histocompatibility complex molecules, procoagulant and anticoagulant factors, biologically active products are responsiblefor atherosclerosis, and the vascular lesions of hypertension. Vascular smooth muscle cells(VSMC)are the predominant cellular element of the vascular media, involved in vascular repair and atherosclerosis[60]. Also smooth muscle cells have the capacity to proliferate and synthesize collagen, elastin, and proteoglycans and elaborate growth factors and cytokines.

Intimal Thickening: A Stereotyped Response to Vascular Injury

Vascular injury—associated with endothelial cell dysfunction or loss—stimulates smooth muscle cell recruitment and proliferation and associated matrix synthesis resulting in intimal thickening. The resulting neointima is typically completely covered by endothelial cells. Thus, intimal thickening is the response of the vessel wall to any insult. In contrary,

neointimal smooth muscle cells are motile, undergo cell division, and acquire new biosynthetic capabilities and its functions are regulated by cytokines, growth factors derived from platelets, endothelial cells, and macrophages, as well as thrombin and activated complement factors and this healing response results in intimal thickening that may impede vascular flow.

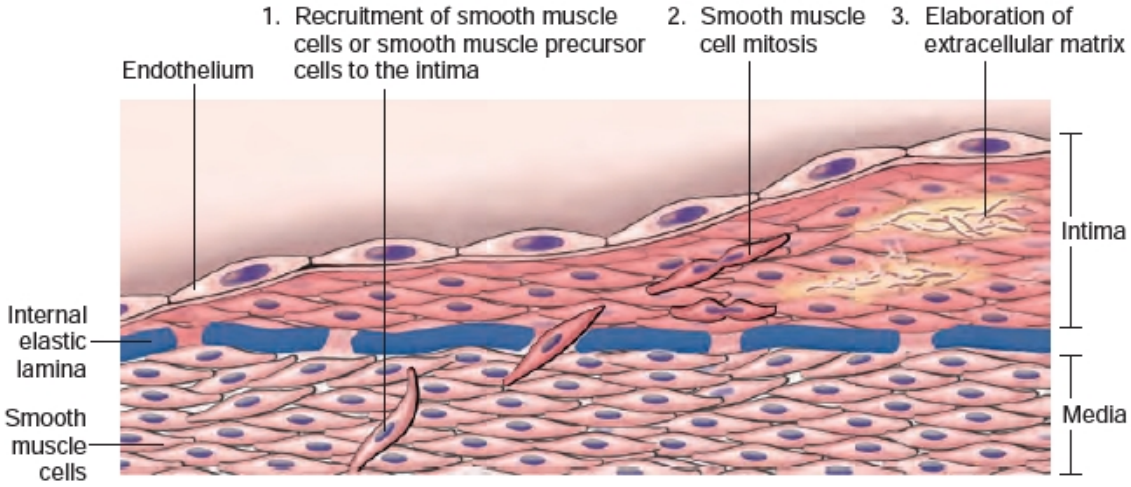
Atherosclerosis, from Greek root words meaning “gruel” and “hardening,” is involved in the pathogenesis of coronary, cerebral and peripheral vascular disease. Risk factors have been identified through prospective analyses (e.g., the Framingham Heart Study) and have roughly multiplicative effect[61].

Diets low in cholesterol and/or high in polyunsaturated fats lower plasma cholesterol levels.Omega-3 fatty acids (abundant in fish oils) are beneficial. Statins act by inhibiting hydroxyl methylglutaryl coenzyme A (HMG CoA) reductase, the rate-limiting enzyme in hepatic cholesterol biosynthesis, have been used widely to lower serum cholesterol levels.

Risk Factors for Atherosclerosis

Major		Minor
NON-modifiable		*Modifiable*
Increasing age		Obesity
Male gender		Physical inactivity
Family history		Stress ("type A" personality)
Genetic abnormalities		Postmenopausal estrogen deficiency
		High carbohydrate intake
Modifiable		
Hyperlipidemia		Alcohol
Hypertension		Lipoprotein Lp(a)
Cigarette smoking		Hardened (trans)unsaturated fat intake
Diabetes		*Chlamydia pneumoniae*

Premenopausal women are relatively protected against atherosclerosis. After menopause the incidence of atherosclerosis related diseases increases in women. Assessment of systemic inflammation is done by C-reactive protein (CRP)[62]. Lipoprotein(a) levels are also associated with disease risk.



Stereotypical response to vascular injury

Pathogenesis of Atherosclerosis

"Response to injury" hypothesis model

⇩

Atherosclerosis is a chronic inflammatory and healing response of the arterial wall to endothelial injury.

⇩

Lesion progression occurs through interaction of modified lipoproteins LDL, monocyte-derived macrophages, and T lymphocytes with endothelial cells and smooth muscle cells of the arterial wall.

⇩

Endothelial injury and dysfunction, causing increased vascular permeability, leukocyte adhesion, and thrombosis

⇩

Accumulation of lipoproteins (mainly LDL and its oxidized forms) in the vessel wall

⇩

Monocyte adhesion to the endothelium, followed by migration into the intima and transformation into macrophages and foam cells

⇩

Platelet adhesion

⇩

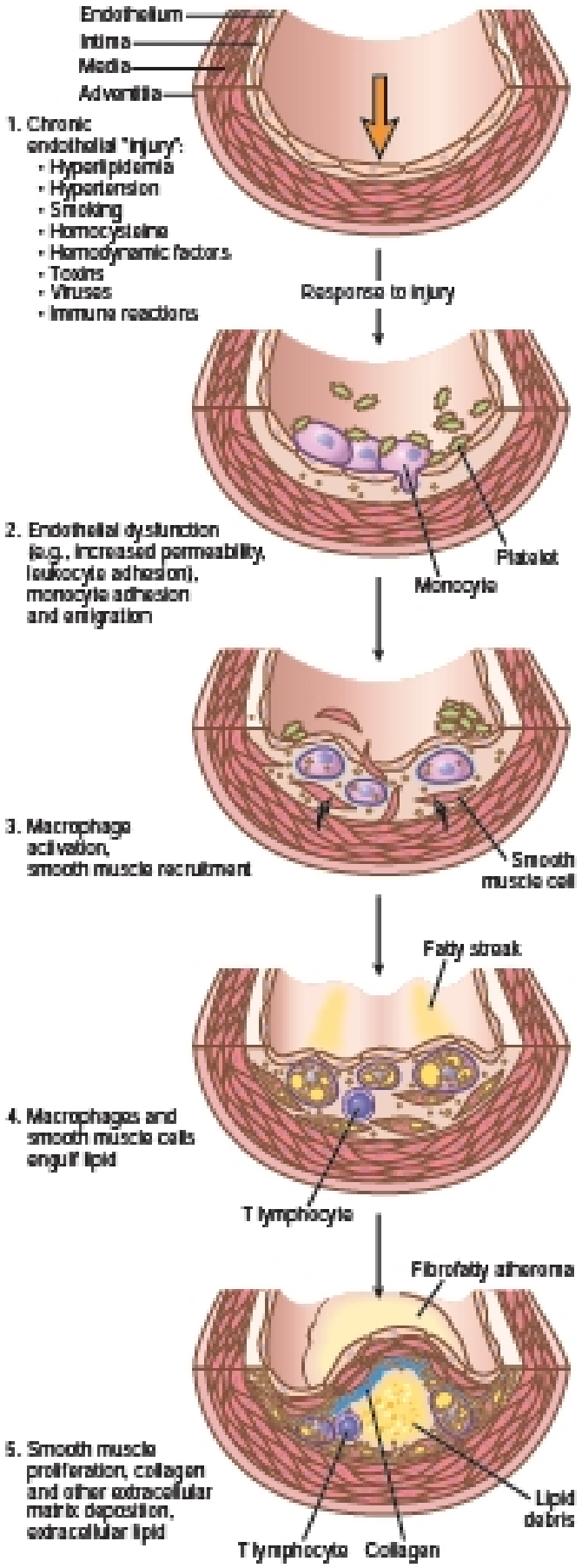
Factor released from activated platelets, macrophages, and vascular wall cells, inducing smooth muscle cell recruitment, either from the media or from circulating precursors

⇩

Smooth muscle cell proliferation, extracellular matrix production, and recruitment of T cells.

⇩

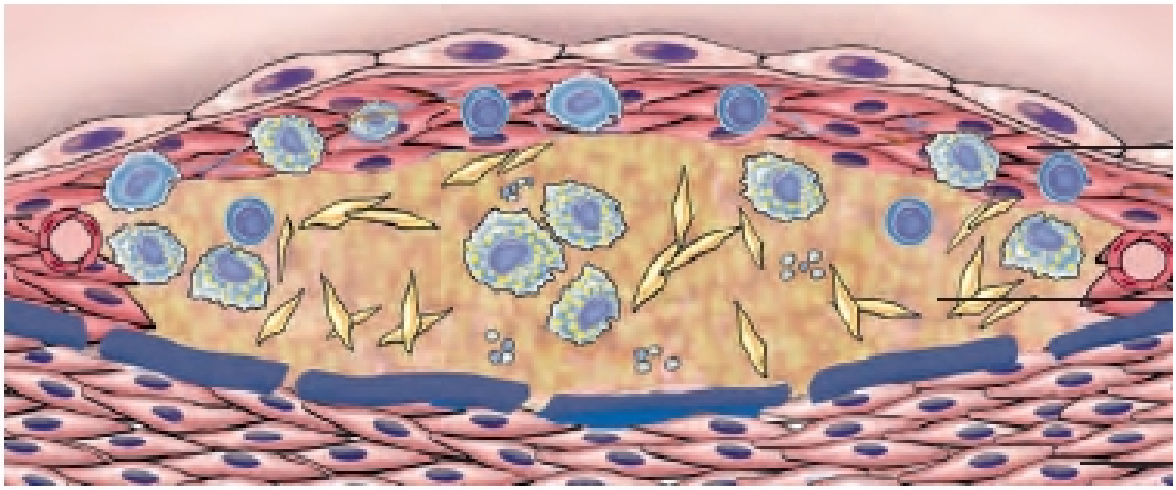
Lipid accumulation both extracellularly and within cells (macrophages and smooth muscle cell)


Endothelium
Intima
Media
Adventitia
1. Chronic endothelial "injury":
• Hyperlipidemia
• Hypertension
• Smoking
• Homocysteine
• Hemodynamic factors
• Toxins
• Viruses
• Immune reactions
Response to injury
2. Endothelial dysfunction (e.g., increased permeability, leukocyte adhesion), monocyte adhesion and emigration
Platelet
Monocyte
3. Macrophage activation, smooth muscle recruitment
Smooth muscle cell
Fatty streak
4. Macrophages and smooth muscle cells engulf lipid
T lymphocyte
Fibrofatty atheroma
5. Smooth muscle proliferation, collagen and other extracellular matrix deposition, extracellular lipid
Lipid debris
T lymphocyte
Collagen

Inflammation

Chronic inflammation is triggered by the accumulation of cholesterol crystals and free fatty acids in macrophages and other cells. The resulting inflammasome activation leads to the production of the pro-inflammatory cytokine IL-1 and macrophage and T cell activation[63].

Intimal smooth muscle cell proliferation and extracellular matrix deposition convert a fatty streak into a mature atheroma and contribute to the progressive growth of atherosclerotic lesions. Intimal smooth muscle cells have a proliferative and synthetic phenotype distinct from the underlying medial smooth muscle cells. Platelet-derived growth factor fibroblast growth factor, and transforming growth factor-α estimulate smooth muscle cells to synthesize extracellular matrix (collagen), which stabilizes atherosclerotic plaques. The key processes in atherosclerosis are intimal thickening and lipid accumulation, which together form plaques and vessels involved are the abdominal aorta, the coronary arteries, the popliteal arteries, the internal carotid arteries, and circle of Willis.



