“Carotid artery intimal media thickness and Ankle brachial index as predictors for Atherosclerosis in Prediabetic patients aged between 18-50years in tertiary care hospital, Kolar, Karnataka.”

By

Dr. SURYA PRASAD R .MBBS

DISSERTATION SUBMITTED TO THE SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

In partial fulfilment of the requirements For the degree of

DOCTOR OF MEDICINE

IN

General Medicine

Under the guidance of

Dr. VIDYASAGAR C.R., MD

Associate Professor

Under Co-Guidance Of

Dr Anil Kumar Sakalecha

Professor

DEPARTMENT OF GENERAL MEDICINE,

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR-563101

APRIL 2017

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**Carotid artery intimal media thickness and Ankle brachial index as predictors for Atherosclerosis in Prediabetic patients aged between 18-50years in tertiary care hospital, kolar, Karnataka."** is a bonafide and genuine research work carried out by me under the guidance of **Dr. VIDYASAGAR CR,** MD, Associate Professor**,** Department of General Medicine. SDUMC, Kolar.

Date:

Place: Kolar **Dr SURYA PRASAD R**

CERTIFICATE BY THE GUIDE

This is to certify that this dissertation entitled **"Carotid artery intimal media thickness and Ankle brachial index as predictors for Atherosclerosis in Prediabetic patients aged between 18-50years in tertiary care hospital, kolar, Karnataka."** Is a bonafide research work done by **Dr. SURYA PRASAD R** in partial fulfillment of the requirement for the degree of **Doctor Of Medicine In GENERAL MEDICINE**, SDUMC, Kolar.

Date:

Place: Kolar

SIGNATURE OF THE GUIDE

Dr. VIDYASAGAR C.R. M.D.
Associate Professor,
Department Of General Medicine
Sri Devaraj Urs Medical College,Tamaka,
Kolar.

CERTIFICATE BY THE CO-GUIDE

This is to certify that this dissertation entitled **"Carotid artery intimal media thickness and Ankle brachial index as predictors for Atherosclerosis in Prediabetic patients aged between 18-50years in tertiary care hospital, Kolar, Karnataka."** Is a bonafide research work done by **Dr. SURYA PRASAD R** in partial fulfillment of the requirement for the degree of **Doctor Of Medicine In GENERAL MEDICINE**, SDUMC, Kolar.

Date:

Place: Kolar

SIGNATURE OF THE CO-GUIDE

Dr ANIL KUMAR SAKALECHA
PROFESSOR
RADIO-DIAGNOSIS
Sri Devaraj Urs Medical College,
Tamaka,
Kolar.

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that this dissertation entitled **"Carotid artery intimal media thickness and Ankle brachial index as predictors for Atherosclerosis in Prediabetic patients aged between 18-50years in tertiary care hospital, Kolar, Karnataka."** Is a bonafide research work done by **Dr. SURYA PRASAD R** in partial fulfillment of the requirement for the degree of **Doctor Of Medicine In GENERAL MEDICINE**, SDUMC, Kolar.

Dr. PRABHAKAR K M.D.
Professor & HOD
Department of General Medicine,
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Date:

Place: Kolar

Dr. HARENDRA KUMAR ML M.D.
Principal,
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Date:

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

ETHICS COMMITTEE CERTIFICATE

This is to certify that the Ethics committee of Sri Devaraj Urs Medical College

& Research Center, Tamaka, Kolar has unanimously approved

Dr. SURYA PRASAD R

Post-Graduate student in the subject of

DOCTOR OF GENERAL MEDICINE

at Sri Devaraj Urs Medical College, Kolar to take up the Dissertation

Work entitled

"Carotid artery intimal media thickness and Ankle brachial index as predictors for Atherosclerosis in Prediabetic patients aged between 18-50years in tertiary care hospital, kolar, Karnataka"

to be submitted to the

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA.

Date :
Place : Kolar

Member Secretary
Sri Devaraj Urs Medical College,
Kolar–563101

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION

AND RESEARCH TAMAKA, KOLAR, KARNATAKA

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research, Kolar, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic/research purpose.

Dr. SURYA PRASAD R

Date :

Place : Kolar

ACKNOWLEDGEMENT

No academic work is single handedly accomplished. This work is no exception. Words fail me in expressing my heart felt and humble gratitude to my guide ***Dr. VIDYASAGAR C.R.,*** *M.D., Professor, Department of General Medicine, for the guidance and encouragement all along in completing my study. His encouragement, sense of punctuality, research oriented approach, the painstaking effort to weed out errors and his affection during the entire course of study leaves me permanently indebted to him.*

I am extremely grateful to ***Dr Anil Kumar Sakalecha,*** *M.D, Professor, Department of Radio-Diagnosis, Sri Devaraj Urs Medical College, Tamaka, Kolar, for his constant guidance which has gone a long way in preparation of this dissertation.*

It is with deep sense of gratitude and respect, I have taken an opportunity to thank my teacher ***Dr. PRABHAKAR K,*** *M.D, Professor and HOD, Department of General Medicine, Sri Devaraj Urs Medical College, Tamaka, Kolar, for his constant inspiration and valuable guidance at various stages of preparation of this dissertation.*

I am equally thankful to ***Dr. B.N.RAGHAVENDRA PRASAD****, ex-HOD, Dept. Of General Medicine, without whose support the inception of this work would have been impossible and who has helped me through all stages of this work.*

I express my deep sense of gratitude and humble thanks to ***Dr.Lakshmiaiah V, Dr.P.N.Venkatarathnamma and Dr.Raveesha A****, Professors for their advice and constant encouragement throughout the present study.*

I express my sincere thanks and gratitude to ***Dr. Purnima Hegde*** *M.D, Professor and HOD, Department of Radio-Diagnosis, Sri Devaraj Urs Medical College, Tamaka, Kolar, for guidance and encouragement and inputs for the study.*

I express my gratitude to ***Dr. S.R.PRASAD****, professor & director of Post Graduate studies for his encouragement invaluable inputs for the study.*

I would like to thank all my teachers, ***Dr. Srinivasa.S.V , Dr.Harish Kumar, Dr. Reddy Prasad, Dr.Naveen.L, Dr.Santoshi Malkarnekar, Dr.Naga Sumanth Reddy, Dr. Niveditha, Dr. Prasanna and Dr. Vishwanath Reddy*** *from the Department of General Medicine for their heartfelt support at all times.*

I would like to acknowledge the opportune help and permission rendered by the Medical Director, Principal and Medical superintendent, SDUMC/RLJH, in conducting this study.

I humbly thank ***Dr.Vijay, Dr.Krishna prasad ,Dr Yugandhar reddy, Dr Kishore, Dr Anitha, Dr.Rahul, Dr Sandeep Reddy , Dr Uphar Gupta, Dr Chandhan, Dr Arun, Dr Sabahari Girish, Dr Sridhar*** *my senior postgraduates for their help and guidance to complete my dissertation.*

I thank all my colleagues ***Dr Sudhir, Dr Harish, Dr Arun, Dr Likitesh, Dr Harshitha, Dr Spoorthi, Dr Spandana, Dr Yasin, Dr Charan Reddy, Dr Shiva Prasad, Dr Varun*** *and junior post graduates for their timely suggestion throughout the preparation of this manuscript.*

I am also thankful to all the Nursing Staff, Technical Staff and non-teaching staff for their invaluable help without which this study would not have been possible.

I thank my parents ***Mrs Lakshmi and Ramesh****, my younger brother* ***Manu Prasad R, Banu Prasad R*** *and other family members for their constant source of encouragement, and support throughout the entire career.*

Last but not the least I am grateful to all those patients who were the subjects for the study, without whose cooperation this work would not have been possible.

Dr. SURYA PRASAD R

LIST OF ABBREVATIONS

ADA	American Diabetes Association
AGEs	Advanced Glycation End products
ABI	Ankle Brachial Index
ASE	American Society of Echocardiography
BMI	Body Mass Index
CIMT	Carotid Intimal Medial Thickness
CVD	Cardiovascular Disease
CCA	Common Carotid Artery
CAD	Coronary Artery Disease
CT-CAG	CT Coronary Angiography
DM	Diabetes Mellitus
ESRD	End Stage Renal Disease
FBS	Fasting Blood Sugar
HbA1c	Glycosylated Haemoglobin
HDL	High Density Lipoprotein
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
LDL	Low Density Lipoprotein
NGT	Normal Glucose Tolerance
NF-kB	Nuclear Factor kappa B
PVD	Peripheral Vascular Disease
PPBS	Post Prandial Blood Sugar
TG	Triglycerides
UKPDS	United Kingdom's Prospective Diabetes Study
WHR	Waist Hip Ratio

ABSTRACT

Atherosclerosis still remains as the major cause of death and premature disability in developed societies. Current prediction estimates that by the year 2020 cardiovascular diseases notably atherosclerosis will become the leading global cause of total disease burden. Atherosclerosis typically occurs over a period of many years, usually decades[1].

Pre-diabetes is characterized by a long period of insulin resistance during which a compensatory increase in pancreatic cell function maintains normal glycaemic at the expense of fasting and postprandial hyperinsulinaemia which later advances in to increase fasting plasma glucose state[4]. Insulin resistance is a central pathogenesis feature of Pre-diabetes, the incidence of which is rising substantially. The principal cause of end organ damage In Pre diabetes is premature cardiovascular atherosclerosis.

It is important to identify these conditions to prevent the incidence of diabetes and to take measures to prevent the vascular complications.

The progression of CIMT is influenced by cardiovascular risk factors and is directly related to the risk factors of the future cardiovascular events[9]. CIMT has therefore become a valuable research tool in clinical trials in the assessment of therapeutic agents directed against atherosclerosis[10]. Studies have demonstrated association between cardiovascular risk and increased risk and increase CIMT in people with Pre-diabetes and Type 2 Diabetes[11].

OBJECTIVES AND METHODOLOGY:

To identify prediabetes and to assess carotid intimal media thickness (CIMT) and Ankle brachial index (ABI) and hence cardiovascular risk in these patients.

This study was conducted in R. L. Jalappa hospital and research Centre Tamaka, Kolar, total of 82 patients were studied out of which 41 Prediabetic, 41 with normal glycemic control, age and gender matched, demographic data of patients was collected , BMI, waist-hip ratio, ABI was calculated. Both the groups were subjected for bilateral carotid artery Doppler using bright mode (B mode) ultrasound for the measurement of carotid artery intimal thickness.

RESULTS:

In this study, abnormal CIMT was observed in 7 (17.1%) out of 41 Prediabetic patients. This difference in CIMT findings between two groups was statistically significant. Pre diabetics are at 8 times higher risk of developing abnormal CIMT than non-diabetics .Abnormal CIMT was associated with greater BMI,WHR, low HDL, high triglycerides and abnormal ABI.

CONCLUSION:

Prediabetes was associated with higher risk of developing subclinical atherosclerosis when compared to non-diabetic patients.

CIMT and ABI being a non-invasive marker of subclinical atherosclerosis should be routinely used to diagnose potential problems and treatment outcomes in patient diagnosed with prediabetes.

Lifestyle modification should be adopted to prevent the conversion of Prediabetes into Type 2 Diabetes Mellitus and thus prevention of its complication.

KEY WORDS:

Prediabetes, Diabetes, Subclinical Atherosclerosis, CMIT, ABI.

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system[1].

People with IFG (Impaired Fasting Glucose) have been shown to have endothelial dysfunction and are at increased risk of cardiovascular disease[2].CIMT (Carotid Intimal Media Thickness) has been observed to be increase in people who would subsequently develop diabetes vascular complication due to atherosclerosis are a major cause of morbidity and mortality in type 2 diabetes. Atherosclerosis is a major risk factor which is accelerated in diabetes[3].

Insulin resistance is a central pathogenetic feature of Pre-diabetes, the incidence of which is rising substantially. The principal cause of end organ damage in Pre diabetes is premature cardiovascular atherosclerosis and patient with Pre diabetes have a similar risk of fatal cardiovascular events as non-diabetic patient who have sustained a myocardial infraction.

Pre-diabetes is characterized by a long period of insulin resistance during which a compensatory increase in pancreatic cell function maintains normal glycaemic at the expense of fasting and postprandial hyperinsulinaemia which later advances in to increase fasting plasma glucose state[4]. Insulin resistance is well established as a independent risk factor for the development of cardiovascular atherosclerosis and pre-diabetes[5].

Endothelial dysfunction precedes the development of atherosclerosis and is believed to play a central role in the pathophysiology[6]. Atherosclerosis still remains as the major cause of death and premature disability in developed countries. Current prediction estimates that by the year 2020 CVD (cardiovascular diseases) notably atherosclerosis will become the leading global cause of total disease burden. Atherosclerosis typically occurs over a period of many years, usually decades[1]. CIMT is a surrogate marker of atherosclerosis and provides a non-invasive method for the risk assessment of CVD. It is a strong predictor of future cardiovascular events and is associated with conventional markers of cardiovascular risk such as diabetes[7]. CIMT is a well-established index of atherosclerosis that correlates with prevalent and incident coronary artery disease[8].

Pre-diabetes, though not a disease entity by itself is associated with a significant degree of risk for both macro vascular and increasingly micro vascular pathology. It is important to identify these conditions to prevent the incidence of diabetes and to take measures to prevent the vascular complications. We need programmes to prevent the development of the Pre-diabetic state, as well as diabetes from Pre-diabetes and its associated complication[1].

The progression of CIMT is influenced by cardiovascular risk factors and is directly related to the risk factors of the future cardiovascular events[9]. CIMT has therefore become a valuable research tool in clinical trials in the assessment of therapeutic agents directed against atherosclerosis[10]. Studies have demonstrated association between cardiovascular risk and increased risk and increase CIMT in people with Pre-diabetes and Type 2 Diabetes[11].

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

1. To identify subjects with Pre-diabetes.

2. To assess carotid intimal media thickness (CIMT) and Ankle brachial index (ABI) in these patients.

3. To assess cardiovascular risk in these patients.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

PRE DIABETES

DEFINITION:

Pre-diabetes is a state where blood sugar level is higher than normal but not yet high enough to be classified as Type 2 Diabetes Mellitus, without intervention Pre-diabetes is likely to become type 2 diabetes in 10 years or less.

The term Pre-diabetes has had a checkered history. Alberti[12] states that it was first used to denote abnormalities of pregnancy (eg. high birth weight babies, hydramnios) or a strong family history of Type 2 Diabetes. However, in 1980, the world Health organisation (WHO) [13] discarded the term largely because many subjects with borderline glucose level do not convert to diabetes and because many would be alarmed unnecessarily. These problems still pertain. Yet in 2005, the American Diabetic Association (ADA) reintroduced Pre-diabetes to cover impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) but not other risk factors for diabetes[14].

In 2008, WHO's diabetic task force again repudiated the term and discouraged its use[15]. Instead, they suggested "intermediate hyperglycemia" to signify IGT and IFG. The ADA nonetheless continues to use Pre-Diabetes and defined it as IFT, IGT, and now HbA1C of 5.7% to 6.4%[16].

Diagnostic criteria

ADA (JANUARY 2016):

DIAGNOSTIC METHOD	CRITERIA
FASTING PLASMA GLUCOSE (Impaired fasting glucose)	100-125mg/dl (5.6-6.9 mmol/L)
2-hr PLASMA GLUCOSE (impaired glucose tolerance)	140-199mg/dl (7.8-11.0 mmol/L)
HbA1C	5.7-6.4 % (39-46 mmol/L)

Table No 1: ADA 2016 classification for diabetes mellitus

Screening for Pre-Diabetes:

- Testing should be considered in all adults of any age who are overweight or obese (BMI>25kg/m^2) , and who have one or more diabetes risk factor:
    - ❖ Physical inactivity
    - ❖ First-degree relative with diabetes
    - ❖ High-risk race or ethnicity (African-American, Latino, Native American, Asian American, Pacific Islander)
    - ❖ Women who delivered a baby weighing >9 lb or who have previously been diagnosed with GDM
    - ❖ HDL-C <35 mg/dL and/or TG >250 mg/dL
    - ❖ A1C ≥5.7%, IGT, or IFG
    - ❖ Hypertension (≥140/90 or on treatment)
    - ❖ History of cardiovascular disease
    - ❖ Conditions associated with insulin resistance (Severe obesity, acanthosis nigricans, polycystic ovarian syndrome)

Pathogenesis of Pre-Diabetes

Individuals with impaired fasting glucose (IFG) have a 20–30% chance of developing diabetes over the next 5–10 years[17, 18]. The risk is even greater if they have combined IFG and impaired glucose tolerance (IGT). Furthermore, IFG and IGT are associated with increased risk of cardiovascular events[19].