Atherosclerotic plaques have three principal components: (1) smooth muscle cells, macrophages, and T cells; (2) extracellular matrix, including collagen, elastic fibers, and proteoglycans; and (3) intracellular and extracellular lipidand a fibrous cap, with a necrotic core, containing lipid (primarily cholesterol and cholesterol esters), foam cells (lipid laden macrophages and smooth muscle cells),fibrin, thrombus, and plasma proteins; The periphery of the lesions show neovascularization[64].Atherosclerotic plaques undergo ,rupture or ulceration, Hemorrhage or Atheroembolism and Aneurysm formation- Atherosclerosis-induced pressure or ischemic atrophy of the underlying media, with loss of elastic tissue, causes weakness and potential rupture.

Large elastic arteries (e.g., aorta, carotid, and iliac arteries) and large and medium-sized muscular arteries (e.g., coronary and popliteal arteries) are the major targets of atherosclerosis.

At early stages of atherosclerotic stenosis, outward remodeling of the vessel media tends to preserve the size of the lumen. Critical stenosis produce tissue ischemia, when there is 70% decrease in luminal cross-sectional area.

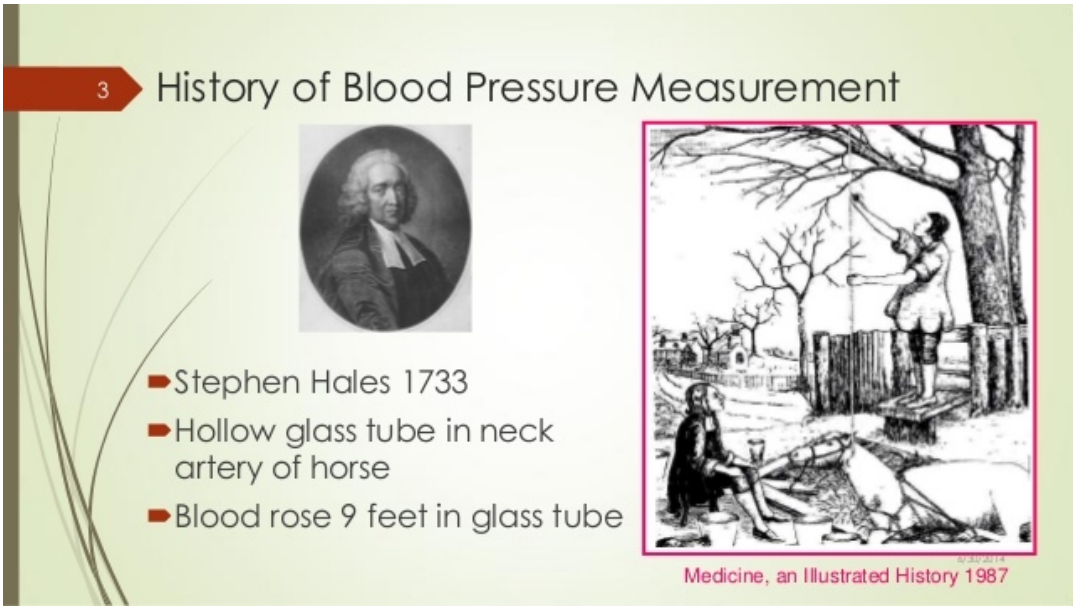
The major structural component of the fibrous cap is the collagen and accounts for its mechanical strength and stability. Collagen in atherosclerotic plaque is produced primarily by smooth muscle cells so that loss of these cells results in a less sturdy cap[65]. Moreover, collagen turnover is controlled by metalloproteinases (MMPs), enzymes elaborated largely by macrophages and smooth muscle cells within the atheromatous plaque; conversely, tissue inhibitors of metalloproteinases (TIMPs) produced by endothelial cells, smooth muscle cells, and macrophages modulate MMP activity. Conversely, statins have a beneficial therapeutic effect by stabilizing plaques through a reduction in plaque inflammation. Thrombin is a potent activator of smooth muscle cells and can thereby contribute to the growth of atherosclerotic lesions.

HYPERTENSION AND VASCULAR WALL

BLOOD PRESSURE

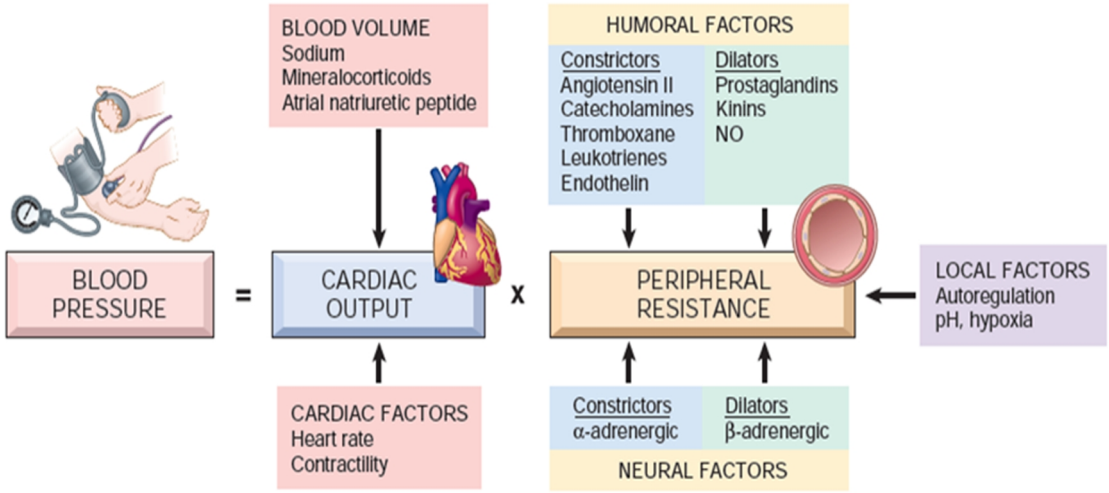
Physician William Harvey (1578–1657), described the circulation of blood in his book "*De motucordis*". The English clergyman Stephen Hales made the first published measurement of blood pressure in 1733[66]. In the year 1828, mercury sphygmomanometer was discovered by Bernoulli.

The first report of elevated blood pressure in a person without evidence of kidney disease was made by Frederick Akbar Mahomed in 1874 using a sphygmograph. Cuff-based sphygmomanometer by Scipione Riva-Rocci in1896 allowed blood pressure to be measured in the clinic. In 1905, NikolaKorotkoff improved the technique by describing the Korotkoff sounds.



BP = CARDIAC OUTPUT X TOTAL PERIPHERAL RESISTANCE

- Cardiac output is a function of stroke volume and heart rate.
- Peripheral resistance is regulated predominantly at the level of the arterioles by neural and hormonal inputs.



Blood pressure regulation

Systolic pressure: It is defined as the maximum pressure which is reached during the cardiac cycle. It indicates the force of contraction of heart.

Diastolic pressure: It is defined as the minimum pressure attained during the cardiac cycle. It depends on the total peripheral resistance.

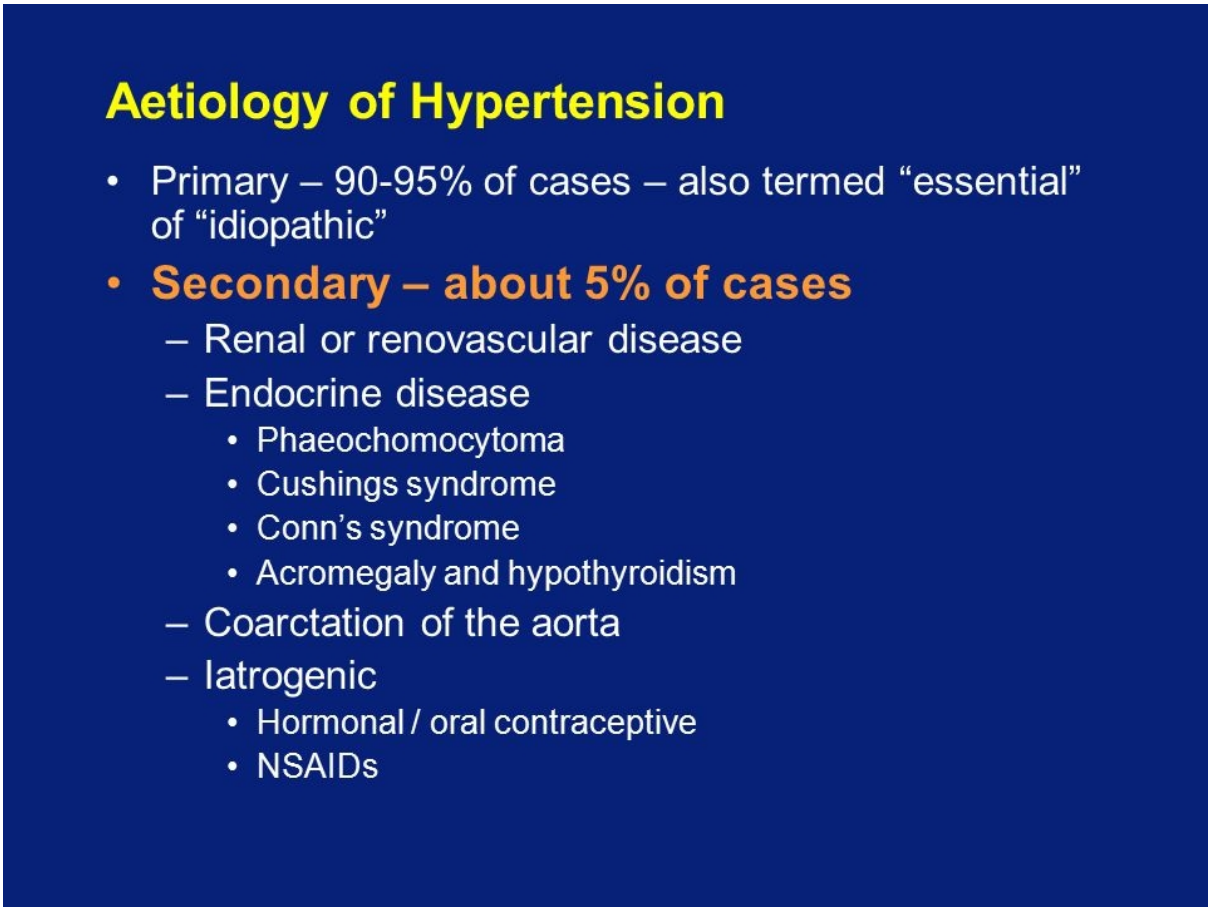
Hypertension causes arterial wall thickening and loss of elasticity – Arterioscleosis means “hardening of the arteries”.

Classification of hypertension for adults aged >18yrs according JNC

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	90-119	60-79
Prehypertension	120-139	80-89
stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	>160	>100
Isolated systolic Hypertension	>/=140	<90

Sustained diastolic pressures above 89 mm Hg or sustained systolic pressure above 139 mm Hg are associated with increased risk of atherosclerotic disease, and are thus considered clinically significant[67].Hypertension causes cardiac hypertrophy and heart failure, multi-infarct dementia, aortic dissection, and renal failure. Hypertension remains asymptomatic until late in its course.

As per Framingham heart study, rise in systolic blood pressure by 20mm Hg and the risk for cardiac failure increases by 56%[80]. This was proposed by Adler et al[80]

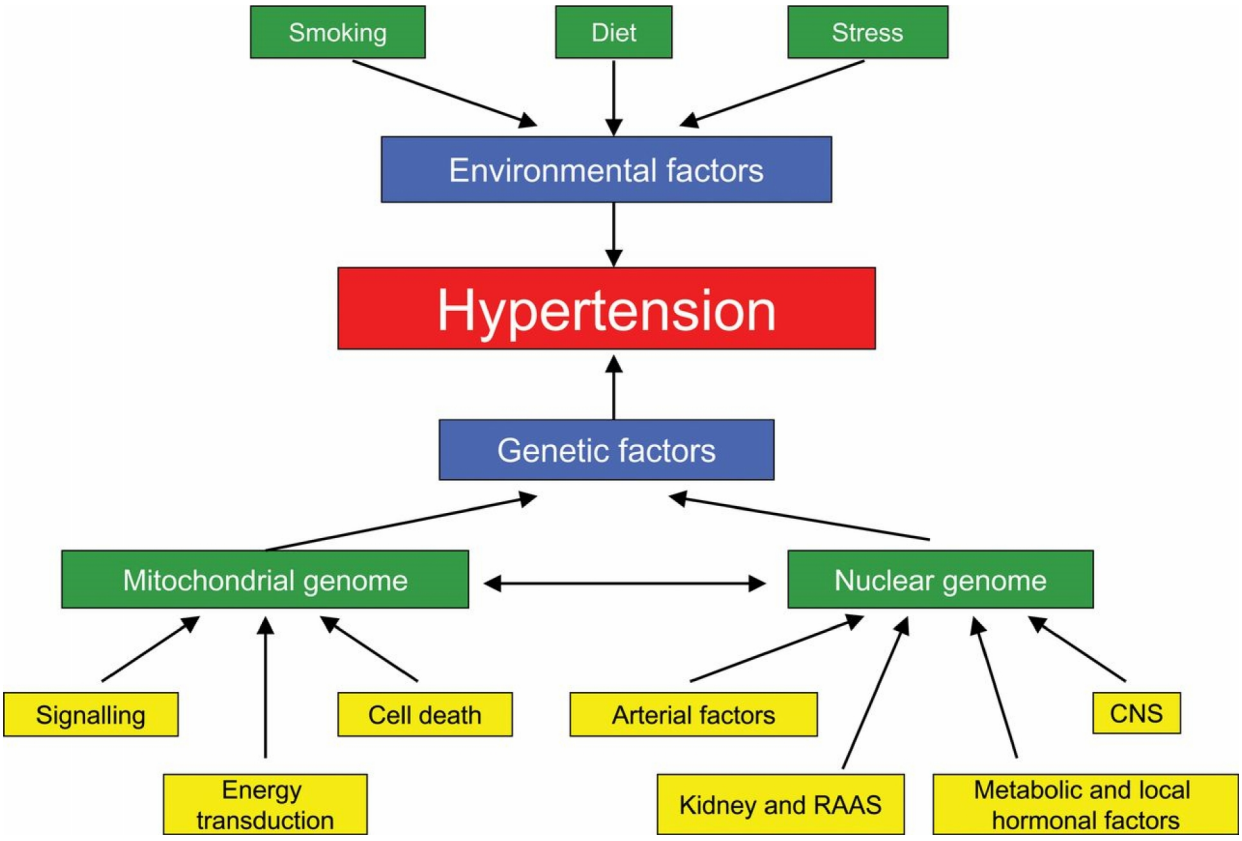


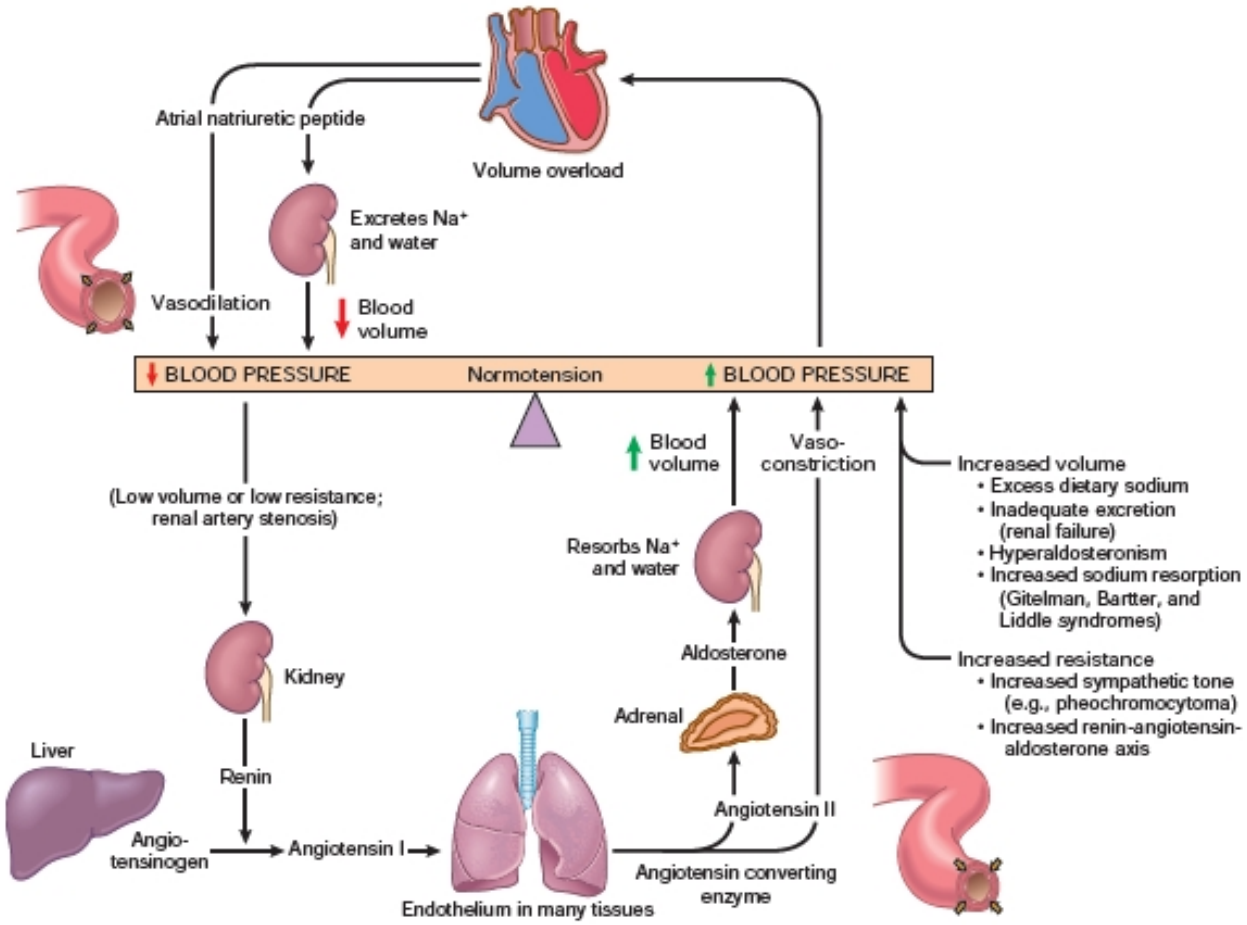
Pathogenesis of Hypertension

Hypertension is a disorder with multiple genetic and environmental contributions.

- Vast majority causes (90% to 95%) of hypertension is idiopathic.

- In renovascular hypertension, renal artery stenosis induces renin secretion and increases vascular tone and blood volume via the angiotensin-aldosterone pathway.
- Single-gene disorders
- Gene defects affecting enzymes involved in aldosterone metabolism
- Mutations affecting proteins that influence sodium reabsorption e.g.,Liddle syndrome, epithelial Na+ channel proteins





Mechanisms of Essential Hypertension

- Genetic factors influence blood pressure regulation, by altering net sodium reabsorption in the kidney. Cumulative effects of polymorphisms in genes affect blood pressure;
- Reduced renal sodium excretion in the presence of normal arterial pressure may be a key initiating event in essential hypertension, a final common pathway for the pathogenesis of hypertension. “Resetting of pressure natriuresis” plays a role[68].

- Renin is an enzyme produced by renal juxta glomerular cells, myo epithelial cells that surround the glomerular afferent arterioles released to increase sodium resorption by the proximal tubules as needed and also cleaves plasma angiotensinogen to angiotensin I.
- Vaso constrictive influences or stimuli that cause structural changes in the vessel wall, can lead to an increase in peripheral resistance and may also play a role in essential hypertension.
- Environmental factors like obesity, smoking, physical inactivity, and heavy salt consumption, stress are all noted in hypertension.

Hypertension not only accelerates atherogenesis but also causes degenerative changes in the walls of large and medium arteries[69].

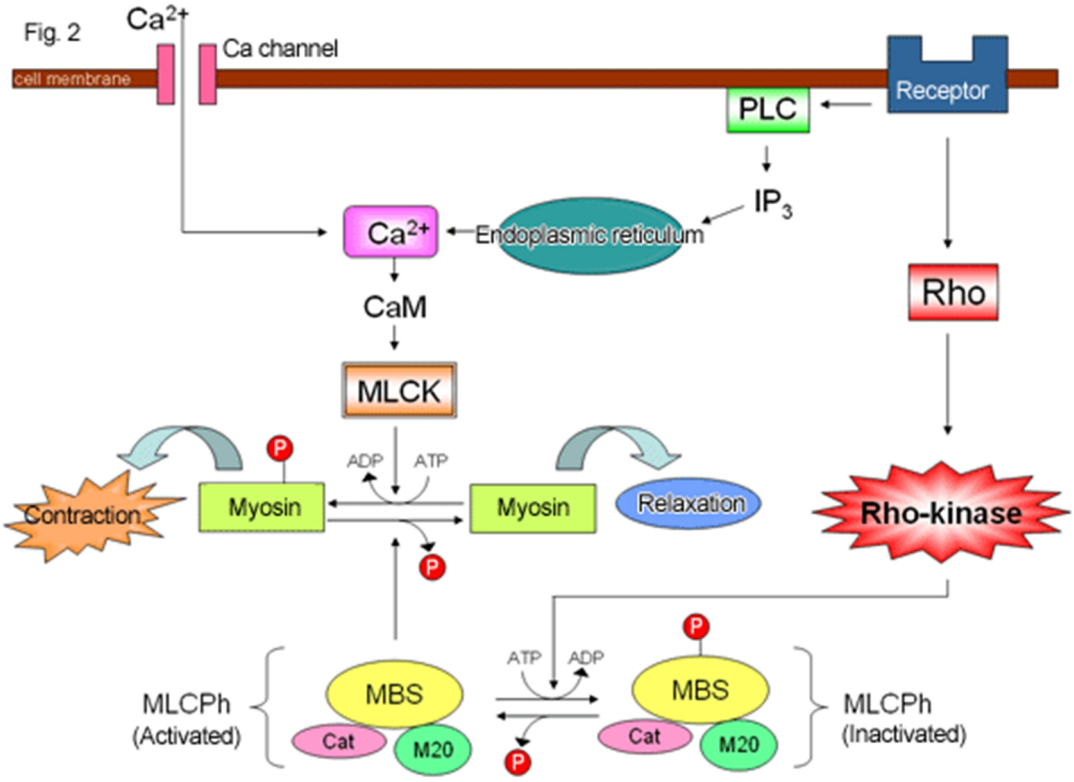
Hypertension induced structural changes in vasculature:

Hypertension is a disorder of heart and blood vessels. They adapt their structure in response to altered load. This occurs physiologically and pathologically in hypertension. Increased pressure exerts an increased load on a thin walled chamber or tube by increasing wall tension according to Laplace's law. A rise in tension results in increased wall tensile stress. Normalisation of wall tensile stress can be achieved either by an increase in wall thickness or by a reduction in chamber/ lumen diameter, or both.