Glucose concentration begins to increase when glucose appearance exceeds glucose disappearance and continues to increase until these two rates are once again equal. In the fasting state, glucose appearance is determined by the rate of glucose release from the liver with perhaps a small contribution by the kidney. Together, these processes are referred to as endogenous glucose production (EGP). The situation is more complex following food ingestion when glucose appearance equals the sum of EGP and the rate of appearance of the ingested glucose[20]. When considered in the light of the prevailing glucose and insulin concentration, EGP is increased in individuals with mild and severe type 2 diabetes.

Weyer et al. are the only investigators who have measured EGP in individuals with IFG. Fasting EGP was increased in Pima Indians with IFG, regardless of whether they had NGT or IGT. In contrast, fasting glucose production was not elevated in Pima Indians with IGT and NFG concentrations. Fasting insulin concentrations were elevated in those subjects, this implies the presence of hepatic insulin resistance. Glucose and insulin suppress glucose production and enhanced insulin secretion can potentially compensate for a defect in insulin action, hepatic insulin resistance does not necessarily mean that excessive EGP is the cause of postprandial hyperglycemia in individuals with IFG and/or IGT. Conversely, effective compensation via these mechanisms could normalize postprandial suppression of EGP, thereby enabling some individuals with IFG to maintain normal postprandial glucose concentrations.

IMPAIRED GLUCOSE TOLERANCE

Normal fasting plasma glucose is <100 mg/dl (<5.6 mmol/L) or a 2-h plasma Glucose in response to a 75-g oral glucose tolerance test (OGTT) of <140 mg/dl (<7.8 mmol/L). IGT is recognized as an intermediate level of post-prandial glucose that carries essentially no risk for microvascular complications[21].

It is diagnosed exclusively by OGTT; the 2-hour plasma glucose is 140 to 199 mg/dl (7.8 to 11.0mmol/L). According to recent NHANES (National Health and Nutrition Examination Survey) data[22], overall IGT prevalence in U.S. adults <20 years of age is 13.8%. The prevalence rises progressively with age.

In the European DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) study, IGT rose from 2.90/0 in 30 to 39 year-old men to 15.1 % in 70 to 79 year-old men[23].

One disadvantage of testing for IGT is the necessity for OGTT another is that the results are not reproducible. Nonetheless, it is a relatively strong, albeit variable, predictor of Type 2 diabetes[24]. A predominant metabolic characteristic is insulin resistance in muscle, which exists along with defective insulin secretion[25].

In most Western countries, conversion rates for isolated IGT range from 4.35% to 6.35% per year[26]. In the DPP (Diabetes Prevention Program) study, in which IFG also was common, conversion to diabetes, was approximately 10% yearly[27].

IMPAIRED FASTING GLUCOSE

IFG was introduced by the ADA in 1997 to classify fasting plasma glucose levels of 110 to 125 mg/dl (6.1 to 7.0mmol/L) [28].

By these criteria, the estimated U.S. prevalence of IFG in adults >20 years of age was approximately 6.9%[29]. In 2003, the ADA changed its definition of IFG from a fasting level of 110 to125 mg/dl to 100 to 125 mg/dl[29]. The rationale for the ADA's change was several-fold. First, glucose levels of 100 to 110 mg/dl carry higher risk for diabetes compared with normoglycemia. Second, receiver-operator characteristic analysis of several studies found that 100 mg/dl is a threshold level of fasting glucose that maximizes sensitivity and specificity for predicting diabetes. Third, the expert committee postulated that reducing the threshold for IFG would make the prevalence of IFG and IGT concordant.

However, the latter did not work out. Prevalence of IFG in the United States after lowering the threshold jumped from 6.9% to 25.7%, which was double the 12.9% for IGT[22].

Ethnic breakdown for IFG prevalence showed 21.1 % in non-Hispanic blacks, 25.1% in non-Hispanic whites, and 26.1 % in Mexican Americans. Other populations had similar increases after this change in IFG definition, for example, from 11.8% to 37.6% in Denmark and from 10.6% to 37.6% in India[15]. There have been 2 major criticisms of the ADA's change in definition of Pre-diabetes based on fasting glucose levels.

GLYCATED HEMOGLOBIN (HbA1c)

In 2009, an expert committee organized by the ADA, the International Diabetes Federation, and the European Association for the Study of Diabetes[30] recommended that HbA1c become an alternative to plasma glucose for diagnosing Type 2 diabetes. Advances in the measurement of HbA1c and growing evidence of its association with plasma glucose underlie this recommendation.

HbA1c gives a better measure of overall glycemic exposure and likely risk for long-term complications. There is no need for fasting or timed samples and HbA1c is less affected by conditions to produce perturbations in glucose levels. Moreover, it is a better guide to clinical management of patients. For these reasons, it is likely that HbA1c will become a standard approach to the diagnosis and clinical management of Type 2 diabetes. For the diagnosis of diabetes, the expert committee recommended an HbA1c threshold of 6.5%. Whether HbA1c can also be used to identify pre-diabetes is an important question. The WHO expert committee advised against its use for this purpose, citing lack of sufficient evidence[15].

The ADA/International Diabetes Federation/European Association for the Study of Diabetes expert committee was noncommittal; it speculated on a range of 6% to 6.5%, but did not recommend it. The ADA proposed a Pre-Diabetes range of 5.7% to 6.4%[16], which accords with updated NHANES data[31].

Pre-Diabetes and the metabolic syndrome

An elevated glucose level is one component of the current consensus definition of the metabolic syndrome[32, 33]. Others are abdominal obesity, elevated blood pressure, elevated triglycerides, and reduced high-density lipoprotein (HDL) cholesterol. Any 3 of these 5 components confer a diagnosis of the syndrome.

Most individuals with the metabolic syndrome have abdominal obesity. Excess adipose tissue releases excess fatty acids and a variety of adipokines that seemingly elicit metabolic risk factors that predispose to both diabetes and CVD[34]. To manifest the syndrome in obese persons, one must also have metabolic susceptibility; the latter in turn can be conferred by other factors (e.g., genetics, physical activity, and drugs). Many investigators believe that insulin resistance mediates all the metabolic risk factors of the metabolic syndrome[35]. The role of insulin resistance in causing hyperglycemia is well established, but whether insulin resistance per se elicits dyslipidaemia and hypertension is uncertain. Regardless, most persons with the metabolic syndrome are insulin-resistant[36].

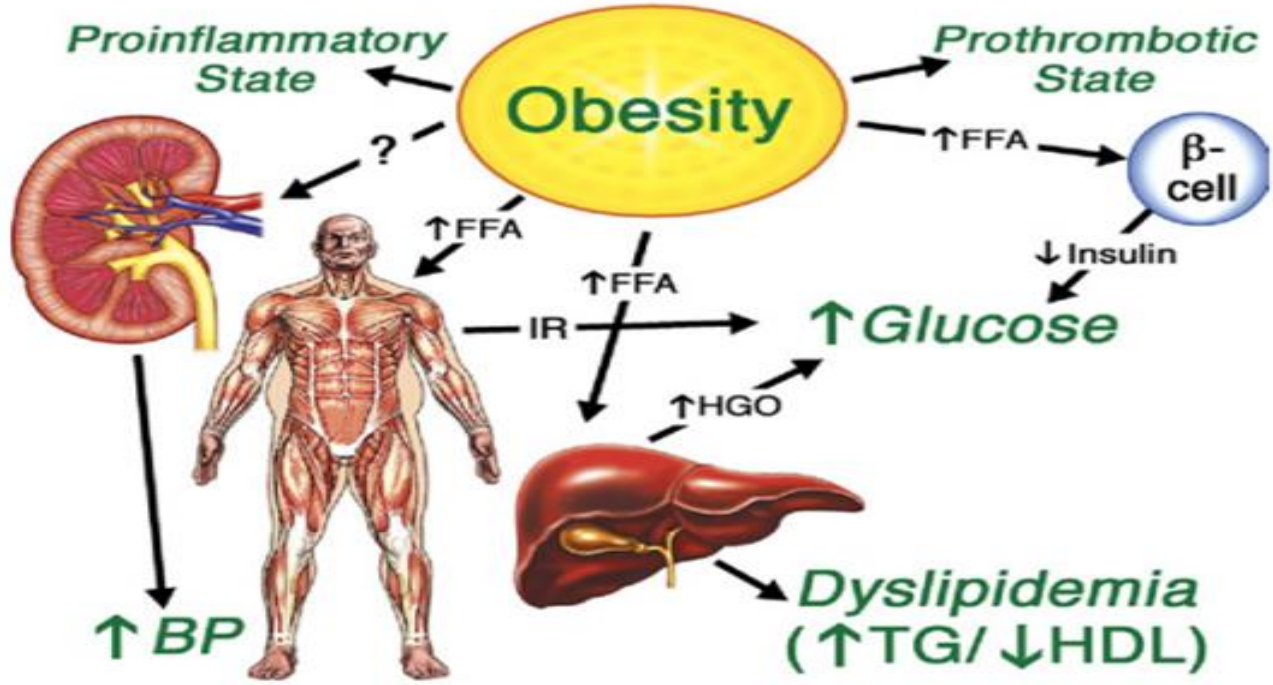
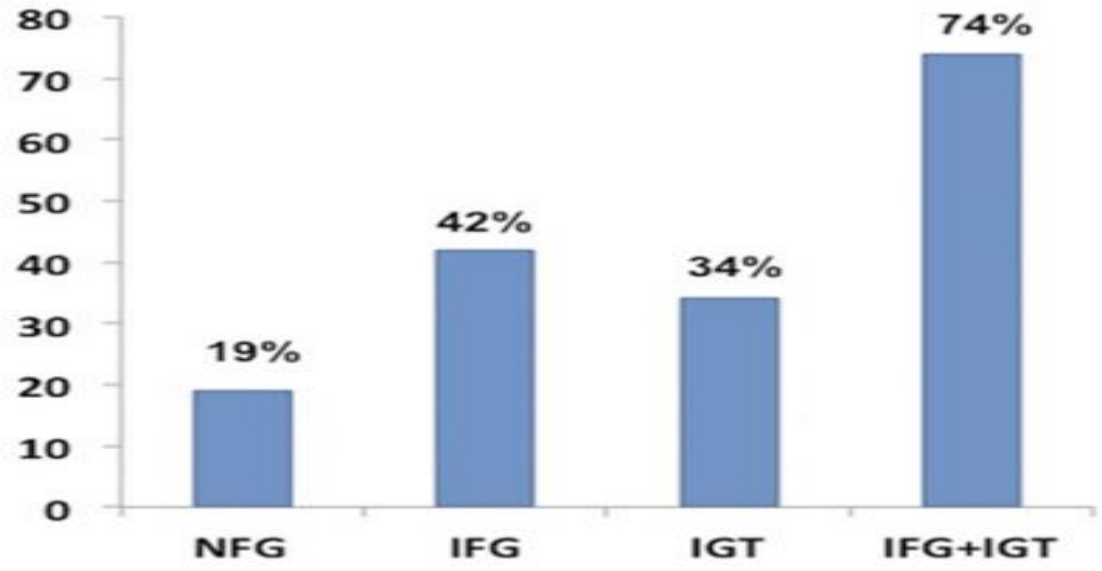


Figure1 : Metabolic Pathways Underlying Pre-Diabetes and Metabolic Syndrome



Graph 1: Prevalence of Metabolic Syndrome in Different Categories of Pre-Diabetes in an European Population[37]

Goals for Pre-Diabetes Intervention

The major detrimental outcomes in persons with prediabetes are macrovascular diseases and type 2 diabetes, and the leading contributors to microvascular disease.

Macrovascular disease occurs both before and after onset of diabetes, whereas microvascular disease occurs almost exclusively several years after conversion to diabetes.

Prevention of Macrovascular Disease

Persons with pre-diabetes have metabolic syndrome, which undoubtedly is a risk factor for macrovascular disease. Moreover, prediabetes increases with age, and aging itself is accompanied by increased risk. Therefore, it is reasonable to intensively intervene on all CVD risk factors in patients with prediabetes.

First-line management is lifestyle intervention: weight reduction in obese subjects, reduced intakes of dietary saturated and trans-fatty acids, cholesterol, and sodium, and increased physical activity. The use of drugs to control CVD risk factors likewise deserves consideration. Targets of therapy include dyslipidemia, hypertension, and prothrombotic factors.

The prime lipid targets are atherogenic lipoproteins—low-density lipoprotein (LDL) and very LDL. In patients with CVD plus metabolic syndrome, LDL cholesterol levels should be reduced to <70 mg/dl, and LDL + very LDL cholesterol (non-HDL cholesterol) to <100 mg/dl. Statins are first-line drugs to achieve these reductions. If these goals are not attained with a statin, a second-line LDL-lowering drug can be used: nicotinic acid, bile acid

sequestrant, or ezetimibe. If CVD is not present, goals are an LDL cholesterol <100 mg/dl and a non-HDL cholesterol <130 mg/dl. In most patients, a statin alone usually is sufficient to achieve this goal.

Blood pressure should be lowered to <130/<85 mm Hg, and preferably to <120/<80 mm Hg. Any of the standard blood pressure–lowering drugs (e.g., angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, calcium blockers, diuretics, beta-blockers) can be employed. Drugs like beta-blockers and higher doses of thiazide diuretics raise glucose levels and predispose patients to conversion to diabetes[38].

Prevention of Microvascular Disease:

The only way to prevent (or delay) microvascular disease in patients with pre-diabetes is to prevent (or delay) the development of diabetes. Unfortunately, there is no proven way to prevent the decline in beta cell function in persons destined to have diabetes. Therefore, priority must be given to reducing insulin resistance. This is best achieved by lifestyle intervention—weight reduction and increased physical activity. The DPP[24] demonstrated the efficacy of this approach. The DPP found that metformin therapy also could delay conversion of pre-diabetes to diabetes in about 40% of subjects. This has led to a recommendation on the part of some diabetologists for the use of metformin in persons with IFG plus IGT and other metabolic syndrome risk factors[27].

Public Health Prevention:

The public at large is increasingly concerned about the diabetes epidemic. Most people know relatives or friends who have diabetes so that they have first handed knowledge of the suffering imposed by this chronic disease. Therefore, when a person is told that he or she has Pre-diabetes, this person's concern is usually increases substantially. This provides an incentive for effective intervention. It further offers the opportunity to detect the metabolic syndrome, which carries greater risk for macrovascular CVD.

Use of the concept of Pre-diabetes can be useful tool for intervention to prevent both macrovascular and microvascular disease.

Atherosclerosis

HISTORICAL REVIEW

- The phenomenon of thickening of arteries is known since the age of Egyptian Mummies
- 1449-1519- Leonardo Da Vinci described thickening of tunica of blood vessels in aged people
- Rokinstansky proposed the incrustation theory for pathogenesis of atherosclerosis
- 1904-Marchanintroduced the term atherosclerosis
- 1957-proposed that Intimal thickening results from fibrin deposition with subsequent organisation of fibroblast and secondary accumulation of lipids
- 1979- Garret etal proposed that monocyte accumulation in Sub-endothelial space was responsible for formation of fatty streak.
- 1985- Daves etal proposed that plaque fissuring with thrombosis as the cause of acute coronary syndrome

Atherosclerosis derives its name from the Greek words ‘sclerosis’ meaning hardening and ‘athere’ meaning gruel (accumulation of lipid). Atherosclerosis remains the major cause of death and premature disability in developed societies. Current predictions estimate that by the year 2020 cardiovascular diseases, notably atherosclerosis, will become the leading global cause of total disease burden.

Atherosclerosis of the coronary arteries commonly causes myocardial infarction (MI) and angina pectoris. Atherosclerosis of the arteries supplying the central nervous system frequently provokes strokes and transient cerebral ischemia. In the peripheral circulation, atherosclerosis causes intermittent claudication and gangrene and can jeopardize limb viability. Involvement of the splanchnic circulation can cause mesenteric ischemia. Atherosclerosis can affect the kidneys either directly (e.g., renal artery stenosis) or as a common site of atheroembolic disease.

The presence of diabetes increases the risk of CVD beyond that seen with the metabolic syndrome alone[39] strong epidemiology evidence supports an association between glycemic control and CVD risk[40].

The United Kingdom prospective diabetes study (UKPDS) provided additional insight into the relationship between glycemic control and CVD in patient with Type 2 diabetes, indicating a linear relationship between HbA1c and CVD endpoints, particularly myocardial infraction[41].

High glucose concentrations have been shown to lead to diacylglycerol accumulation and protein kinase C activation in vascular cells, and to increased glucose flux through the aldose reductase pathway. These pathways have been linked to increased inflammation via increased nuclear factor K-B activation.

Pathogenesis of atherosclerosis

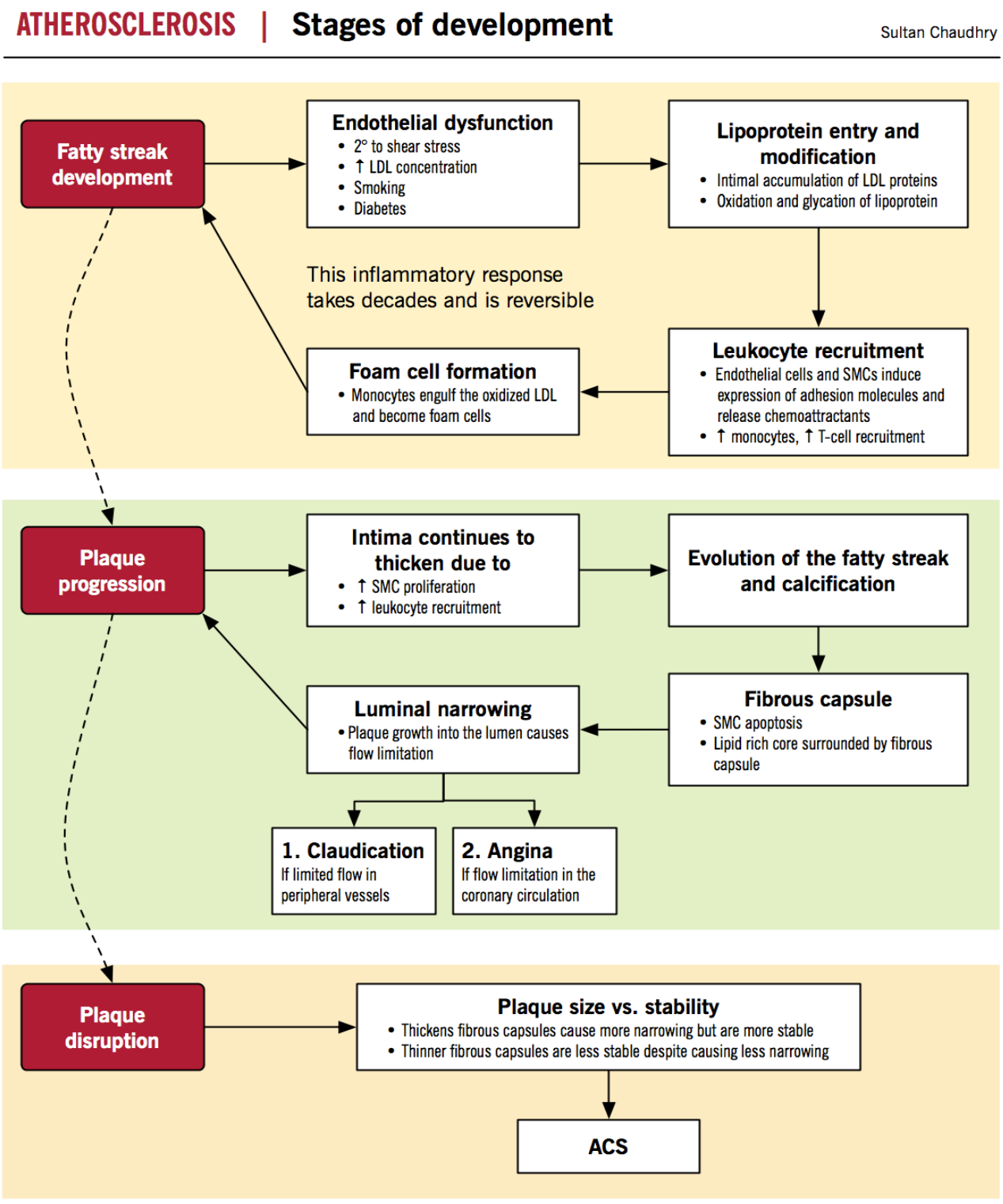


Figure 2: stages of atherosclerosis

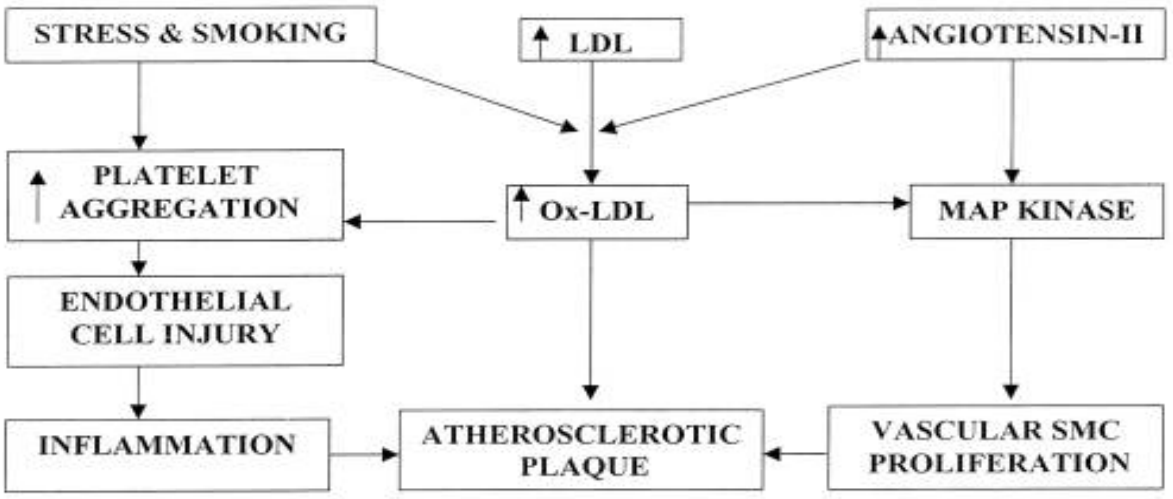


Figure 3: Schematic design depicting the involvement of oxidized low density lipoprotein (oxLDL), injury of endothelial cells and proliferation of vascular smooth muscle cells (SMC) in the development of atherosclerotic plaque. MAP Mitogen-activated protein

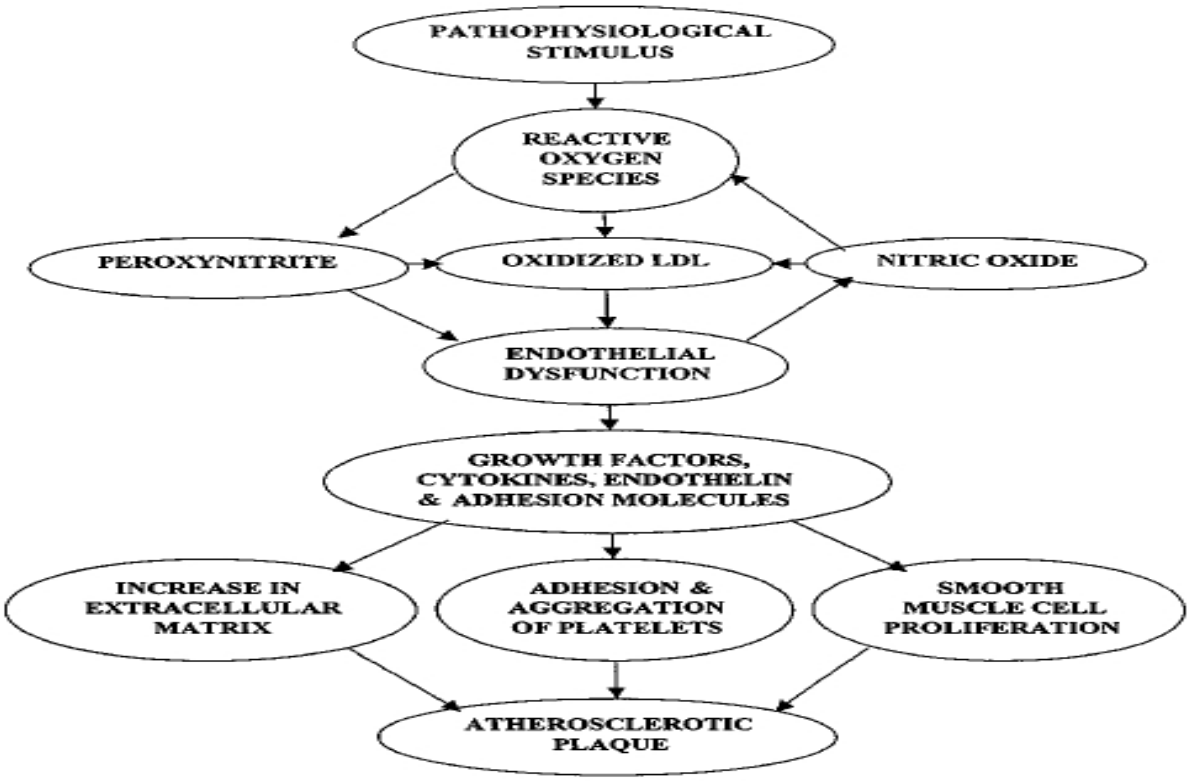


Figure 4: Schematic diagram depicting the involvement of reactive oxygen species, endothelial dysfunction, growth factors, cytokines and adhesion molecules in the genesis of atherosclerosis. LDL Low density lipoprotein

CAROTID INTIMA MEDIA THICKNESS (CIMT)

The burden of coronary artery disease (CAD) continues to rise globally, as developing nations, including India, are adopting to lifestyle changes with predisposition to cardiovascular diseases (CVD).[42]

In India, incidences of CAD have doubled over the last three decades. By 2015, CVDs alone would amount to 1.5 million deaths, including 34% of male and 32% of female global deaths.[43]

According to a study, presence of modifiable risk factors account for more than 90% of the (CV) risk. Their presence cannot always be interpreted as the presence of atherosclerotic heart diseases, nor their absence guarantees atherosclerotic lesion-free arterial tree.[44]

Atherosclerosis, the precursor of CV events, keeps progressing insidiously without symptoms, afflicting large sections of arterial tree including carotid and coronary arteries. Hence, increasing the population awareness about factors causing CVD and recognizing novel screening modalities to evaluate subclinical atherosclerosis is of paramount importance for prevention of CAD, stroke, and peripheral vascular disease.

DEFINITION:

CIMT is defined as the area of tissue starting at the luminal intimal interface and the media adventitia interface of CCA. Since B-mode (bright-mode) ultrasonography is a safe, non-invasive, and cost-effective to measure CIMT, a recent study more precisely defined CIMT as the double-line pattern visualized by B-mode vascular ultrasound formed by two parallel echogenic lines representing junction of the vessel lumen with intima and media-adventitia interface.[44]

In 1986, Pignoli and colleagues[45] for the first time reported ultrasound imaging to measure IMT of carotid arteries.

In 1991, Salonen and colleagues[46] showed for the first time the in vivo use of ultrasound imaging for the evaluation of atherosclerotic changes in the carotid arteries. They demonstrated close histological relationship between coronary, Cerebral and carotid atherosclerotic diseases. Since then, the ultrasonographic assessment of easily accessible arteries has become a surrogate marker for evaluation of less accessible vessels such as coronary and cerebral arterial system.

Ultrasound imaging provided information on IMT, the presence and type of plaque, calcification and wall diameter. These information enabled assessment of presymptomatic lesion, atherosclerotic burden, and reduced death and disabilities from CVD.

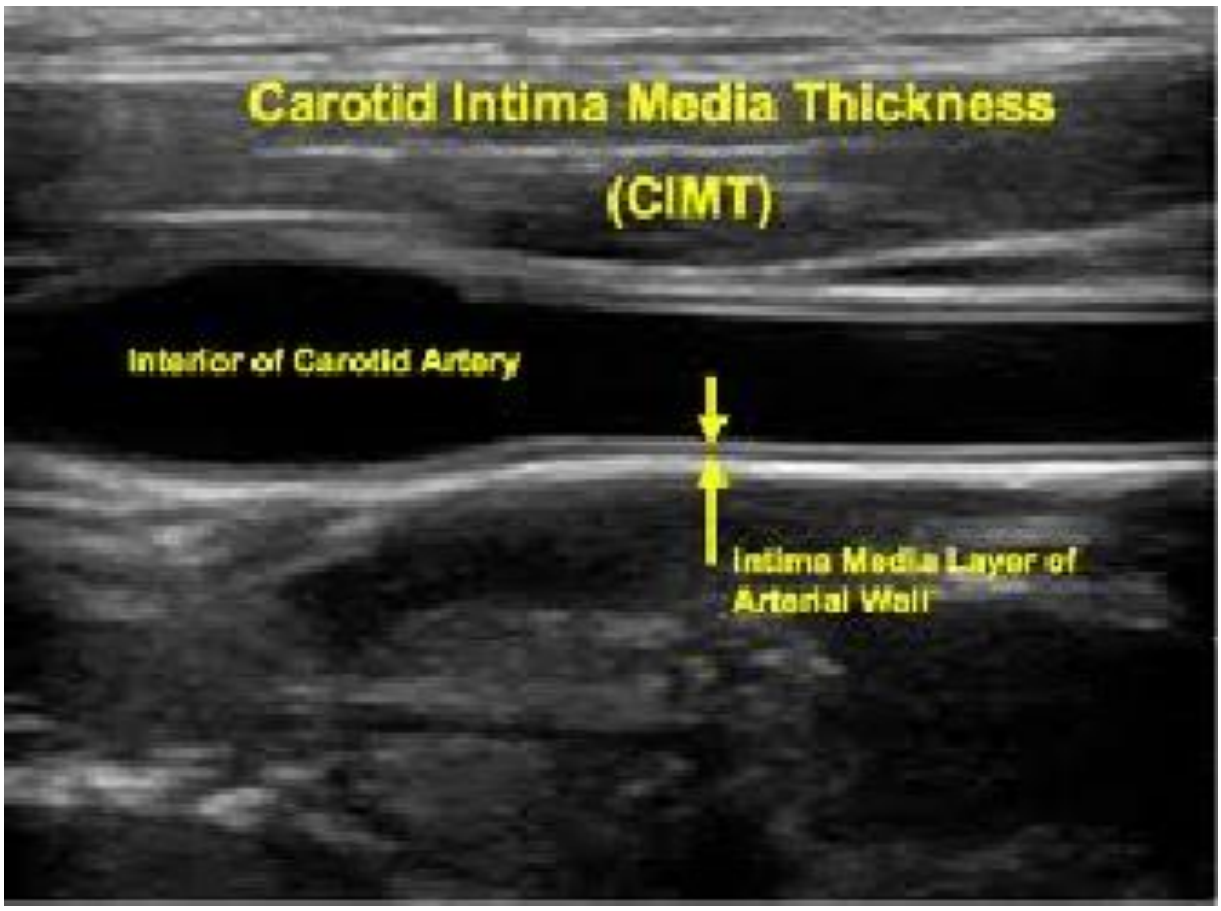


Figure 5: B mode Ultrasound of common carotid artery

GUIDELINES FOR CIMT MEASUREMENT

The American Society of Echocardiography (ASE) in a consensus statement has standardized the technique for CIMT assessment.[48] The current guidelines recommend the use of state-of-the art linear-array ultrasound transducers that can operate at a fundamental frequency of at least 7 MHz to scan carotid arteries. Depending on scanning protocol, the specific predetermined bilateral sites in the vicinity of carotid bifurcation are selected for taking CIMT measurements.

Other segments of the carotid artery used for CIMT measurements are CCA and the internal carotid artery (ICA), CIMT of the CCA has better reproducibility than ICA or carotid bifurcation due to its ease of access and proximity to the surface and runs relatively parallel to the skin.

The patient lies supine, with their neck a little extended by placing a pillow under their shoulders. The patient should be comfortable and excessive extension of the neck should be avoided. Some patients may not be able to lie supine; if this is the case they can usually be examined adequately in a sitting position. The examiner can sit beside the patient's thorax and scan the neck from this position, or sit at the patient's head and scan the neck from this location.