The elevated pressure causes an increase in wall tension that is largely experienced by vascular myocytes and the extracellular matrix of the blood vessel[70]. The diameter of large elastic arteries such as the aorta or carotid is increased in hypertension. There is also an increase in wall thickness (or at least intima–media thickness (IMT) as measured by ultrasound)19 The rise in pressure distends the vessel, while the increased media thickness normalises media stress. Blood vessels do not obey Hooke's law and are non-linearly elastic—i.e., they become stiffer when distended.Pro-hypertensive factors contribute to endothelial barrier dysfunction[72]. For example, angiotensin-II (Ang-II) disrupts the blood brain barrier in spontaneously hypertensive rats (SHR) and aldosterone can diminish endothelial nitric oxide synthase activity via rearrangement of the actin cytoskeleton. RhoA the master regulator of actin cytoskeleton formation, an improvement in endothelial barrier function could be another mechanism. Hence RhoA/ROCK inhibition (e.g. fasudil) acts as an anti-hypertensive therapy. Similar to vasoactive molecules, novel mediators of endothelial permeability and actin cytoskeleton dynamics are emerging.

Overall, the metabolism of endothelial cells becomes dysfunctional promoting a pro-contractile, pro-inflammatory, and pro-oxidative milieu in hypertension.

Role of Tunica Media -Vascular Smooth Muscle Cells



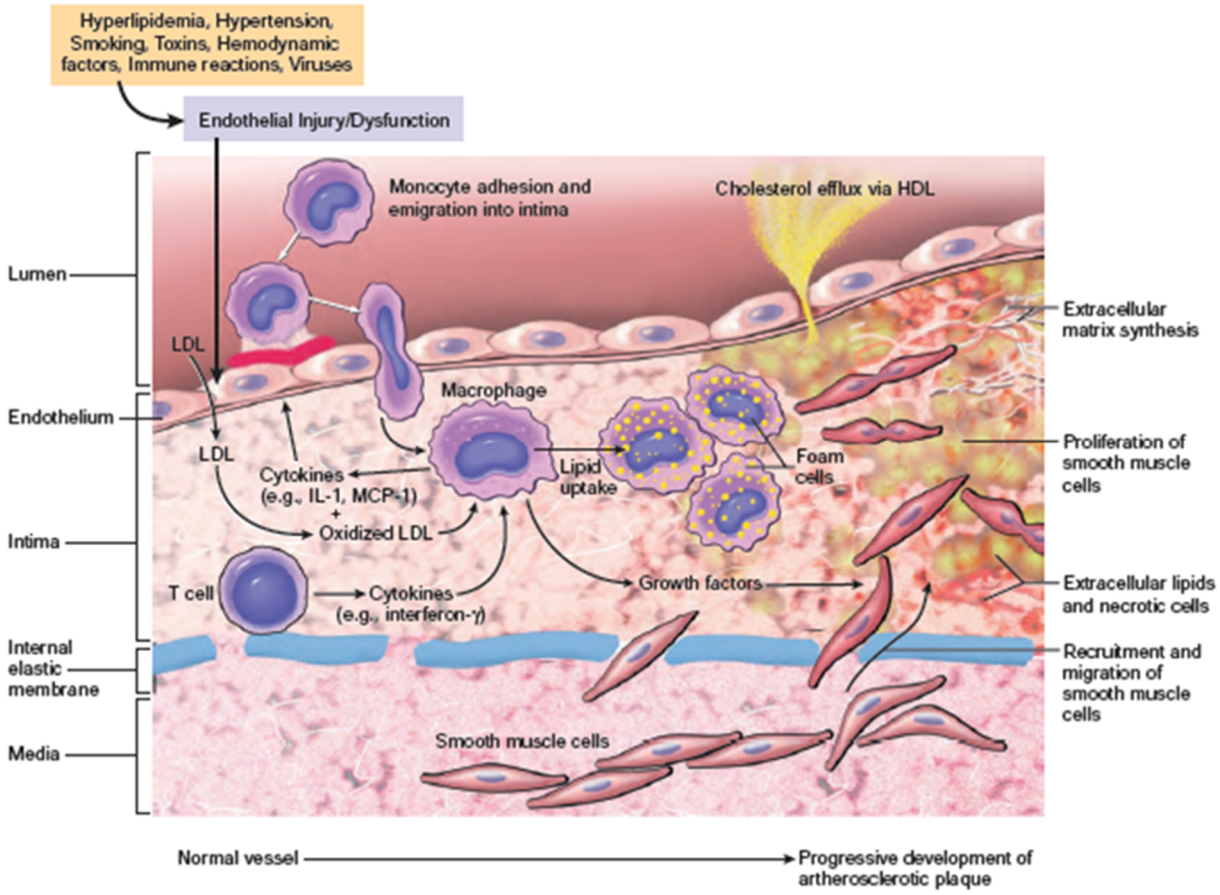
VSMCs are embedded in a network of elastin-rich extracellular matrix and the basement membrane, which surrounds each VSMCs and separates the VSMCs-containing medial cell layer from the endothelium (73). VSMCs structural changes in hypertension are termed VASCULAR REMODELING. Vascular remodeling is classified as hypertrophic, eutrophic or hypotrophic. Remodeling can be inward (reduced luminal diameter) or outward (increased luminal diameter) [74]

The most common type in hypertension is inward remodeling, causing a reduction of the luminal diameter under passive conditions. Outward remodeling is generally seen during antihypertensive treatment, and in conditions of increased flow

During hypertension, VSMCs undergo hyperplasia and hypertrophy which is responsible for the vascular inward remodeling and subsequent development of increased total peripheral resistance

Fibroblasts are the principal cells for vascular remodeling in response to injury[75]. However, during hypertension, fibroblasts also undergo a morphological change, with proliferation and migration into the tunica media . This response to injury also leads to the production of chemokines, cytokines, adhesion molecules, reactive oxygen species and matrix metalloproteinases, along with proliferation of the vasa vasorum, resulting in irreversible functional and structural remodeling of the vessel wall. The peri vascular adipose tissue (PVAT) anticontractile action is lost in hypertension.

In dysfunctional PVAT (e.g., hypertension), immune cell infiltrates in the perivascular adipose tissue also contributes to the low-grade inflammation seen in multiple cardiovascular diseases.



Sequence of cellular interactions in atherosclerosis

.

STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), Version 22. Descriptive quantitative data were presented as frequencies or means ± standard deviation (SD). Correlation of two continuable variables were done using Pearson Correlation test. One-way ANOVA was used to compare the groups. Cross tabulation were used to check the association between categorical variables. P value of <0.05 was considered statistically significant. .

RESULT

A total of 100 subjects between 31–60 years were included in the study (mean age: 46.23±8.56 years).There were 49 males and 51 females in the study group.

The demographic characteristics of the subjects by age group are shown in Table 2 and Graph 2

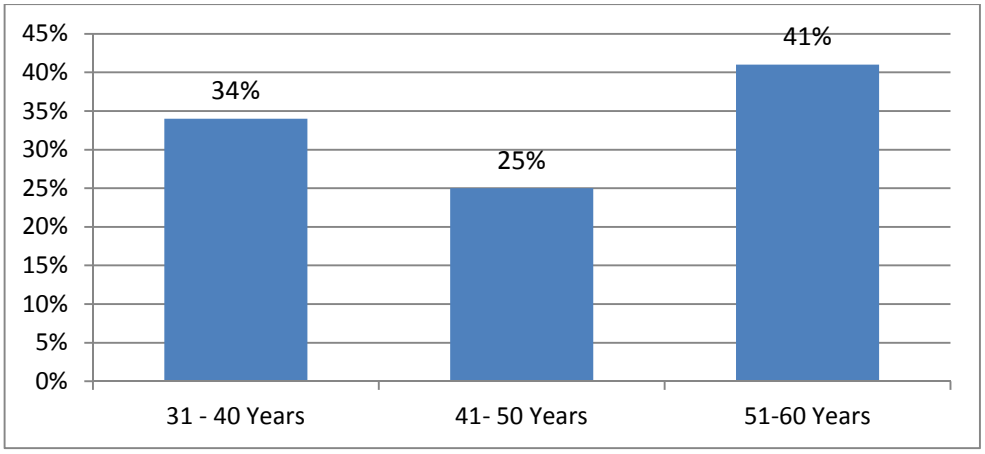
Table 2

Age group distribution

AGE Group (in years)	Frequency	Percent
31-40	34	34.0%
41- 50	25	25.0%
51-60	41	41.0%
Total	100	100.0%

Graph -2

Age group distribution



All subjects were grouped into three groups age wise, 31 - 40, 41 - 50 and 51 – 60 years with a frequency of 34, 25 and 41 respectively. Among the subjects, age group 51-60 years has the highest frequency (shown in figure 1 and graph 1)

By gender wise classification females are higher in number (59%), which is shown in table 3 and graph 3

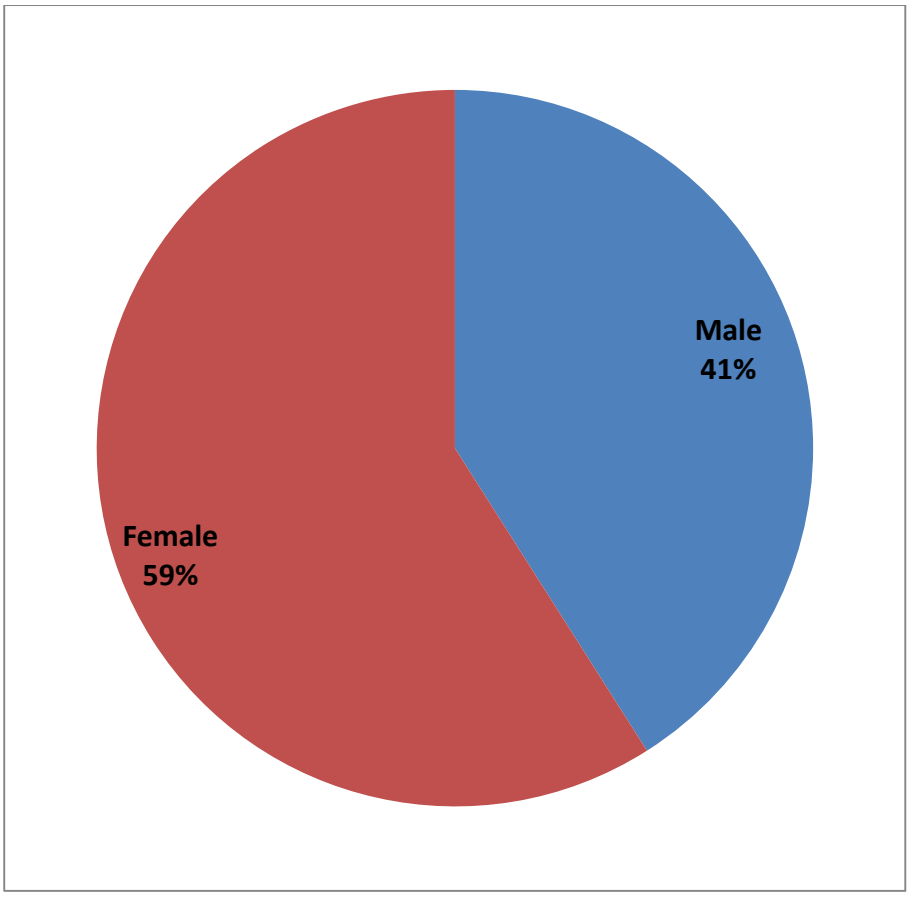
Table -3

GENDER DISTRIBUTION

SEX	Frequency	Percent
Male	41	41.0%
Female	59	59.0%
Total	100	100.0%

Graph -3

GENDER DISTRIBUTION



The BMI of participants is classified into four categories based on Asian Indian criteria. Among them, over weight category has the highestfrequency (41%), Obesity category (32%) and normal BMI (26%) respectively. Mean BMI of these categories is 26.53±4.03.