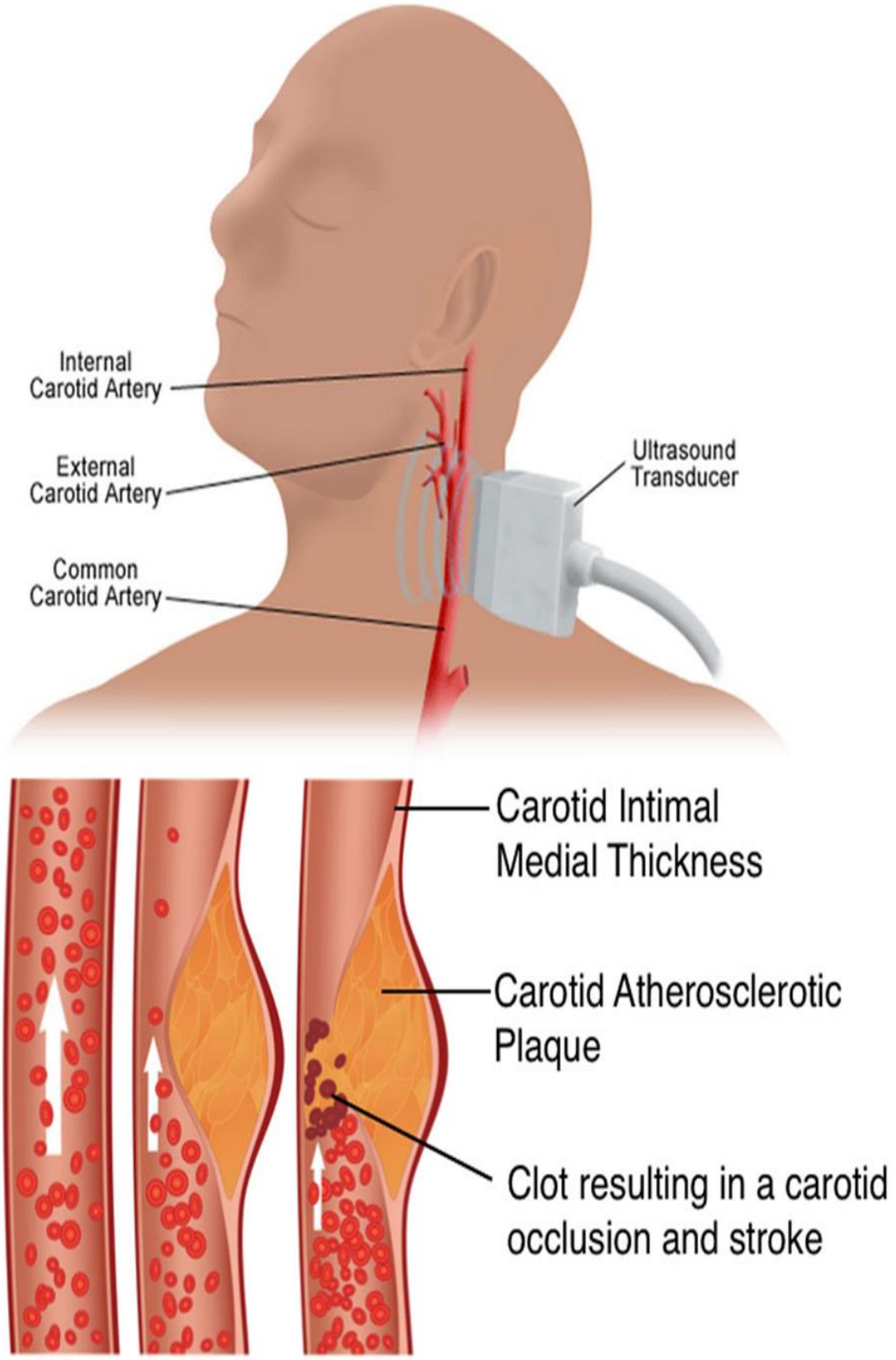


Figure 6: method of carotid artery intimal thickness measurement and atherosclerotic changes in the vessels

A high-frequency transducer (7–14 MHz) is used and the examination starts with a transverse scan of the carotid artery from as low in the neck as possible, to as high in the neck as possible behind the angle of the mandible. This approach will allow the depth and course of the vessels to be ascertained, together with the level of the bifurcation and the orientation of its branches.

Colour Doppler is then activated and the vessels are examined in the longitudinal plane, again from the lower neck upwards. Areas of abnormal flow are identified with colour Doppler, an initial assessment of their significance is made and the need to undertake a spectral examination can be considered.

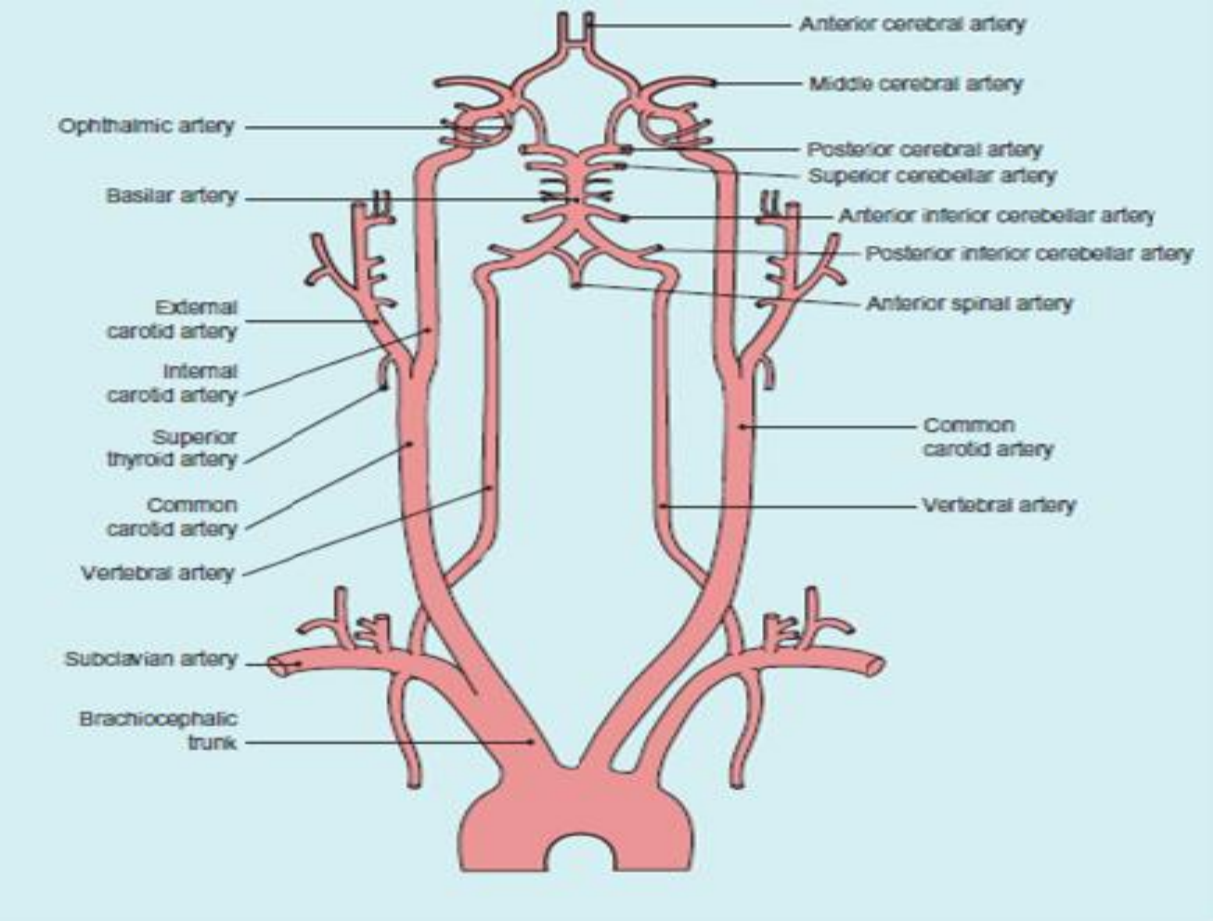


Figure 7:Carotid and vertebral arteries.

Identification of the Internal and External Carotid Arteries

The common carotid artery on the right arises from the brachiocephalic artery behind the right sternoclavicular joint, where the origin can usually be seen on ultrasound. On the left it usually arises directly from the aorta, so that its origin on the left cannot be seen on scanning from the neck. The level of the carotid bifurcation is usually at about the level of the upper border of the laryngeal cartilage but it may vary.

THE EXTERNAL CAROTID ARTERY

- Branches present
- Anterior position
- Waveform characteristics:
  - ✓ High resistance pattern with relatively little diastolic flow
  - ✓ Appears more pulsatile on colour Doppler
  - ✓ Dicrotic notch is more prominent
- Positive ‘temporal tap’

THE INTERNAL CAROTID ARTERY

- The other branch of the bifurcation
- Bulb at origin
- Posterior position and course angled posteriorly
- Less pulsatile waveform on colour Doppler with relatively high diastolic flow

Optimization of images is done by adjusting patient's neck position especially in anterior scanning planes, an rolled towels are given under neck and legs for comfort, with the use of external landmarks such as the Meijer arc or similar device, transducer angle standardized. The six values of mean CIMT (three on each side) are obtained and averaged to get mean CIMT.[49]

Reliance on a single absolute threshold abnormality will result in under-detection of diseases in younger individuals and over-detection in older individuals.[50]

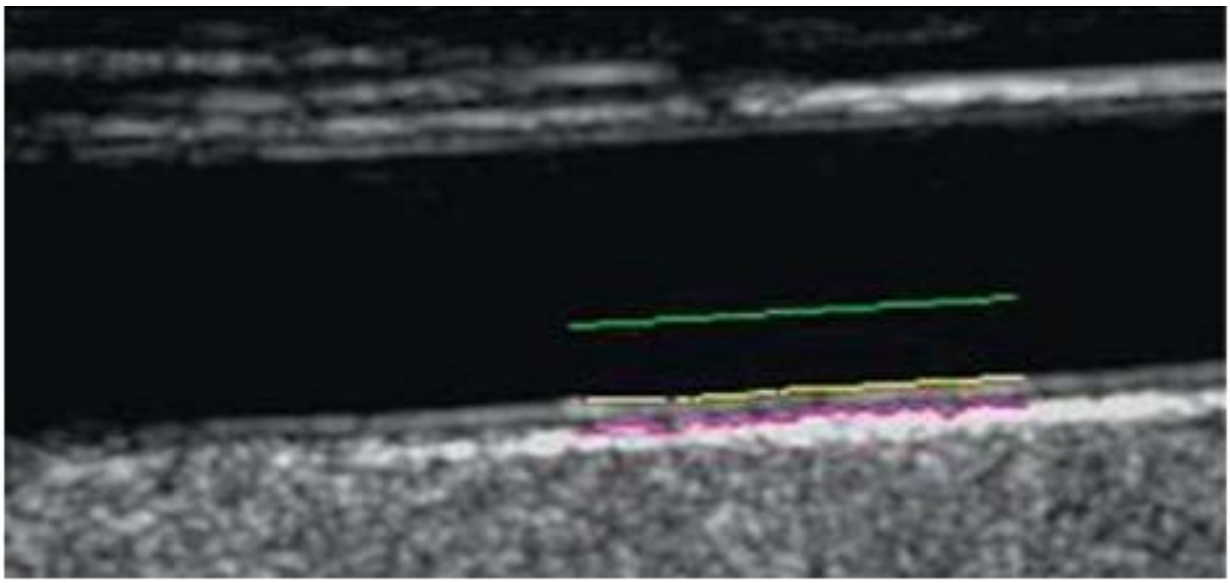


Figure 8 . Intima-media thickness (IMT) definition – IMT is measured as the distance between lumen-intima (yellow line) and media-adventitia (pink line) interfaces.

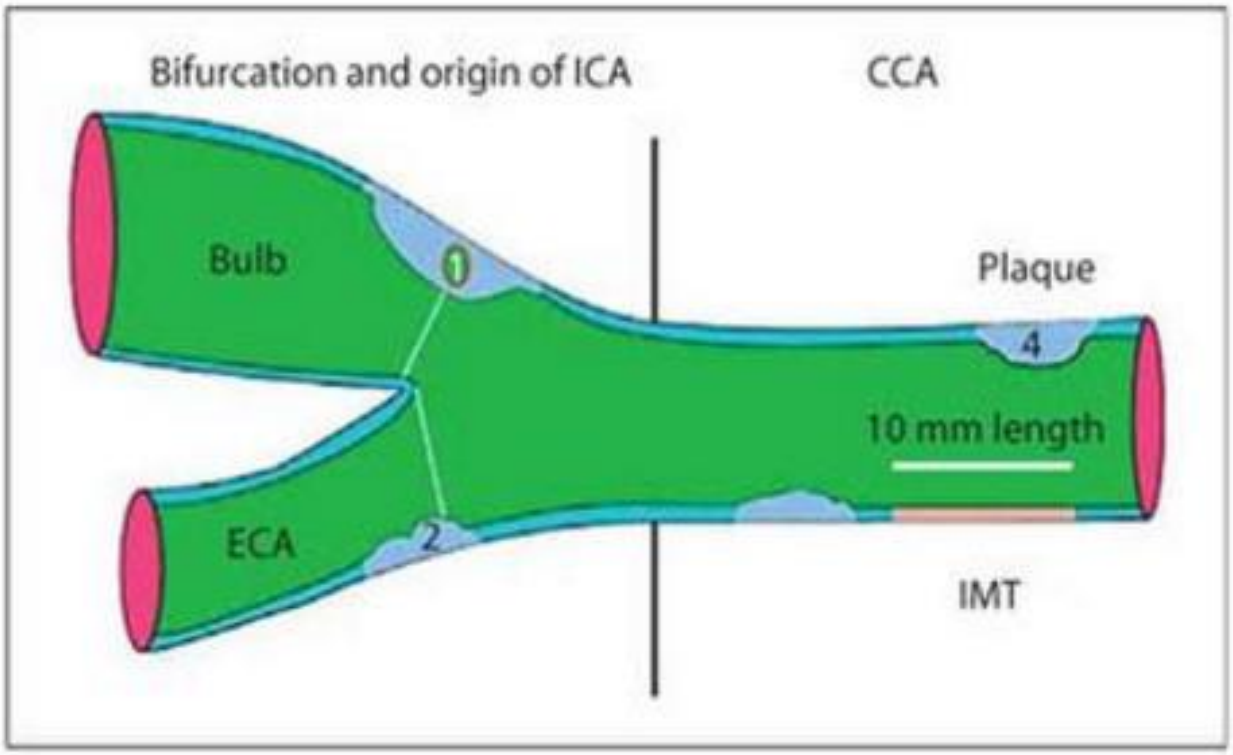
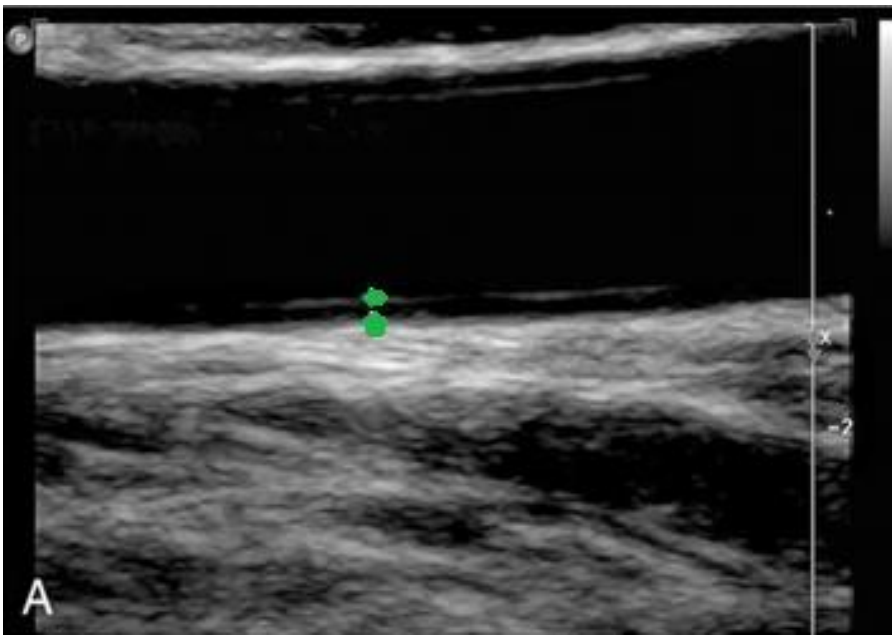
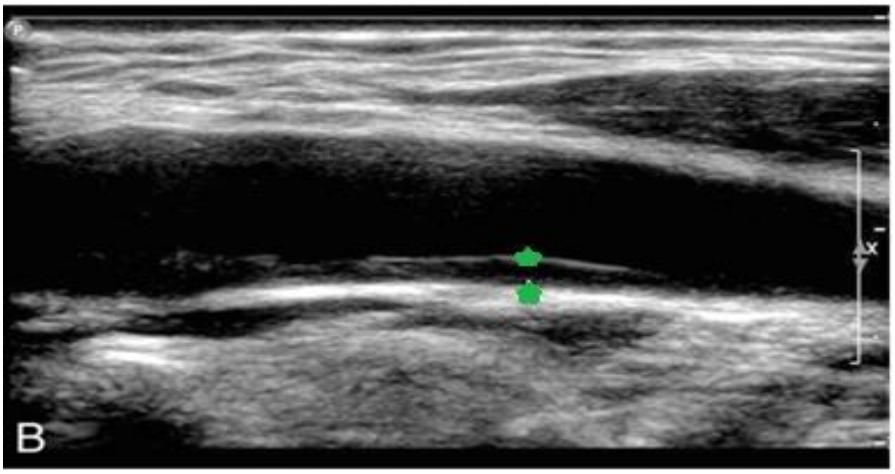


Figure 9 : Proper location for IMT measurement

(A) A normal intima-medial thickness (IMT) of 0.7 mmmeasured in the upper common carotid artery.



(B) Moderate thickening of the IMT at 1.2 mm



(C) More marked intimal thickening of 1.4 mm.

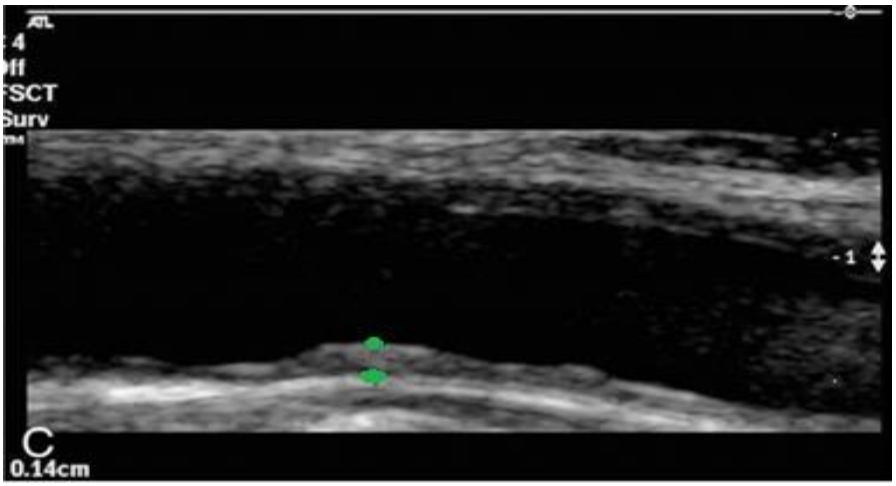


Figure 10: Doppler images showing various changes in CIMT

In healthy middle-aged adults, CIMT values between 0.6 and 0.7 mm have been considered normal, while CIMT of 1 mm or more has been associated with significant increased absolute risk of CHD.[51]

In healthy Indian adults, the average and maximum CIMT values reported were 0.67 and 0.70 mm, respectively.[52] The measurement of CIMT varies with age and values> 1.0 mm are considered abnormal in younger population and confer increased absolute risk of CHD.[50,53]
In a cross-sectional study, apparent age-related increase in common CIMT was observed in both the genders (approximately 0.010 mm/year in seemingly healthy men and ~0.014 mm/year in seemingly healthy women), whereas it is 0.010 mm for both genders in the ICA. Patients with known CAD had three times higher rate of CIMT progression than patients without known CAD (0.030 mm/year vs. 0.010 mm/year, respectively).[54]

According to the ASE guidelines, [48] patients at intermediate CVD risk [Framingham Risk Score (FRS) 6%-20% without established coronary heart disease (CHD)], peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm) were the potential candidates for CIMT measurement.

The carotid plaque was identified by ultrasound to refine CVD risk assessment. Other patient categories that were considered for CIMT measurement and carotid plaque detection included

1. Patients with family history of premature CVD in a first-degree relative (men less than 55 years old, women less than 65 years old)
2. Patients with severe abnormalities in single risk factor (e.g., genetic dyslipidemia) aged less than 60 years who otherwise would not serve as the candidates for pharmacotherapy
3. women aged less than 60 years old with at least two CVD risk factors

The present consensus on echocardiography reported CIMT values >/=75th percentile as the upper limit of normal across age, gender, race/ethnicity, and served as the indicators of increased CVD risk. CIMT values increase with age and are generally more in men than women. Thickness of CIMT has been reported to be the highest in African Americans, least in Hispanics, and intermediate in Whites.[50]

In 2010, Liviakis et al. also supported recommendation of the ASE guidelines to use CIMT in 75th percentile as the upper cut-off limit.[45] Patients with these elevated CIMT values were considered for aggressive treatment for atherosclerosis. The CIMT values between 25th and 75th percentiles were considered as average and indicative of unchanged CVD risk.

At these CIMT values, physicians might consider treatment initiation. The guidelines suggested that patients with CIMT values </= 25th percentile may be considered to have lower CVD risk. But lowering treatments than standard care in such patients remained to be confirmed, and therefore recommended reporting of these broad levels of risk based on CIMT values.[48]

A strong correlation between incident CVD and increasing CIMT has been reported in the age group of 42-74 years. But comparatively strong relationship between increasing risk factor burden, emerging risk factors, and CIMT has been observed in young adults aged 18-42 years.

The finding of the Carotid Atherosclerosis Progression Study with 2436 individuals younger than 50 years reported that CIMT predictive value for future vascular events was at least as high in younger subjects as in older subjects, and the relative risk associated with the increased CIMT was considerably higher in individuals younger than 50 years[55].

CIMT FOR PREDICTION OF CV RISK

In 2004, Kablak-Ziembicka et al.[56] reported a correlation of CIMT and extent of CAD in 558 consecutive patients with mean age of58.8 years. They showed that there was an increase in CIMT as the CAD progressed and patients with CIMT value of 1.15 mm had 94% higher risk of CAD. Every 0.1 mm increase of CIMT was reported to increase the risk of myocardial infarction (MI) by 11%.

CIMT for monitoring response to therapy:

Atherosclerotic vascular changes are known to precede cardiovascular death and disability. CIMT has gradually become a choice among clinician for detection of subclinical or accelerated atherosclerosis disease by virtue of being cheap and unsophisticated.

In clinical practices it was reported to be useful in evaluating the effectiveness of prevention therapy.[57]Hence, clinicians may make therapeutic decision based on CIMT reports. Lifestyle changes, including smoking cessation, regular exercise, healthy diet choices, and weight loss have been observed to profoundly influence initiation, development, and progression of atherosclerosis.

The landmark study reporting the influence of lifestyle changes on atherosclerosis progression was Monitored Atherosclerosis. Regression Study which directly correlated various lifestyle modifications with annual reduction of CIMT.[48]

The CIMT progression was annually reduced by 0.065, 0.0033, and 0.028 mm after reduction of body weight index by 5 kg/m2, dietary cholesterol intake by 100 mg/day, and quitting smoking by10 cigarettes/day, respectively. Cumulatively, changes in these lifestyle measures had led to an annual decrease in CIMT by 0.13 mm.[56, 58]

However, CIMT progression rate in obese controls subjects was three times higher than in lean subjects. This study importantly highlighted the role of weight reduction on retardation of atherosclerosis progression.[59]

In 2003, Wu et al.[60] reported the relationship between progression of atherosclerosis and dietary intake. They showed that progression of CIMT was retarded with intake of pectin (a viscous fiber) and with increased physical activity.[60, 61]

In a recent review, Cobble and Bale suggested CIMT to be an important tool for day-to-day clinical practice to detect CV risk in patients and also that laboratory reports of CIMT would act as motivator for patients to reduce CV risk.[58]

ADVANTAGES OF CIMT

- CIMT can be used repeatedly and reproducibly with no adverse effects on the patients. It can be performed noninvasively with no risk of vessel dissection, vessel closure, or coronary spasm

- CIMT scanning protocol can detect atherosclerotic diseases in early and asymptomatic stages

- CIMT directly visualizes vasculature unlike indirect biomarkers such as low- density LDL-C or even the more advanced biomarkers like high-sensitivity C-reactive protein or lipoprotein-associated phospholipase A2 (Lp-PLA2)

- CIMT with plaque interrogation can be performed in any basic ultrasound ambulatory setting with favorable speed and cost factors

- CIMT can be easily quantified via automated boundary detection software, and the carotid interrogation is radiation free and thus safer than other imaging tests such as coronary calcium scoring or CT-CAG

- CIMT allows for observation of the arterial wall, the actual site of the atherosclerotic disease, rather than the lumen

- CIMT is not dependent on calcification of the plaque as assessment tools such as coronary artery calcification score.

CHALLENGES OF CIMT TESTING

There are also a few shortcomings of this procedure; however, some of them were resolved.[62,63]

- There is no standardized protocol for measurement of CIMT, which might lead to inaccurate estimation of the progression and regression of the CIMT during the follow-up studies or in the evaluation of any therapeutic intervention on the measured CIMT

- Resolution: Implementation of edge detection software programs improved reproducibility and reduced reader variation[64]

- Different portions of the carotid artery have been used to measure the CIMT, common carotid, bifurcation, internal carotid, and combined CIMT, which may influence the value of the measured CIMT

- Resolution: Iglesias del Sol and colleagues measured CIMT at the common carotid, bifurcation, internal carotid, and combined CIMT, and they found that all the measurement sites had the same ability to predict future cardiovascular events[65]

- Measurement of CIMT involves a combined measure of the intimal and medial layers of the arterial wall, whereas the atherosclerotic process is restricted in the intimal layer, particularly in its early phase and CIMT is only an indirect assessment of the

possible atherosclerotic burden in the coronary arteries, as in CIMT, carotid arteries and not coronary arteries are visualized since CAD is the commonest cause of cardiovascular related death. The detection of atherosclerosis in the carotid by CIMT may not represent atherosclerosis in coronary arteries

- Resolution: In a systematic review, Bots and colleagues reviewed 34 studies on the relationship of CIMT to coronary atherosclerosis. Thirty of these studies showed a modest positive relationship, the magnitude of which was similar to that found in autopsy studies. The modest relationship between CIMT and coronary atherosclerosis most likely reflects variability in atherosclerosis development between the vascular beds rather than limitations of CIMT measurements.

CIMT IN INDIAN CLINICAL SCENARIOS

Asian Indians have been an ethnically vulnerable race for developing metabolic syndrome and diabetes, both of which are well known contribution to the pathogenesis of atherosclerosis vascular disease[65].The subclinical diabetes is reported as an important vascular risk for Asian Indians[66].

Atherosclerosis is known to develop in patient of hypertension, chronic autoimmune vasculitis or arthritis, polycystic ovarian syndrome, and in patient receiving dialysis. Several studies on Indian population have reported various clinical scenarios using CIMT as endpoints of the study.[51,66,67]

In 2003, Hansa et al.[68] reported association of CIMT with CAD and CV risk factors in the Indian population which included 101 patients with established CAD, and 140 control subjects with no CAD.CIMT as measured at three predefined sites (carotid bifurcation, CCA, and ICA) on each side was significantly higher in the coronary disease group compared to the controls. The results of this study indicated that increased values of average and maximum CIMT were significantly associated with the presence of CAD and this association was independent on the presence of other conventional CV risk factor.[52]

The Chennai Urban rural Epidemiology Study (CURES-2), an epidemiological study published in 2004, reported association of CIMT and arterial stiffness with retinopathy in Asian Indians who were at high risk group for diabetes and CAD[69],The data from the study showed an association between early atherosclerosis and diabetes retinopathy in urban south Indian population.

A prospective study in 2006 reported efficacy of CIMT in predicting the prevalence of CAD in a patient population of end stage renal disease (ESRD) using CAG as standard. The study reported that CIMT can be used as a screening tool for the evaluation of CAD in patients with end stage renal disease (ESRD), and in the absence of other risk factors, patients with IMT less than 0.75 mm may not need a pre transplant CAG.[70] The study reported higher CIMT in diabetic who had CAD, even when the CAD was not clinically overt, and suggested that the CIMT was reliable surrogate marker for subclinical CAD in diabetes patient.

In 2008, Mahajan et al.[71] published a study that was regarded as the second only Indian study examining the extent of atherosclerosis in rheumatoid arthritis (RA) patients. The study reported that RA patients had significantly greater CIMT values than age- sex-matched controls, indicating the association of RA with premature atherosclerosis.

A recent study by Madhuri et al.[72] reported relation of the CIMT with age and found a significant association between advancing age and CIMT and age is an independent risk factor for increased IMT which predicts future coronary events. The intima media thickness (IMT) of the common carotid artery measured by ultrasound imaging has been shown to be reliable and early marker of systemic atherosclerosis. Routine use of this

technique in clinical settings could improve our ability to decide on preventive therapies to reduce the risk for development of clinical.

Hansa G et al[52] .studied association between CIMT and prevalent CAD in Indian subjects and found significantly increased CIMT in patients with established CAD. There was a significant association between risk factor count and the average and maximum intima-media thickness values in the combined study population. These results indicate that raised values of average and maximum carotid intima-media thickness are significantly associated with the presence of coronary artery disease and there association is independent of the presence of other conventional cardiovascular risk factors.

Kasliwal et al [73.], association between CIMT and prevalent CAD in Indian subjects, CIMT was found to predict the presence of left main CAD with reasonable accuracy. Mean CIMT value more than 1.0mm had 92% specificity for the presence of left main CAD.[73]

A multivessel angioscopic study by Osamu kurihara et al.[74] reported relationship between prediabetes and coronary atherosclerosis - Coronary atherosclerosis and plaque vulnerability were more advanced in prediabetic than in nondiabetic patients and was comparable between prediabetic and diabetic patients. Slight or mild disorders in glucose metabolism, such as prediabetes, could be a risk factor for CAD, as is diabetes itself.

Study done by Andrea L.C. Schneide et al.[75] To examine the magnitude and types of hospitalizations among persons with prediabetes, undiagnosed diabetes, and diagnosed diabetes showed that persons with diagnosed diabetes, undiagnosed diabetes, and prediabetes are at a significantly elevated risk of hospitalization due to cardiovascular, endocrine, respiratory, gastrointestinal compared with those without diabetes hospitalizations

Due to its ease of use and reproducibility, CIMT would be the ideal choice for assessing subclinical atherosclerosis in clinical practice.

CIMT as a reliable marker of atherosclerosis and harbinger of CV risk appears to be feasible in Indian population where cost effectiveness is of paramount importance.

Ankle Brachial Index

The ankle-brachial index (ABI) is the ratio of the systolic blood pressure (SBP) measured at the ankle to that measured at the brachial artery.

Originally described by Winsor[76] in 1950, this index was initially proposed for the noninvasive diagnosis of lower-extremity peripheral artery disease (PAD).[77] Later, it was shown that the ABI is an indicator of atherosclerosis at other vascular sites and can serve as a prognostic marker for cardiovascular events and functional impairment, even in the absence of symptoms of PAD.[78,-80]

Measurement of Ankle-Brachial index

Several noninvasive techniques are used to detect limb flow or pulse volume for measuring the ABI, primarily Doppler ultrasound and oscillometric methods. The former uses a continuous-wave Doppler probe for detection of arterial flow. The SBP is determined with a pneumatic cuff, which is first inflated until flow ceases and then deflated slowly until there is reappearance of the flow signal.

The oscillometric technique is based on the assumptions that the maximum oscillations appearing during cuff deflation correspond to the mean arterial pressure.

Other methods used to measure ABI include plethysmography, photoplethysmography, auscultation, and pulse palpation. ABI is obtained by dividing ankle pressure by brachial pressure.