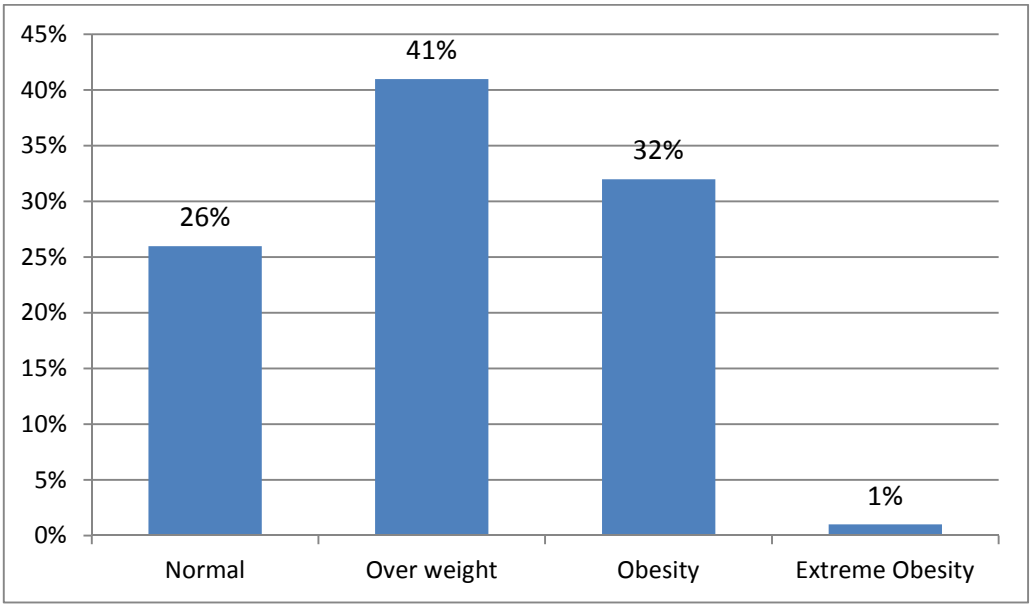
TABLE 4

BMI FREQUENCY DISTRIBUTION

BMI	Frequency	Percent
Normal	26	26.0%
Over weight	41	41.0%
Obesity	32	32.0%
Extreme Obesity	1	1.0%
Total	100	100.0%

GRAPH 4

BMI DISTRIBUTION



The frequency of subjects by Systolic BP classification is tabulated in table no. 5 and is depicted in graph 5

Among these groups, pre hypertensive subjects have the highest frequency (77%), followed by stage I hypertensive (18%) and Normal subjects (5%)

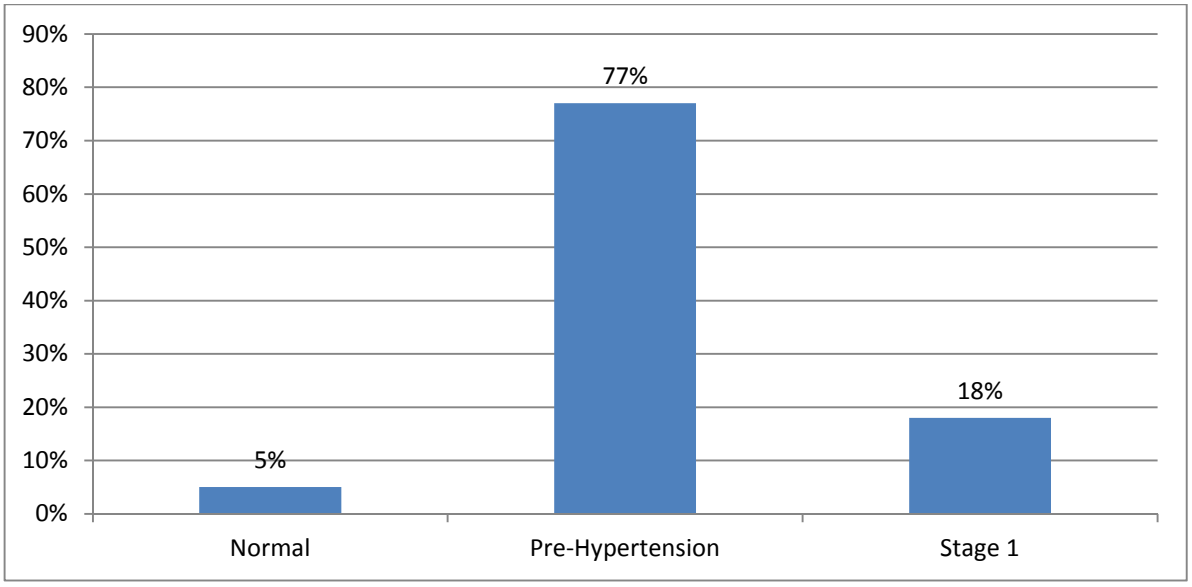
TABLE 5

DISTRIBUTION BY SYSTOLIC BLOOD PRESSURE

SBP	Frequency	Percentage
Normal	5	5%
Pre hypertension	77	77%
Stage 1 Hypertension	18	18%
Total	100	100%

GRAPH 5

DISTRIBUTION BY SYSTOLIC BLOOD PRESSURE



HT classification by DBP is done and tabulated in table no.6 and also shown graphically in graph 6

Stage I hypertensive subjects are higher in number (65%), followed by prehypertensive subjects (29%) and Normal subjects (5%)

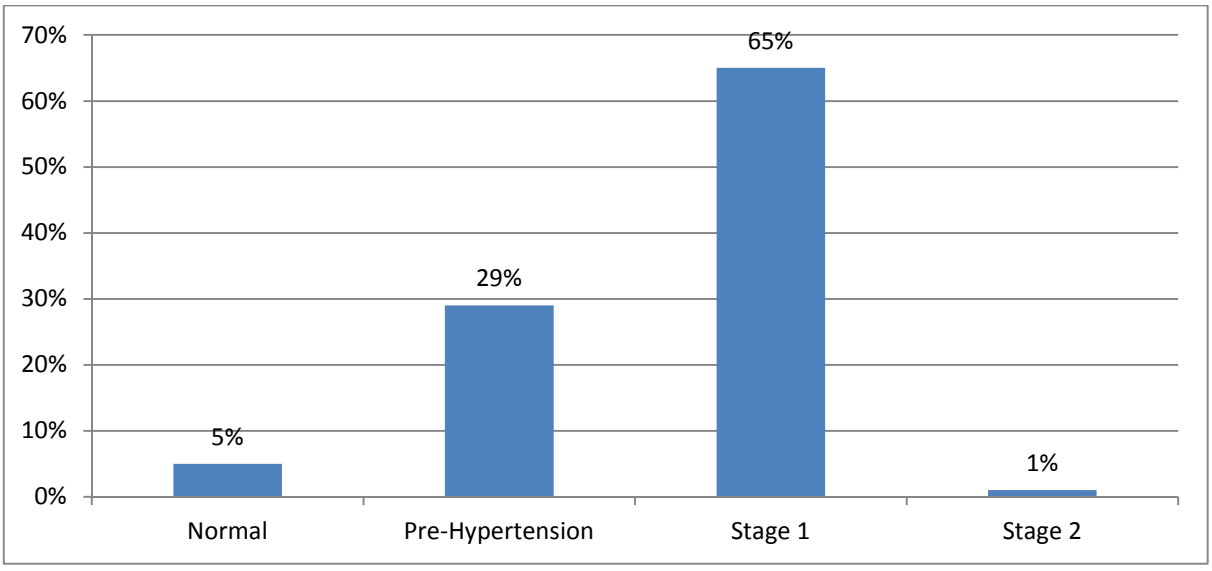
TABLE 6

FREQUENCY DISTRIBUTION BY DIASTOLIC BLOOD PRESSURE

DBP	Frequency	Percentage
Normal	5	5%
Pre Hypertension	29	29%
Stage 1 Hypertension	65	65%
Stage 2 Hypertension	1	1%

GRAPH 6

FREQUENCY DISTRIBUTION BY SYSTOLIC BLOOD PRESSURE



Of the 100 subjects, 100 (100 %) completed the study and carotid artery scanning done. The CIMT measurement was performed in all the subjects.

The percentage of frequency distribution is calculated and represented in table no.7 and pie graph. In that, normal and abnormal values are 80% and 20% respectively.

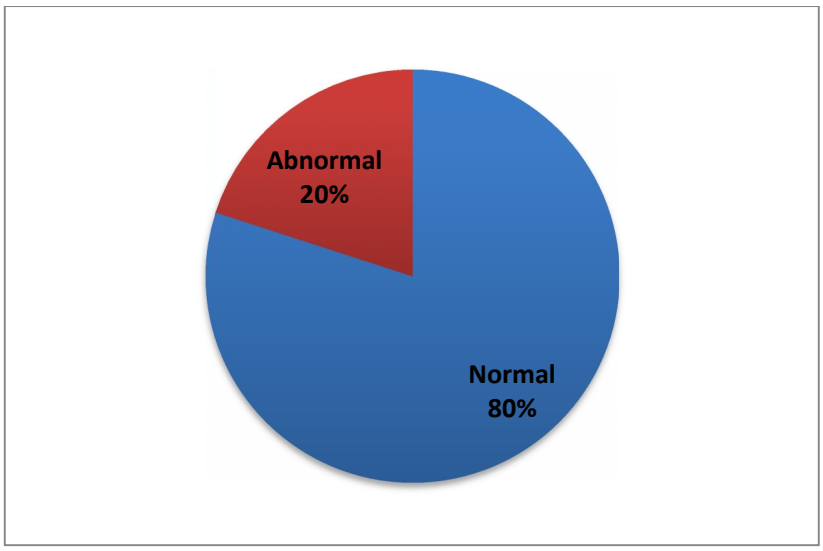
Table No 7

CIMT distribution

CIMT	Frequency	Percent
Normal (<.9 mm)	80	80.0%
Abnormal (>.9 mm)	20	20.0%
Total	100	100.0%

Graph 7

CIMT DISTRIBUTION



Mean CIMT of the right side is0.77±.15 and left side is 0.76 ± .18 and is tabulated in Table 8

TABLE 8

Mean CIMT Side-Side

	Mean CIMT	**SD**	**P value**
Rt side	0.77	0.15	<0.21
Lt side	0.76	0.18	

There is no significant difference between the two sides, p value is < 0.21.

Mean CIMT of the males and females with normal BMI category is 0.81 and 0.58 respectively. Over weight males and females have mean CIMT 0.85 and 0.71 respectively. Obese males and females have mean CIMT 0.93 and 0.76 respectively.

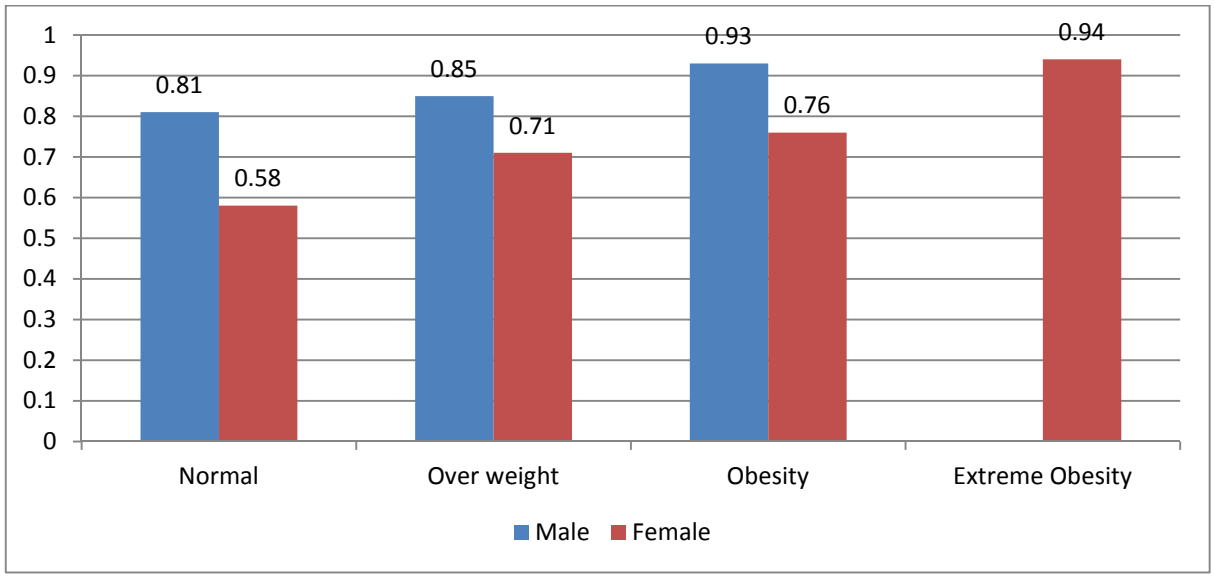
Table 9

BMI vs Gender vs Mean CIMT

BMI	Gender	
	Male	Female
Normal	0.81	0.58
Over weight	0.85	0.71
Obesity	0.93	0.76
Extreme Obesity	-	0.94

Graph 8

BMI vs Gender vs Mean CIMT



Mean CIMT of the normal BMI category by age group wise are 0.57,0.67 and 0.81 respectively. Mean CIMT of the Overweight BMI category by age groupwise are 0.64,0.76 and 0.85 respectively. Mean CIMT of the Obesity category by age groupwise are 0.65,0.78 and 0.96 respectively.