Interpretation of ABI-

- Normal= 1.0-1.4
- Acceptable =0.9-1.0
- Some arterial disease =0.8-0.9
- Moderate arterial disease =0.5-0.8
- Severe arterial disease =<0.5

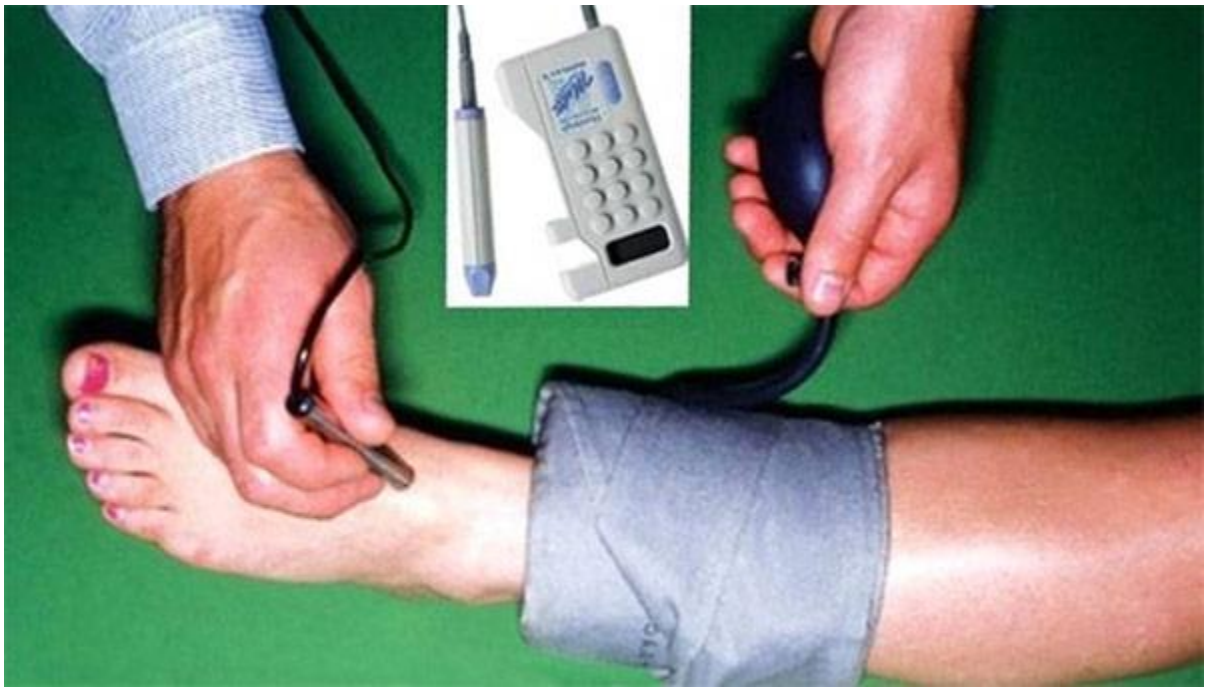


Figure 11: showing measurement of ABI in anterior tibial artery

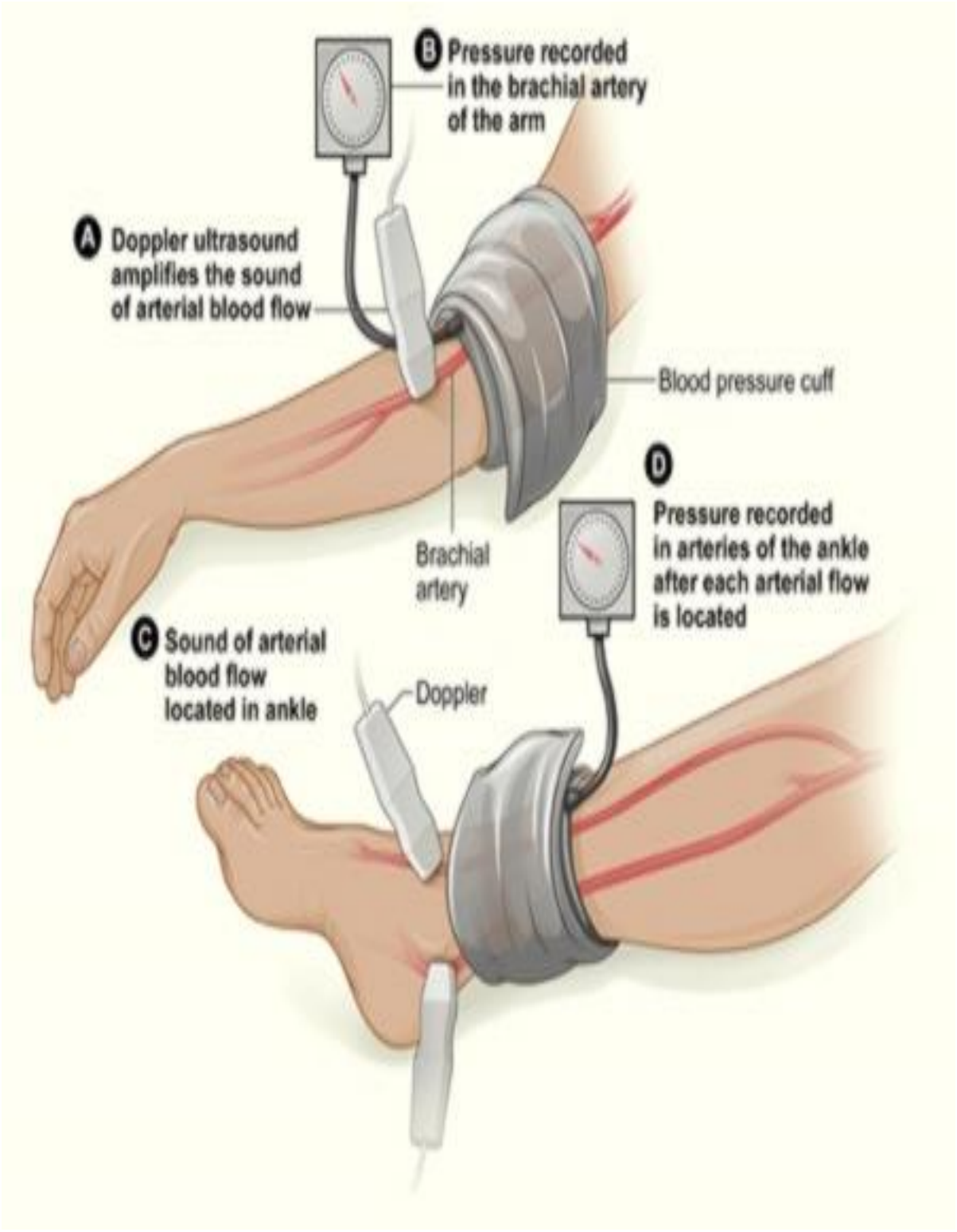


Figure12: measurement of ABI in upper and lower limbs

Why Is SBP Higher in the Ankles than in the Arms-?

The blood pressure waveform amplifies as it travels distally from the heart, resulting in a progressive increase in SBP and a decrease in DBP. The most widely accepted model used to explain the SBP amplification relies on retrograde wave reflection from resistant distal arterioles, which is additive to the antegrade wave.[81] In the legs, remodeling of vessel structure occurs, resulting from increased intraluminal pressure, characterized by increased wall thickening and unchanged inner radius.[82,83] The changes in wall thickness resulting from increased hydrostatic pressure in the lower extremities with walking (vertical position) occur during the second year of life and plausibly explain why the ABI is 1.00 in the newborn and increases to adult values at 2 to 3 years of age.[84] Therefore, both reflected waves and changes in vessel wall thickness and consequently stiffness contribute to SBP amplification.

The systolic pressure is more sensitive indicator of disease as it is earlier to be reduced than diastolic pressure. Thus the basis of the lower extremity pressure measurement is detection of a reduction in systolic blood pressure in the leg, indicating the presence of obstructive arterial disease.

In absence of subclavian or axillary artery disease, the brachial pressure is equal to aortic pressure and therefore is reflective of obstructive lesion between the aorta and brachial artery.

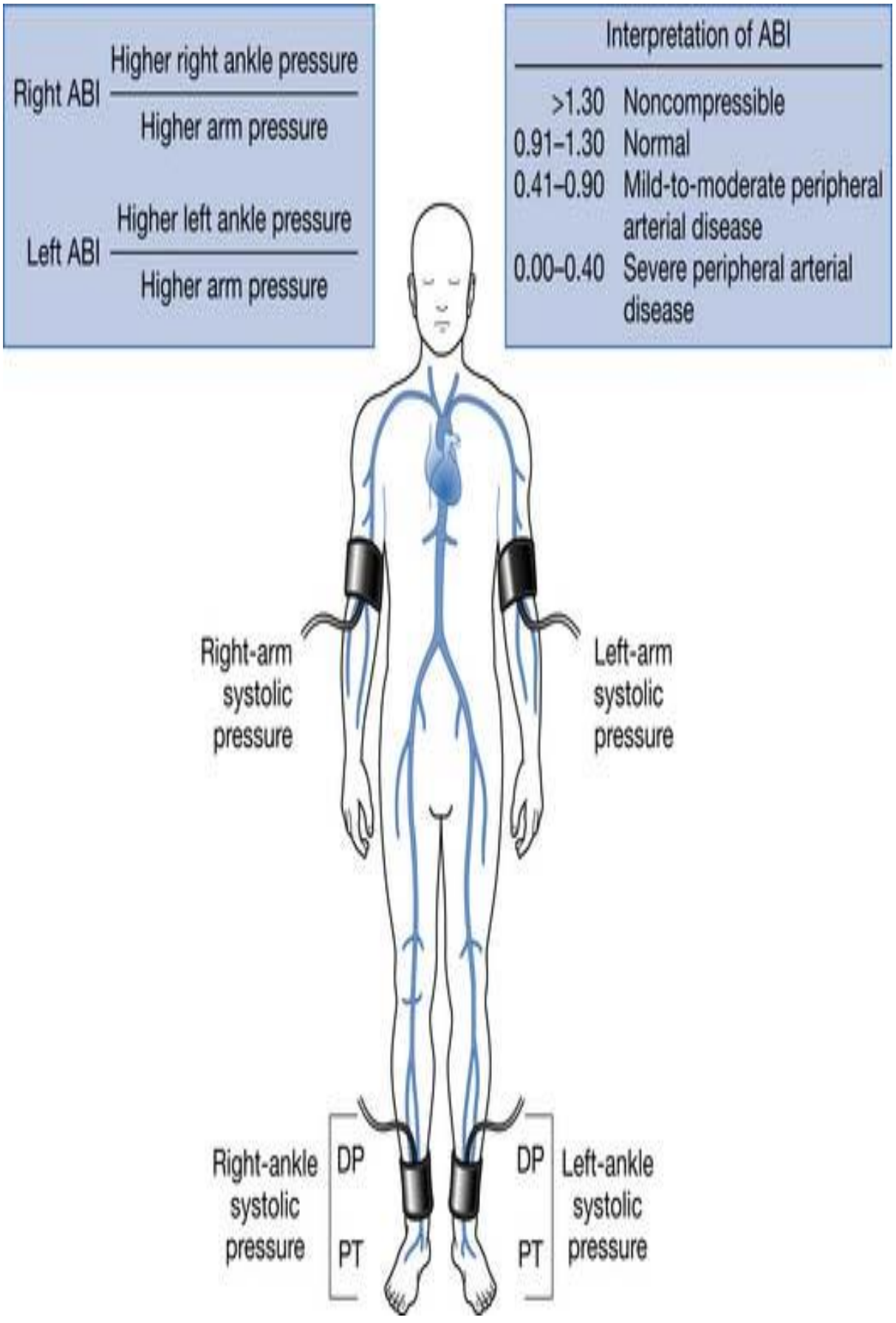


Figure 13: calculation of ABI

ABI: A Marker for CVD Risk and Events

The ABI serves as a measure of systemic atherosclerosis and thus is associated with both atherosclerotic risk factors and prevalent CVD in other vascular beds. A low ABI is associated with many cardiovascular risk factors, including hypertension, diabetes mellitus, dyslipidemia, smoking history, and several novel cardiovascular risk factors (eg, C-reactive protein, interleukin-6, homocysteine, and chronic kidney disease).[85,86,87,88]

A strong and consistent relationship between low ABI and prevalent coronary artery disease and cerebrovascular disease has been demonstrated in several population-based cohort studies that included individuals with existing CVD[89-91]. The prevalence of coronary artery disease among PAD patients ranges from 10.5% to 71% compared with 5.3% to 45.4% among subjects without PAD

The ABI is a measure of the severity of atherosclerosis in the legs but is also an independent indicator of the risk of subsequent atherothrombotic events elsewhere in the vascular system. The ABI may be used as a risk marker both in the general population free of clinical CVD and in patients with established CVD

The ABI has been investigated as a risk predictor in several population-based cohort studies, mostly in Europe[92-95] and North America.[96-99] These studies have consistently found that a low ABI is associated with an increased risk of myocardial infarction, stroke, and both total and cardiovascular-related mortality. Furthermore, the increased risks are independent of established CVD and risk factors at baseline, suggesting that the ABI, as an indicator of atherosclerosis, might enhance the accuracy of risk prediction with established scoring systems.[80]

METHODOLOGY

METHODOLOGY

SOURCE OF DATA:

This study will be conducted on 41 Prediabetic and 41 within normal glycemic control between age group of 18-50years attending the General Medicine outpatient section and inpatients of R. L. Jalappa hospital and research centre Tamaka, Kolar.

Inclusion criteria:

- Age between 18-50years.
- **Study group:** Prediabetes defined as fasting plasma glucose 101-125 mg/dl, Post prandial glucose
- 141-199mg/dl, HBA1C 5.7%-6.4%.
- **Control group:** Normal people with fasting plasma glucose <100mg/dl and post prandial glucose <140mg/dl, HBA1c <5.7%.

Exclusion criteria:

- Chronic kidney disease.
- Congestive Cardiac failure.
- Established Coronary artery disease and stroke.
- Hypothyroidism.
- Patients on statin therapy for more than 6 months.
- Pregnancy.

Method of collection of data

This study was conducted on patients attending the General Medicine outpatient section and inpatient section of R.L.Jalappa hospital and research centre Tamaka, Kolar .Patients who is nondiabetic, of age group between 18-50years was screened for FBS, PPBS, HBA1c, after obtaining informed consent.

Patients with fasting plasma glucose of 101 -125mg/dl, post prandial glucose of 141-199mg/dl, HbA1c 5.7-6.4% was categorized into study group(Prediabetic) and patients with fasting plasma glucose <100mg/dl and post prandial <140mg/dl ,HBA1c<5.7% was categorized into control group.

A predesigned and pretested proforma was used to collect data regarding personal details, treatment history BMI, waist-hip ratio, ABI will be calculated. Both the groups was subjected for bilateral carotid artery Doppler for the measurement of carotid artery intimal thickness.

Carotid intimal medial thickness was measured using B mode ultrasound 'SIEMENS ACUSON^{R} X300 PREMIUM' ultrasound system with high frequency (5-10MHz range) linear traducer color Doppler imaging. The patient was made to lie supine with his/her neck extended and head turned to the contralateral to the side being tested, scan was performed transversely from the proximal common carotid artery moving distally, plagues, nature of plague and the degree of stenosis was noted by using peak systolic velocities and end diastolic velocities.

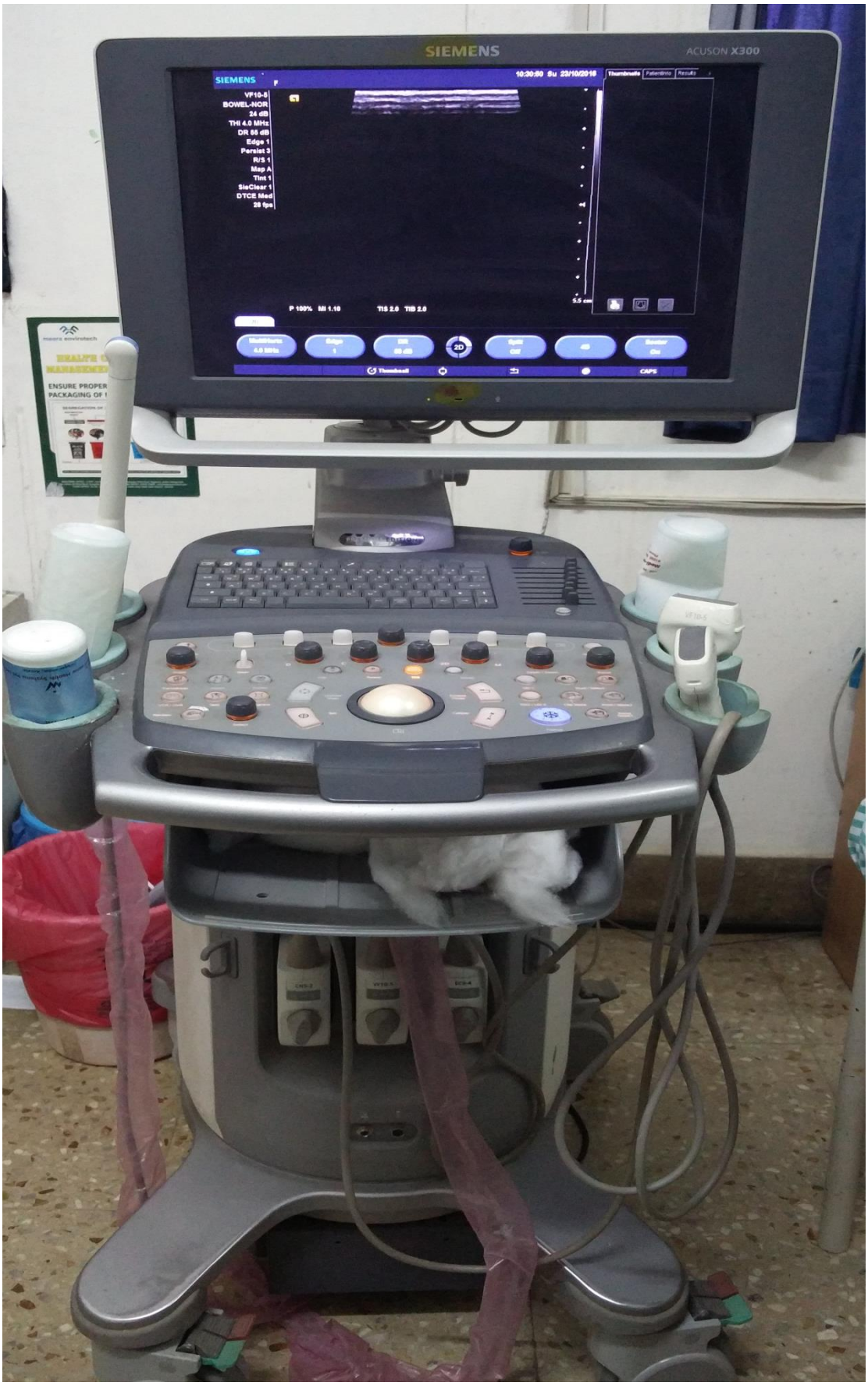


Figure 14: SIEMENS ACUSON^{R} X300 PREMIUM' ULTRASOUND

A consensus conference of the Society of Radiologists in Ultrasound recommended the following criteria for estimating stenosis[108]:

- Normal: ICA PSV < 125 cm/s and no plaque or intimal thickening is visible.
- < 50% stenosis: ICA PSV < 125 cm/s and plaque or intimal thickening is visible.
- 50-69% stenosis: ICA PSV is >125-230 cm/s and plaque is visible.
- >70% stenosis to near occlusion: ICA PSV >230 cm/s and visible plaque and lumen narrowing are seen.
- Near occlusion: A markedly narrowed lumen is seen on color Doppler ultrasound.
- Total occlusion: No detectable patent lumen is seen on gray scale ultrasound, and no flow is seen on spectral, power, and color Doppler ultrasound.

Normal IMT values – median (P50), 25th and 75th percentile (P) IMT values for men and women at different age categories.

Age	P25	P50	P75
Men <30	0.39	0.43	0.48
Men 31-40	0.42	0.46	0.50
Men 41-50	0.46	0.50	0.57
Men >50	0.46	0.52	0.62
Women <30	0.39	0.40	0.43
Women 31-40	0.42	0.45	0.49
Women 41-50	0.44	0.48	0.53
Women >50	0.50	0.54	0.59

Ankle brachial index –

The patient was placed in a supine position with arms and legs at the same level as the heart for 5 min before measurement. Appropriate sized blood pressure cuff for both the arms and ankle was tied; ankle cuff tied between malleolus and calf, arm cuff in cubital fossa, ankle and brachial pressure is measured. ABI is obtained by dividing ankle pressure by brachial pressure.

- Normal= 1.0-1.4
- Acceptable =0.9-1.0
- Some arterial disease =0.8-0.9
- Moderate arterial disease =0.5-0.8
- Severe arterial disease =<0.5

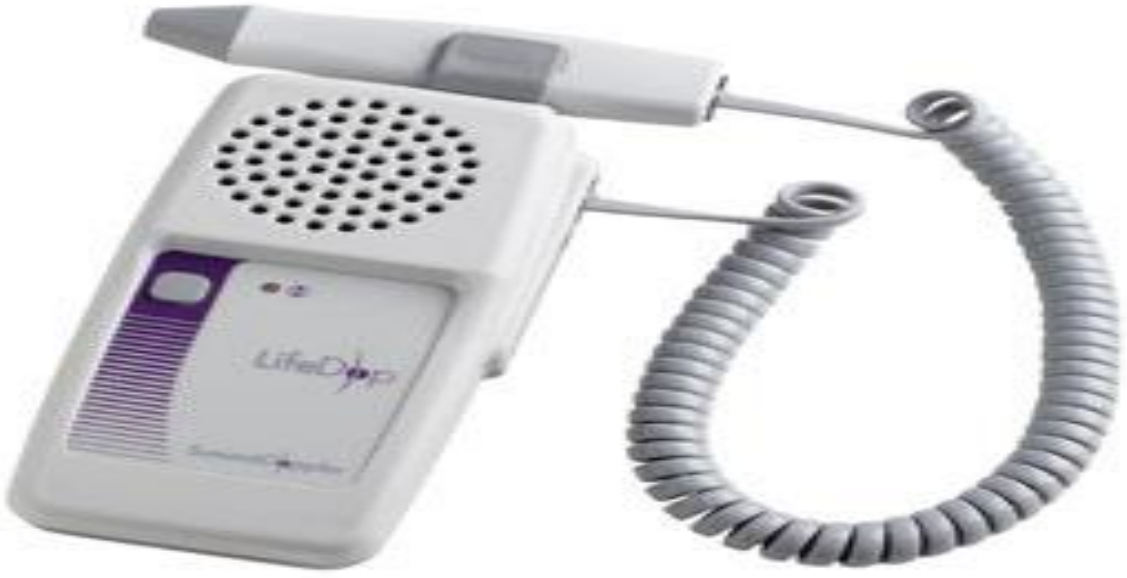


Figure 15: Hand held non-display doppler

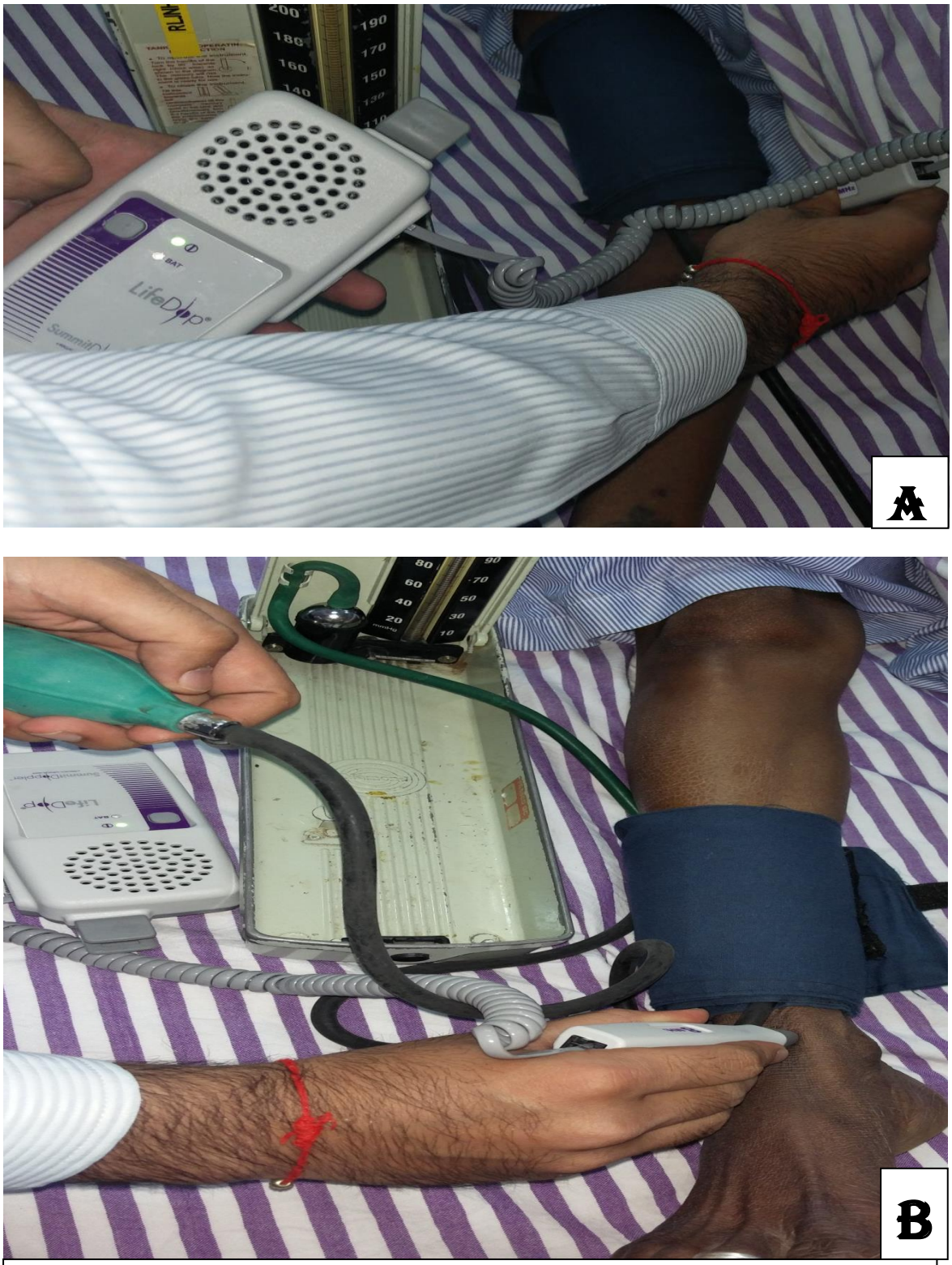


Figure 16: ABI measurement

A- Brachial artery
B- Anterior tibial artery

Sampling procedure:

A comparative randomized case control study was planned. After obtaining approval from the ethical committee board and taking informed consent, Patient were screened for FBS, PPBS, and HBA1c, depending on the inclusion criteria grouped into study and control group.

Study group and control group matched and compared with age, sex, BMI, waist hip ratio, cholesterol levels, smoking, family history of heart disease, hypertension.

STATISTICAL ANALYSIS

Sample size is estimated by using the formula

$$N = \frac{2\,\sigma^2 (Z_\alpha + Z_\beta)^2}{(M_1 - M_2)^2}$$

Z_α=1.96 %(95%confidence level).

Zβ=0.84% with 80% prevalence.

M_1-M_2 = difference in means

- Sample size estimated based on CIMT to detect mean CIMT thickness of 0.10 the sample size required 41 per group with 80% error and 95% confidence level.
- Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two groups.
- P value <0.05 was considered as statistically significant.

ETHICAL CLEARANCE:

Ethical clearance has been obtained from our institution ethical committee

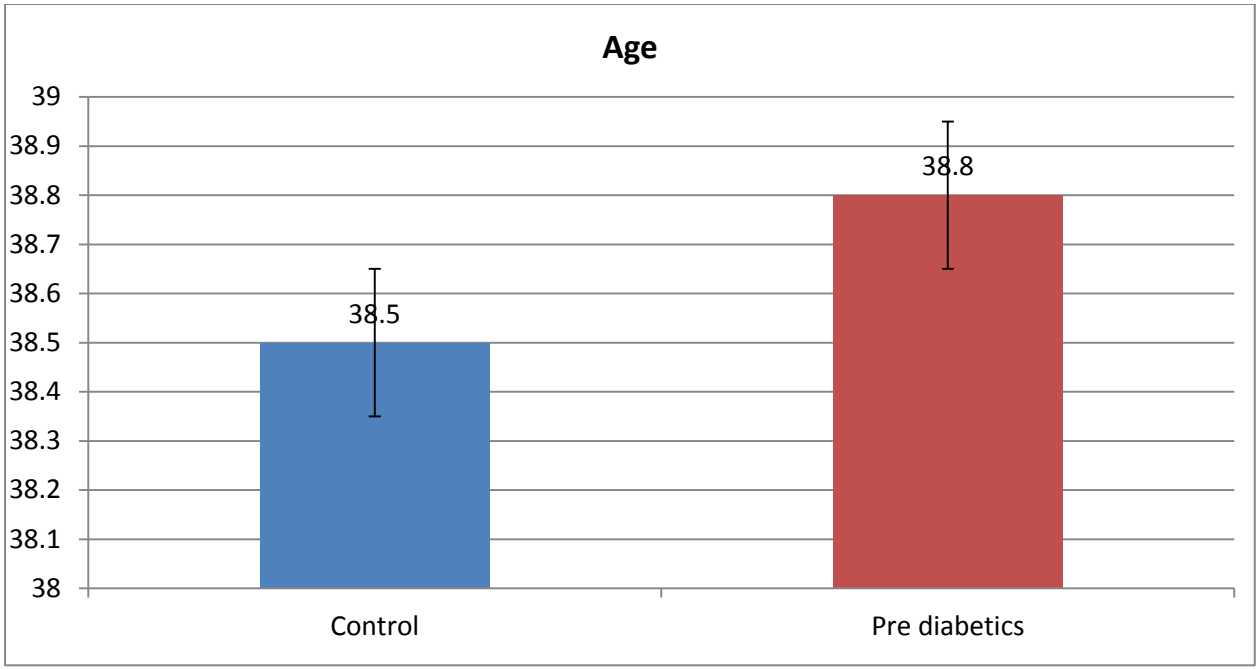
RESULTS

RESULTS

Table 2: Age distribution of subjects in both groups

	Group				P value
	Control		Pre diabetics		
	Mean	SD	Mean	SD	
Age	38.5	7.4	38.8	7.1	0.831

Mean age of subjects in controls was 38.5 ± 7.4 years and in Pre diabetes was 38.8 ± 7.1 years. There was no significant difference in mean age between two groups; hence age matching was achieved between two groups.



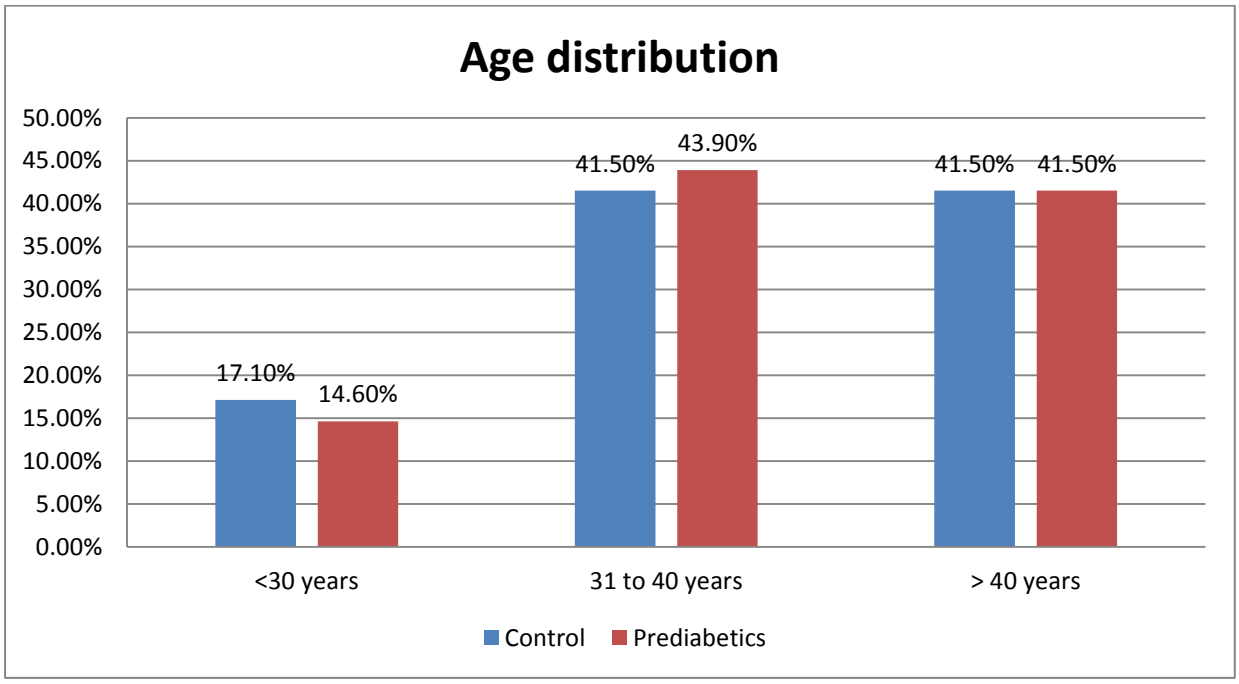
Graph 2: Bar diagram showing Age distribution of subjects in both groups

Table 3: Age distribution of subjects between two groups

		Group			
		Control		Prediabetics	
		Count	%	Count	%
Age	<30 years	7	17.1%	6	14.6%
	31 to 40 years	17	41.5%	18	43.9%
	> 40 years	17	41.5%	17	41.5%

χ 2 = 0.105, df = 2, p =0. 949

Majority of subjects in control and pre diabetics group were in the age group > 30 years. Age matching was achieved between two groups.