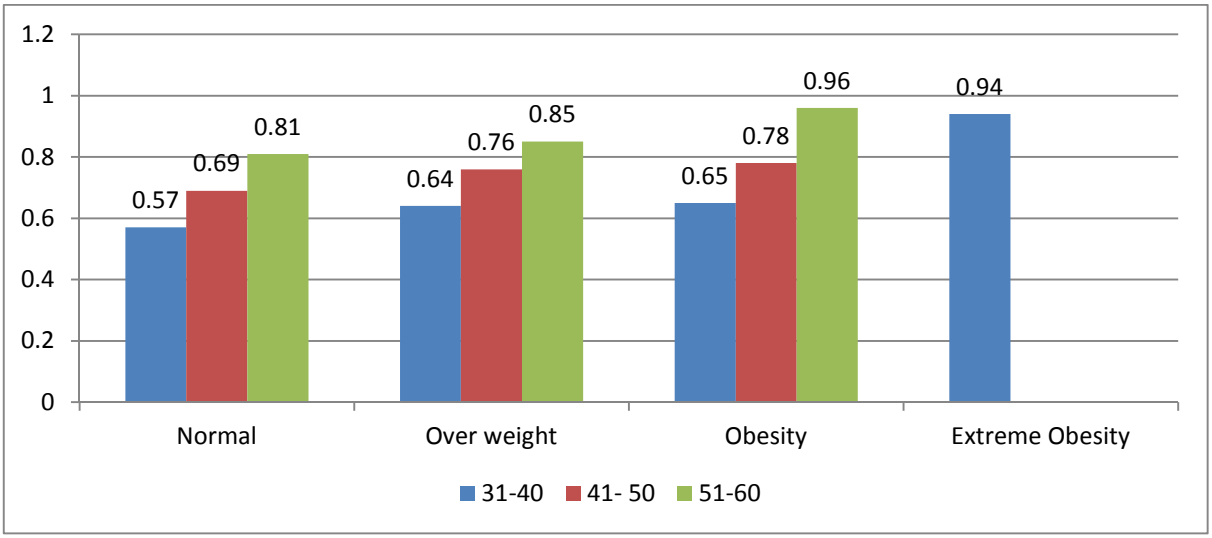
Table 10

BMI vs Age vs CIMT

BMI	31-40	41- 50	51-60
Normal	0.57	0.69	0.81
Over weight	0.64	0.76	0.85
Obesity	0.65	0.78	0.96
Extreme Obesity	0.94		

Graph 09

BMI vs Age vs CIMT



We analysed the relationship statistically between the age, gender, BMI, systolic blood pressure and diastolic blood pressure with carotid artery intima media thickness (CIMT).

Pearson correlation analysis shows Age correlation (r value–0.806 and P value <0.001),Gender correlation (r value 0.12 and p value <0.001), BMI Correlation (r value 0.418 and P value <0.001), systolic blood pressure Correlation (r value – 0.419 and P value < 0.001) and diastolic blood pressure Correlation (r value – 0.473 and P value <0.001).All the parameters show significant positive correlation and p values.

Age has more positive correlation with CIMT.As age advances CIMT is also increased. By genderwise CIMT is increased more in males when compared to females. Overweight and obesity category reflects increased BMI individuals with increased CIMT proportionately.

The Systolic and diastolic blood pressure parameters are positively correlated and increased proportionally with CIMT.

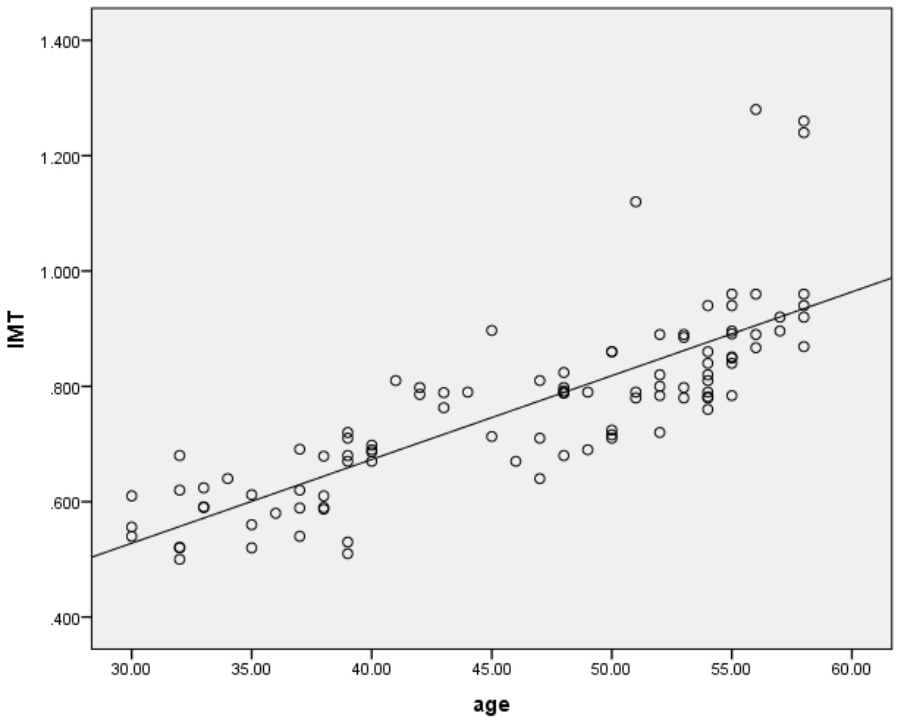
The following datas are shown in the graphs and Tables

GRAPH 10

Correlations Age vs CIMT

Correlation value – 0.806 (Good correlation)

P value - <0.0001



Mean CIMT of all the males is 0.88±0.13 and Mean CIMT of all the females is 0.69±0.12 and has significant p values and are shown in Table and graph

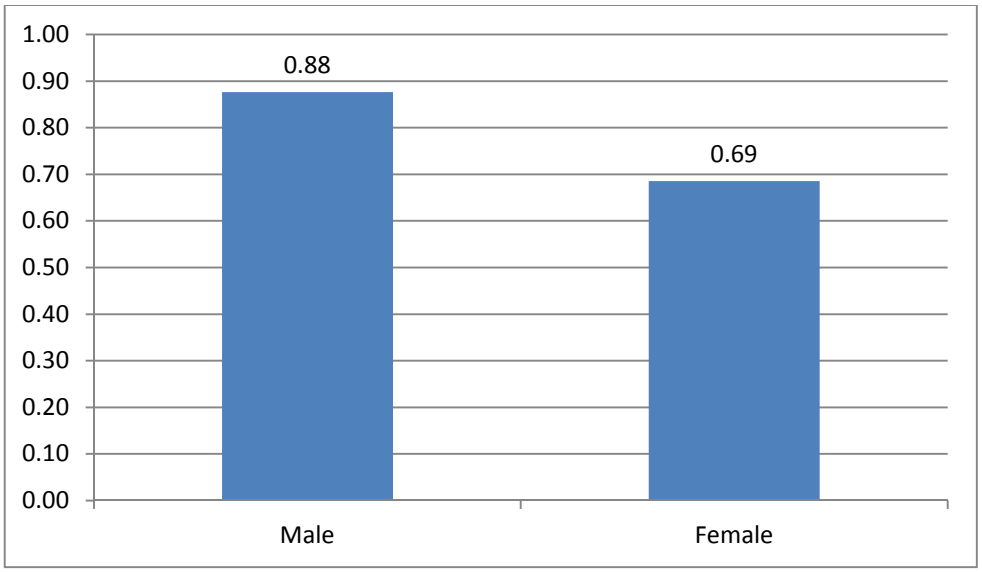
TABLE -11

Gender Vs CIMT

Gender	N	Mean CIMT	Std. Deviation	P value
Male	41	0.88	0.13	<0.0001
Female	59	0.69	0.12	

GRAPH -11

Gender Vs CIMT



Mean CIMT of the normal BMI subjects is 0.64±0.12, Over weight subjects has 0.78±0.11 and overweight people has 0.85±0.16.All categories have significant p values<. .001

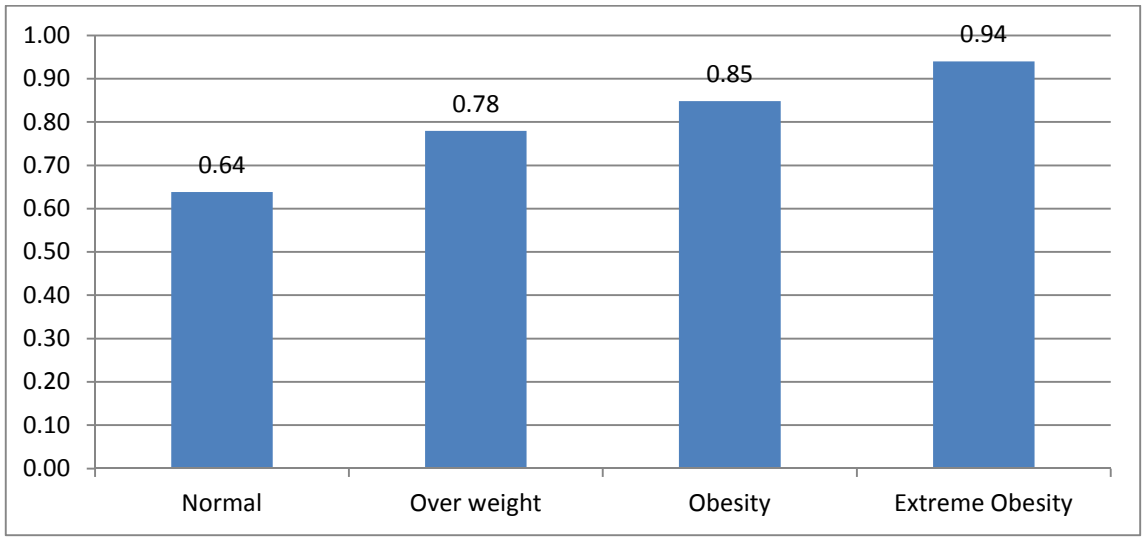
TABLE -12

BMI vs CIMT

BMI	N	Mean CIMT	Std. Deviation	P value
Normal	26	0.64	0.12	<0.0001
Over weight	41	0.78	0.11	
Obesity	32	0.85	0.16	
Extreme Obesity	1	0.94	-	

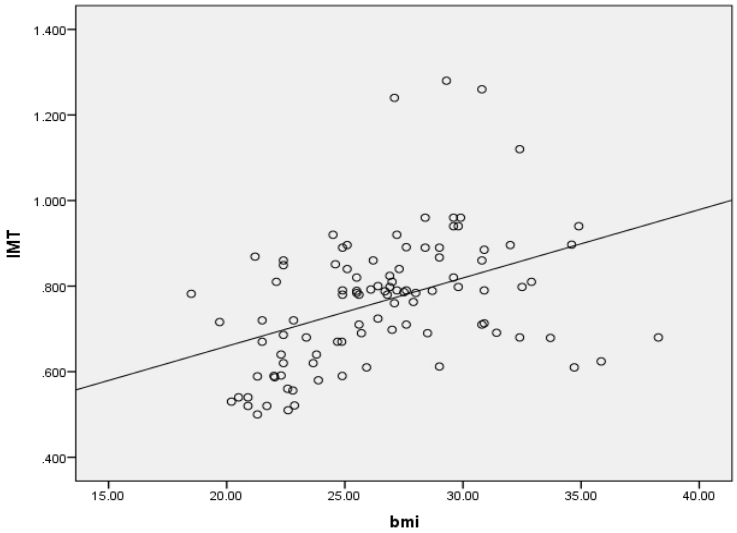
GRAPH -12(a)

BMI vs CIMT



Graph 12 (b)

CORRELATION BMI vs CIMT



BMI Correlation r value = 0.418 and P value <0.001

Mean CIMT of the subjects having normal SBP is 0.52±0.02, Pre hypertensive subjects have 0.78±0.11 and Stage 1 hypertensives have 0.85±0.16.All categories have significant p values <0.001 and has good correlation with CIMT.

Table 13

SBP Vs MEAN CIMT

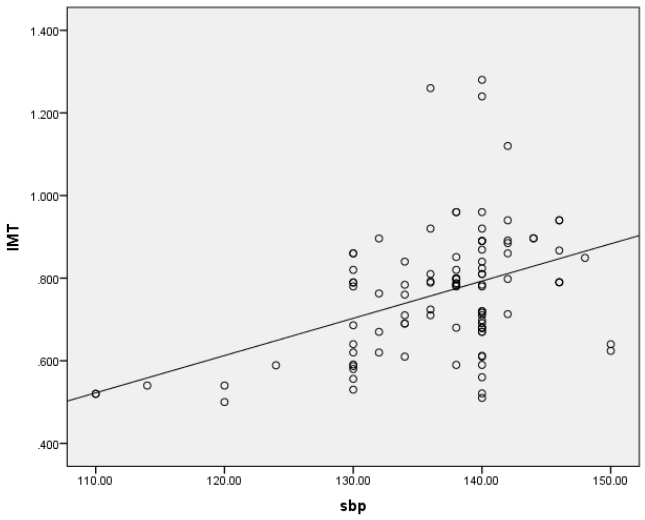
SBP	N	Mean CIMT	Std. Deviation	P value
Normal	5	0.52	0.02	<0.0001
Pre-Hypertension	77	0.76	0.15	
Stage 1 Hypertension	18	0.85	0.12	

Graph -13

Correlations SBP vs CIMT

Correlation value – 0.419 (Moderate correlation)

P value = 0.001



Mean CIMT of the subjects having normal DBP is 0.52±0.02, Pre hypertensive subjects have 0.78±0.11 and Stage 1 hypertensives have 0.85±0.16.All categories have significant p values <0.001 and have good correlation with mean CIMT

Table -14

DBP vs IMT

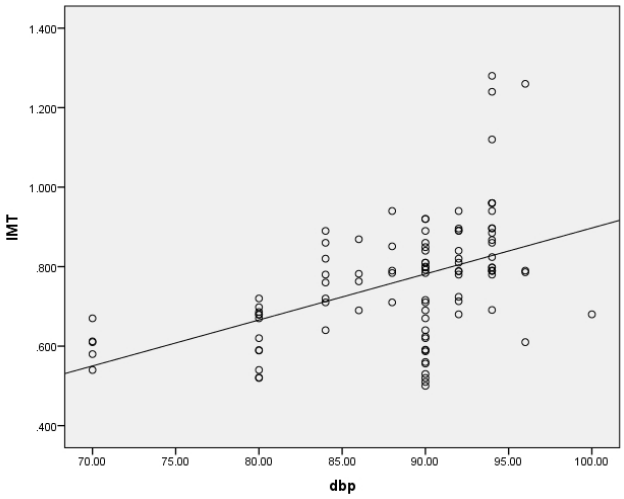
DBP	N	Mean CIMT	Std. Deviation	P value
Normal	5	0.60	0.05	0.009
Pre-Hypertension	29	0.72	0.11	
Stage 1	65	0.80	0.17	
Stage 2	1	0.68	-	

Graph -14

Correlations DBP vs CIMT

Correlation value – 0.473 (Moderate correlation)

P value <0.0001



DISCUSSION

In our study, we found that the mean CIMT of normal healthy persons (including all age group) was 0.77±.16mm.

Levenson J et al, Wendelhag I et al, Deepa R et al, Siva Kumar V et al, Riley WA et al showed the near similar values [61-65].

In our study there was progressive increase in CIMT from 31 to 58 years in all the subjects.

Our study also showed that CIMT is positively correlated with age (P value<0.001) and was higher in the age group of 50-58 years, than lower age groups.

ChatautSP et al,Zavodna E et al, Adeyinka AO et al, Ribeiro AB et al, Savolainen M et al,**Torng PL et al, Coresh J et al, Li S et al, Grobbee DE et al**.,studies consistently showed increased CIMT with age[66-75]

There was significant correlation between CIMT and sex (P value=0.001) and also higher CIMT was seen in males than females in this study.

Torng PL et al,Coresh J et al, Li S et al,Grobbee DE et al.studies showed the similar correlation with gender [72,73,74,75].

In the current study, a positive correlation was observed between CIMT and BMI (r value = 0.32).The change was greater in higher BMI groups (over

weight and obese individuals) than in normal individuals, suggesting a more rapid change in IMT for BMI values > 23.5 kg/m^2

Sorlie P et al , Urbina EM et al,Ducimitere P et al and Sasaki et al have reported similar positive association between CIMT and BMI[76-79].

In our study mean CIMT of hypertensive patients by systolic and diastolic wise criteria are 0.84±.14 and 0.79±.10 mm respectively.

In our study, CIMT correlated positively with SBP and DBP of all the subjects Pearson correlation for SBP (r value=0.41) and DBP (r value=0.47).

This was consistent with **Zavodna E, et al. Ribeiro AB, et al, de Faire U,et al** studies despite differences in the methodology employed in measurement of blood pressure. While blood pressure was taken at presentation in this study; other studies used 24h SBP and DBP measurement method.[80,81,82]

In his study, **Sasaki et al, showed that** vascular remodeling is the cause of carotid arterial changes. In the early atherosclerosis stages, a compensatory mechanism prevents narrowing coincident with an increase in IMT. Although it is a compensatory mechanism, hemodynamic changes still occur in the walls of the arteries resulting in arterial disease.[719]

In hypertensives, higher CIMT values is observed with age which could probably be due to the combined effect of increased blood pressure levels and aging process on the intima media. Also the impact of blood pressure

levels on the intima media has been considered as an accelerated form of aging and hypertensive patients develop aging process in their arterial walls earlier in life than normotensives.

In hypertensives, elevated blood pressure level can cause injury to the endothelium of blood vessels with subsequent thickening of intima media complex via medial hypertrophy,[81,83] a process specifically related to the disease.

Savolainen M et al, de Faire U et al, showed similar results.(80,82)

This thickening of the arterial wall is probably an adaptive mechanism to compensate for the persistent increase in blood pressure levels[80] and the thickening of the vessel wall have been demonstrated in vivo and in vitro.[84] Therefore, increase in blood pressure has a significant effect on the IMT.

Ribeiro AB et al, Simon A et all showed similar results(69,71),

Davis et al. reported cross-sectional associations between c-IMT and cardiovascular risk factors 9,

In the current study, the correlation between carotid atherosclerosis and HTN was significant.

In our study, the method used in arriving at CIMT value involved taking three measurements 1cm proximal to right and left carotid bulb and the mean value of the three measurements were recorded for each side; this was

different from the method employed in some other studies.[80,85] This method is simple, reliable, and reproducible. There is minimal inter- and intra observer error[86].

There was no significant side-side difference noted in the mean CIMT for both left and right sides. **Ibinaiye et al, limbu et al,** noted similar observations(84,85).

CONCLUSION

- OBESITY is an emerging major chronic health problem and a neglected problem globally, with India being one among them. So this study was done to bring out the association between BMI and blood pressure with carotid artery intima media thickness, a surrogate marker of atherosclerosis in the systemic vessels.
- This cross sectional study was done in Tirunelveli Medical College hospital. Sample size was 100. BMI and blood pressure were measured and CIMT was measured using carotid Doppler ultrasonography.

From our study we conclude, that

1) BMI has positive correlation with CIMT values.
2) Blood pressure also has significant positive correlation with CIMT values.
3) Agewise there is a progressive increase in CIMT values.
4) Genderwise, males have a higher CIMT values than female counterparts.

Hence we recommend Carotid Doppler sonography, as a screening tool to be included in the routine Master health checkup programme to monitor the ongoing atherosclerotic changes in vessel wall.

LIMITATIONS OF THE STUDY

This study has its own limitations

- The number of patients in this study is small. Hence generalization of results of the study have to be made with caution.
- The study population involved patients seeking medical care in our hospital which is a tertiary care center and hence they may not represent the general population

FUTURE SCOPE

- In future, this study can be extended among large number of people including both males and females
- Serum leptin, hs CRP and adiposity inflammatory markers can be included to identify the vulnerable population.
- Early detection and timely intervention in the vulnerable population will go a long way in preventing sudden cardiac and cerebro vascular accidents.
- Primary health care providers should be made aware of this potential future screening tool.

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INFORMED CONSENT FORM

Study Title _____

Study Number _____

Subject's Full Name _____

Date of Birth/Age _____

Address _____

1. I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. **OR** I have been explained the nature of the study by the Investigator and had the opportunity toask questions
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the clinical trial/project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)
5. I agree to take part in the above study

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Signatory's Name _____ Date _____

Signature of the Investigator _____ Date _____

Study Investigator's Name _____

Signature of the Witness _____ Date _____

Name of the Witness

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பத்திற்கு)

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 கொடுக்கப்பட்ட அறிவுரைகளின் 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 அளிக்கிறேன்.	☐

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

PROFORMA

Name :

Age/Sex:

Residential Address:

H/o:

Diabetes mellitus	Y	N
Hypertension	Y	N
Thyroid & other endocrine disease	Y	N
Ischemic heart disease	Y	N
Stroke	Y	N
Bronchial Asthma	Y	N
Vasculitis disorders	Y	N
Chronic Steroids usage	Y	N
Statin therapy	Y	N

CLINICAL EXAMINATION

Height: cms

Weight: kgs

BMI:

PR:

BP : mmhg

Respiratory system:

Cardiovascular system:

CNS:

Carotid artery measurement

	Carotid Bulb	**Proximal bulb**	**Distal bulb**
Right Side			
Left Side			

BODY MASS AND OBESITY

- DEFINITION OF OBESITY
- PREVALENCE OF OBESITY
  - GLOBAL SCENARIO
  - INDIAN SCENARIO
- OBESITY AND ANTHROPOMETRY
- BODY MASS INDEX(BMI)
- PATTERNS OF OBESITY
- ENERGY BALANCE
- DIETARY LIPIDS / LIPO PROTEINS
- STORAGE OF LIPIDS AS TRIGLYCERIDES
- ROLE OF HORMONES
- FAT AS AN ORGAN
- PATHOGENESIS OF OBESITY
  - GENES AND ENVIRONMENT
  - INFLUENCES OF CHILDHOOD AND PARENTAL OBESITY
  - MONOGENIC CAUSES OF OBESITY
  - POLYGENIC CAUSES OF OBESITY
  - ROLE OF EDC
  - INTERACTIONS BETWEEN GENES, DEVELOPMENT, AND ENVIRONMENT
  - ROLE OF EPIGENETIC MODIFICATIONS
  - GI FACTORS, BARIATRIC SURGERY, AND THE MICROBIOME
  - THE GUT MICROBIOME AND OTHER GI FACTORS
  - SOCIAL AND ECONOMIC FACTORS
  - ROLES OF SEDENTARY BEHAVIOR, LACK OF EXERCISE, AND NONEXERCISE ACTIVITY THERMOGENESIS
  - FUEL PARTITIONING, INSULIN, AND OBESITY
- COMMON HEALTH CONSEQUENCES OF OVERWEIGHT AND OBESITY
- OXIDATIVE STRESS AND ENDOTHELIAL DYSFUNCTION
- WEIGHT OF THE HEART IN OBESITY

VASCULAR SYSTEM AND ATHEROSCLEROSIS

- STRUCTURE OF VASCULAR WALL
- ENDOTHELIAL CELL
- ENDOTHELIAL CELL INJURY
- HEMODYNAMIC DISTURBANCES
- HYPERCHOLESTEROLEMIA
- VASCULAR WALL RESPONSE TO INJURY
    - INTIMAL THICKENING: A STEREOTYPED RESPONSE TO VASCULAR INJURY
    - RISK FACTOR FOR ATHEROSCLEROSIS
    - PATHOGENESIS OF ATHEROSCLEROSIS
    - RESPONSE TO INJURY HYPOTHESIS MODEL

HYPERTENSION AND VASCULAR WALL

- BLOOD PRESSURE HISTORY
- PATHOGENESIS OF HYPERTENSION
- MECHANISMS OF ESSENTIAL HYPERTENSION
- HYPERTENSION INDUCED STRUCTURAL CHANGES IN VASCULATURE
- ROLE OF TUNICA MEDIA -VASCULAR SMOOTH MUSCLE CELLS

Sl.No	AGE	SEX	Height (cm)	Weight (Kg)	BMI	SBP mmHg	DBP mmHg	CIMT RT	CIMT LT	Mean IMT
1	54	1	166	51	18.5	138	86	0.794	0.77	0.782
2	50	2	162	48	19.7	140	90	0.722	0.71	0.716
3	39	2	156	57	20.2	130	90	0.53	0.53	0.53
4	31	2	142	56	20.5	120	70	0.58	0.5	0.54
5	32	2	145	59	20.9	110	90	0.64	0.4	0.52
6	37	2	153	57	20.9	114	80	0.48	0.6	0.54
7	58	1	169	55	21.2	140	86	0.868	0.87	0.869
8	32	2	147	50	21.3	120	90	0.51	0.49	0.5
9	37	2	153	61	21.3	124	80	0.578	0.6	0.589
10	46	2	159	57	21.5	132	90	0.68	0.66	0.67
11	52	1	164	57	21.5	140	84	0.66	0.78	0.72
12	35	2	150	59	21.7	110	80	0.54	0.5	0.52
13	38	2	155	61	22	140	90	0.6	0.58	0.59
14	38	2	154	55	22.03	130	90	0.594	0.58	0.587
15	54	1	166	58	22.1	140	90	0.82	0.8	0.81
16	33	2	148	60	22.3	130	90	0.682	0.5	0.591
17	34	2	149	53	22.3	150	90	0.68	0.6	0.64
18	37	2	154	64	22.4	130	80	0.68	0.56	0.62
19	40	2	156	59	22.4	130	80	0.702	0.67	0.686
20	54	1	165	56	22.4	130	94	0.86	0.86	0.86
21	55	1	168	56	22.4	148	90	0.998	0.7	0.849
22	35	2	152	63	22.58	140	90	0.62	0.5	0.56
23	39	2	156	61	22.6	140	90	0.52	0.5	0.51
24	31	2	142	60	22.8	130	90	0.552	0.56	0.556
25	39	2	156	66	22.83	140	80	0.74	0.7	0.72
26	32	2	148	48	22.87	140	80	0.442	0.6	0.521
27	39	2	156	54	23.37	138	80	0.69	0.67	0.68
28	32	2	147	62	23.66	132	90	0.74	0.5	0.62
29	47	2	159	61	23.8	130	84	0.65	0.63	0.64
30	36	2	153	48	23.88	130	70	0.56	0.6	0.58
31	58	1	169	61	24.5	136	90	0.94	0.9	0.92
32	55	1	168	59	24.6	138	88	0.862	0.84	0.851
33	39	2	156	60	24.69	140	70	0.67	0.67	0.67
34	40	2	156	50	24.87	140	80	0.67	0.67	0.67
35	33	2	148	59	24.89	138	80	0.68	0.5	0.59
36	44	2	158	72	24.9	130	88	0.82	0.76	0.79
37	51	1	163	63	24.9	140	94	0.76	0.8	0.78
38	52	1	164	63	24.9	140	84	0.91	0.87	0.89
39	54	1	165	65	25.1	134	90	0.85	0.83	0.84
40	55	1	167	61	25.1	132	94	0.912	0.88	0.896
41	48	2	160	72	25.5	130	94	0.818	0.76	0.789
42	54	1	165	71	25.5	130	84	0.81	0.83	0.82
43	55	1	167	71	25.5	134	88	0.788	0.78	0.784

Sl.No	AGE	SEX	Height (cm)	Weight (Kg)	BMI	SBP mmHg	DBP mmHg	CIMT RT	CIMT LT	Mean IMT
44	47	2	159	56	25.6	134	84	0.72	0.7	0.71
45	54	1	166	56	25.6	138	92	0.79	0.77	0.78
46	40	2	156	70	25.7	134	90	0.7	0.68	0.69
47	38	2	155	63	25.92	134	70	0.62	0.6	0.61
48	48	2	161	72	26.1	136	90	0.804	0.78	0.792
49	50	2	162	59	26.2	130	90	0.92	0.8	0.86
50	50	2	162	66	26.4	136	92	0.758	0.69	0.724
51	52	1	163	57	26.4	138	90	0.69	0.91	0.8
52	48	2	161	70	26.7	138	92	0.786	0.79	0.788
53	53	1	164	72	26.8	130	84	0.8	0.76	0.78
54	48	2	161	74	26.9	140	94	0.848	0.8	0.824
55	53	1	164	76	26.9	138	94	0.816	0.78	0.798
56	40	2	157	66	27	140	80	0.706	0.69	0.698
57	47	2	160	78	27	136	90	0.83	0.79	0.81
58	54	1	165	73	27.1	134	84	0.76	0.76	0.76
59	58	1	170	73	27.1	140	94	1.28	1.2	1.24
60	51	1	163	68	27.2	146	94	0.66	0.92	0.79
61	57	1	169	74	27.2	140	90	0.95	0.89	0.92
62	55	1	168	69	27.3	140	92	0.83	0.85	0.84
63	42	2	158	74	27.5	138	96	0.872	0.7	0.786
64	50	2	162	69	27.6	136	88	0.73	0.69	0.71
65	54	1	165	78	27.6	146	96	0.78	0.8	0.79
66	55	1	168	78	27.6	142	92	0.582	1.2	0.891
67	43	2	158	62	27.9	132	86	0.776	0.75	0.763
68	52	1	164	79	28	140	90	0.798	0.77	0.784
69	53	1	165	69	28.4	140	92	0.91	0.87	0.89
70	58	1	170	70	28.4	138	94	0.72	1.2	0.96
71	49	2	162	74	28.5	134	86	0.68	0.7	0.69
72	43	2	158	78	28.7	136	92	0.798	0.78	0.789
73	35	2	152	67	29	140	70	0.624	0.6	0.612
74	56	1	168	76	29	140	90	0.99	0.79	0.89
75	56	1	169	76	29	146	94	0.934	0.8	0.867
76	56	1	169	65	29.3	140	94	1.26	1.3	1.28
77	52	1	164	64	29.6	138	92	0.82	0.82	0.82
78	54	1	167	74	29.6	142	88	0.99	0.89	0.94
79	55	1	168	72	29.6	140	94	0.93	0.99	0.96
80	48	2	162	85	29.8	142	94	0.816	0.78	0.798
81	58	1	170	85	29.8	146	94	0.68	1.2	0.94
82	56	1	168	70	29.9	138	94	0.94	0.98	0.96
83	39	2	156	89	30.8	140	90	0.72	0.7	0.71
84	50	2	162	74	30.8	142	84	0.85	0.87	0.86
85	58	1	170	89	30.8	136	96	1.22	1.3	1.26
86	45	2	158	82	30.9	142	92	0.726	0.7	0.713

Sl.No	AGE	SEX	Height (cm)	Weight (Kg)	BMI	SBP mmHg	DBP mmHg	CIMT RT	CIMT LT	Mean IMT
87	49	2	162	73	30.9	146	94	0.88	0.7	0.79
88	53	1	165	81	30.9	142	94	0.9	0.87	0.885
89	37	2	154	66	31.42	140	94	0.702	0.68	0.691
90	57	1	169	78	32	144	92	0.902	0.89	0.896
91	48	2	161	71	32.4	140	92	0.69	0.67	0.68
92	51	2	163	82	32.4	142	94	1.04	1.2	1.12
93	42	2	158	78	32.5	138	90	0.806	0.79	0.798
94	41	2	158	80	32.9	140	92	0.82	0.8	0.81
95	38	2	155	76	33.7	140	80	0.688	0.67	0.679
96	45	2	159	82	34.6	144	94	0.914	0.88	0.897
97	31	1	145	75	34.71	140	96	0.62	0.6	0.61
98	55	1	168	95	34.9	146	92	0.98	0.9	0.94
99	33	2	149	90	35.85	150	90	0.748	0.5	0.624
100	32	2	148	93	38.27	140	100	0.71	0.65	0.68

CVD-CARDIO VASCULAR DISEASE

BMI-BODY MASS INDEX

AT-ADIPOSE TISSUE

IMT-INTIMA MEDIA THICKNESS

CIMT- CAROTID ARTERY INTIMA MEDIA THICKNESS

CCA-COMMON CAROTID ARTERY

ICA-INTERNAL CAROTID ARTERY

CHD-CORONARY HEART DISEASE

TEE-TOTAL ENERGY EXPENDITURE

REE-RESTING ENERGY EXPENDITURE

TEF-THERMIC EFFECT OF FOOD

VLDL-VERY LOW DENSITY LIPOPROTEIN

LDL- LOW DENSITY LIPOPROTEIN

NPY-NEURO PEPTIDE Y

AgRP-AGOUTI RELATED PEPTIDE

MCH-MELANOCYTE CONCENTRATING HORMONE

MSH- MELANOCYTE STIMULATING HORMONE

PYY-PEPTIDE TYROSINE (3-36)

IAAT-INTRA ABDOMINAL ADIPOSE TISSUE

POMC-PRO OPIO MELANO CORTIN

FTO-FAT MASS AND OBESITY ASSOCIATED

EDC-ENDOCRINE DISRUPTING CHEMICAL

GI-GASTRO INTESTINAL

NO-NITRIC OXIDE

PI3K-PHOSPATIDYL INOSITOL TRI PHOSPHATE

MAPK-MITOGEN ACTIVATED PROTEIN KINASE

VCAM-VASCULAR CELL ADHESION MOLECULE

CRP-C-REACTIVE PROTEIN

VEGF-VASCULAR ENDOTHELIAL GROWTH FACTOR

IL-1-INTER LEUKIN-1

MMP-MATRIX METALLO PROTEINASE

BP-BLOOD PRESSURE

VSMC-VASCULAR SMOOTH MUSCLE

PVAT-PERI VASCULAR ADIPOSE TISSUE

JNC-JOINT NATIONAL COMMITEE

WHO-WORLD HEALTH ORGANISATION