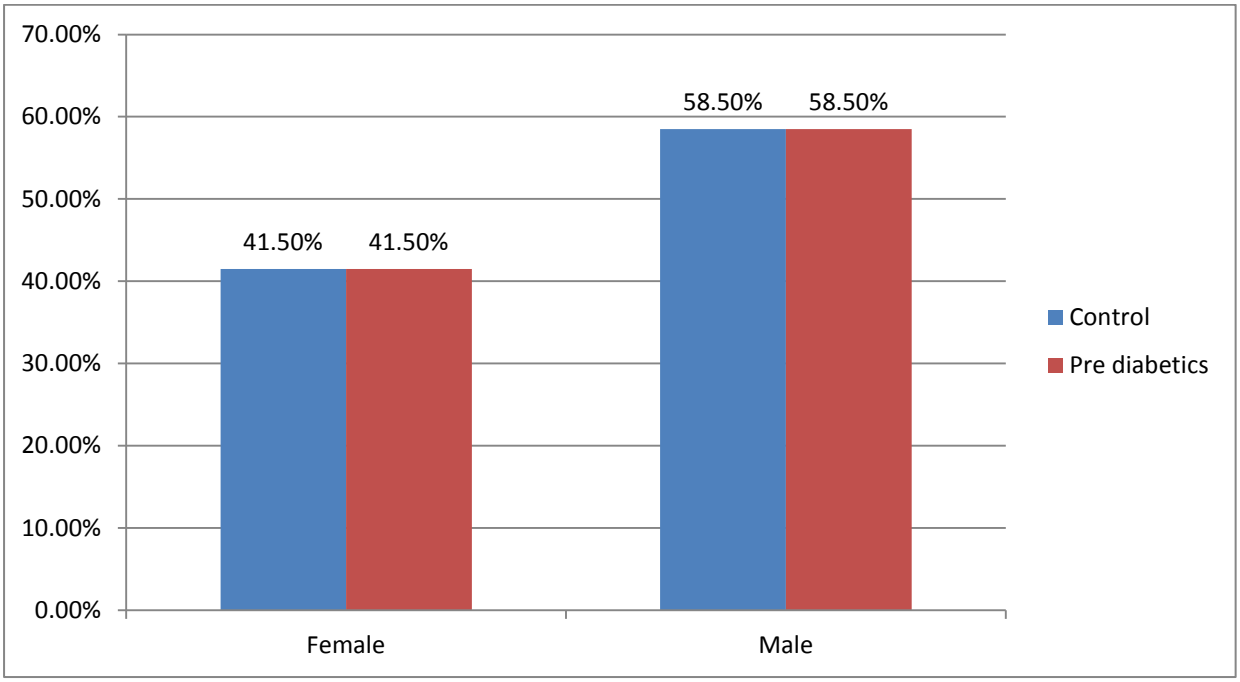
Graph 3: Bar diagram showing age distribution of subjects between two groups

Table 4: Gender distribution of subjects between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
Sex	Female	17	41.5%	17	41.5%
	Male	24	58.5%	24	58.5%

$\chi 2 = 0.000$, df = 1, p = 1.000

In both groups 58.5% were males and 41.5% were females. Hence gender matching was achieved.



Graph 4: Bar diagram showing Gender distribution of subjects between two groups

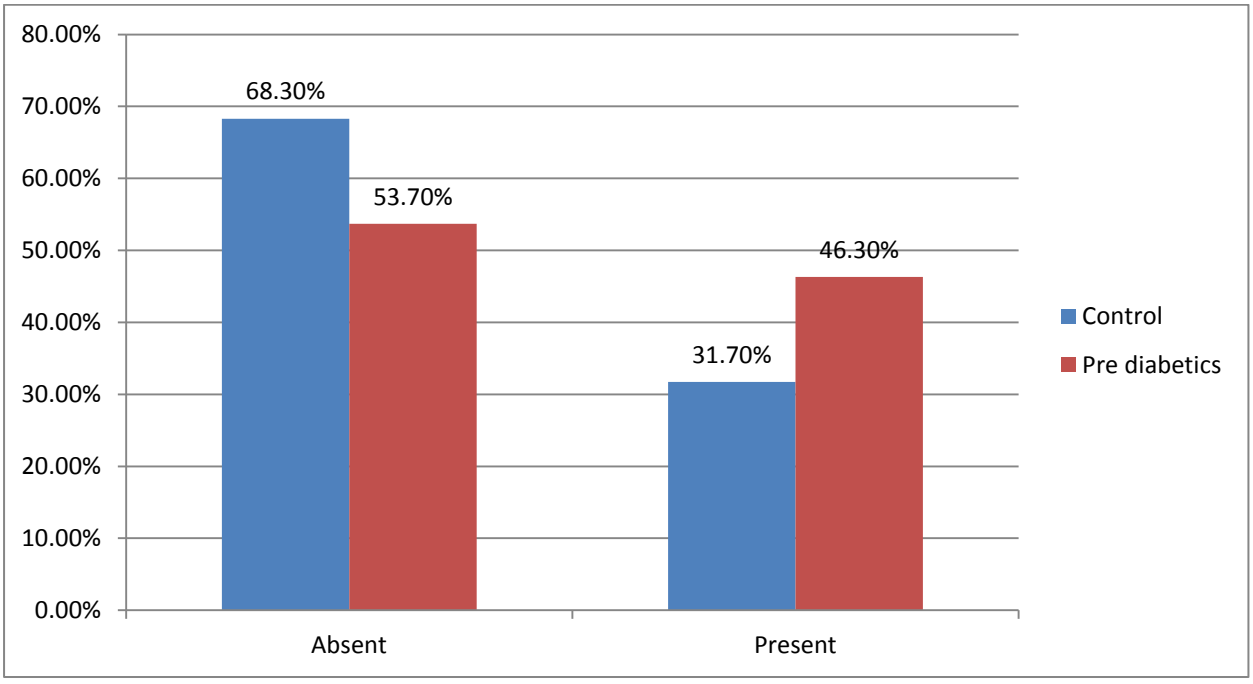
Table 5: Family history of diabetes between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
Family history of diabetes	Absent	28	68.3%	22	53.7%
	Present	13	31.7%	19	46.3%

$\chi 2 = 1.845$, df = 1, p = 0.174

In control group 31.7% and in pre diabetes group 46.3% had family history of diabetes.

There was no significant difference between two groups with respect to family history.



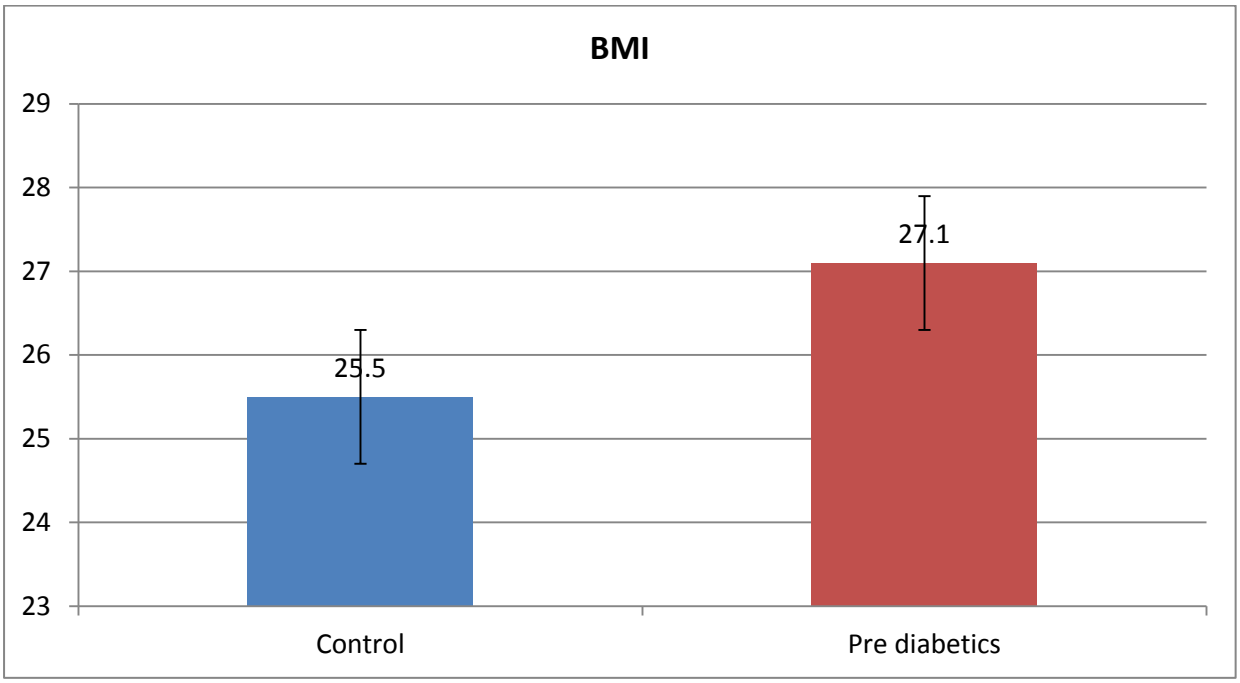
Graph 5: Bar diagram showing Family history of diabetes between two groups

Table 6: Mean BMI comparison between two groups

	Group				P value
	Control		Pre diabetics		
	Mean	SD	Mean	SD	
BMI	25.5	3.4	27.1	5.3	0.122

Mean BMI in control group was 25.5 ± 3.4 and in pre diabetes group was 27.1 ± 5.3.

There was no significant difference in BMI between two groups.



Graph 6: Bar diagram showing Mean BMI comparison between two groups

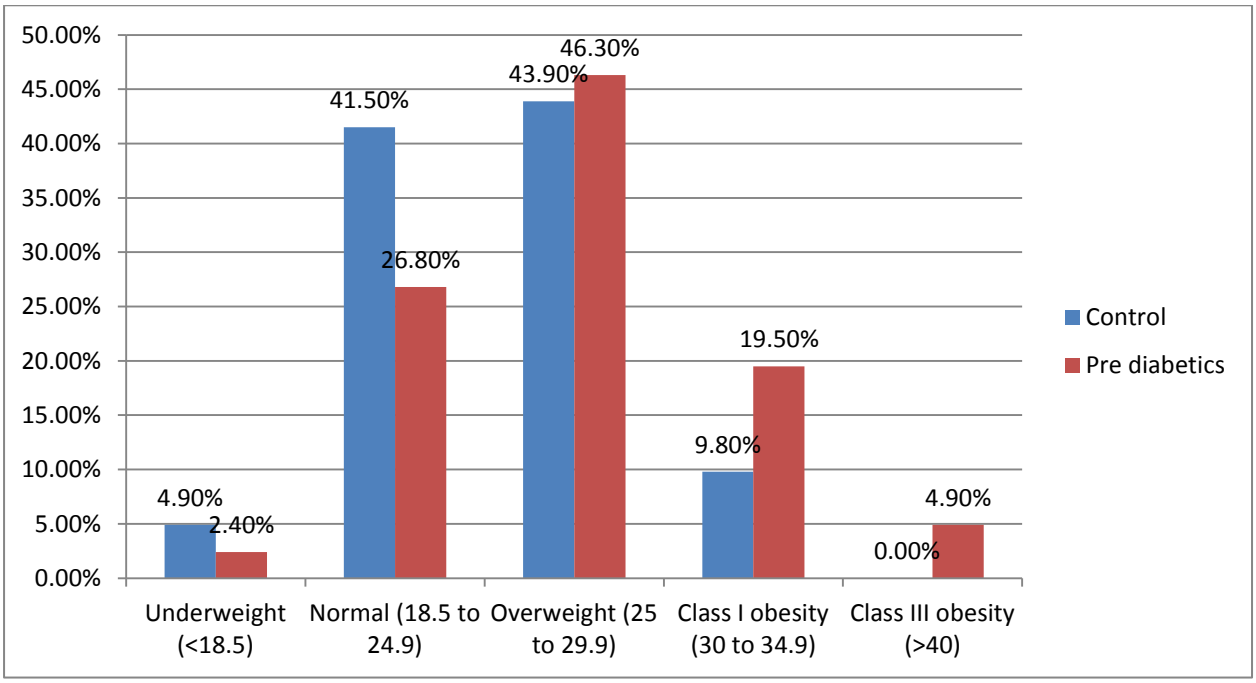
Table 7: BMI classification between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
BMI	Underweight (<18.5)	2	4.9%	1	2.4%
	Normal (18.5 to 24.9)	17	41.5%	11	26.8%
	Overweight (25 to 29.9)	18	43.9%	19	46.3%
	Class I obesity (30 to 34.9)	4	9.8%	8	19.5%
	Class III obesity (>40)	0	0.0%	2	4.9%

$\chi 2 = 4.979$, df = 4, p = 0.289

In the Control group 4.9% were underweight, 43.9% were overweight and 9.8% had Class I obesity. Similarly in Pre diabetics group 2.4% were Underweight, 46.3% were overweight, 19.5% were Class I Obese and 4.9% were class III obese.

There was no significant difference in BMI classification between two groups.



Graph 7: Bar diagram showing BMI classification between two groups

Table 8: Comparison between BMI and Gender in two groups

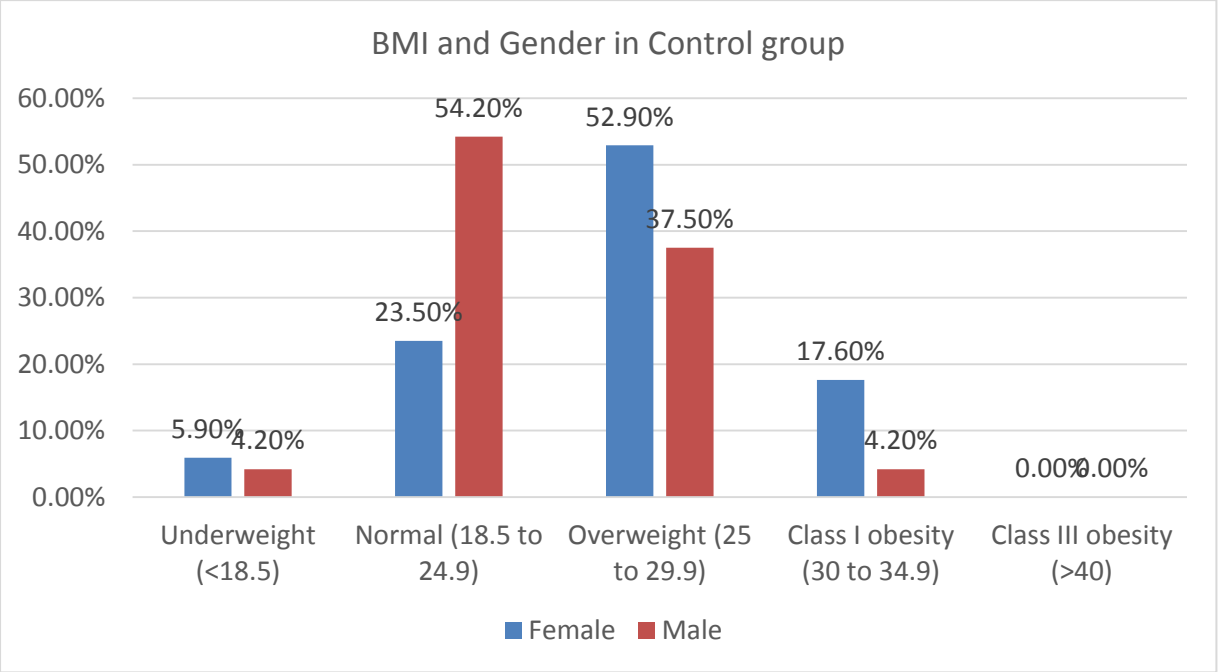
		Group							
		Control				Prediabetics			
		Sex				Sex			
		Female		Male		Female		Male	
		Count	%	Count	%	Count	%	Count	%
BMI	Underweight (<18.5)	1	5.9%	1	4.2%	0	0.0%	1	4.2%
	Normal (18.5 to 24.9)	4	23.5%	13	54.2%	4	23.5%	7	29.2%
	Overweight (25 to 29.9)	9	52.9%	9	37.5%	8	47.1%	11	45.8%
	Class I obesity (30 to 34.9)	3	17.6%	1	4.2%	4	23.5%	4	16.7%
	Class III obesity (>40)	0	0.0%	0	0.0%	1	5.9%	1	4.2%
P value		0.195				0.890			

In Control group among female gender, majority of them were overweight (52.9%) and among males majority of them had normal BMI (54.2%).

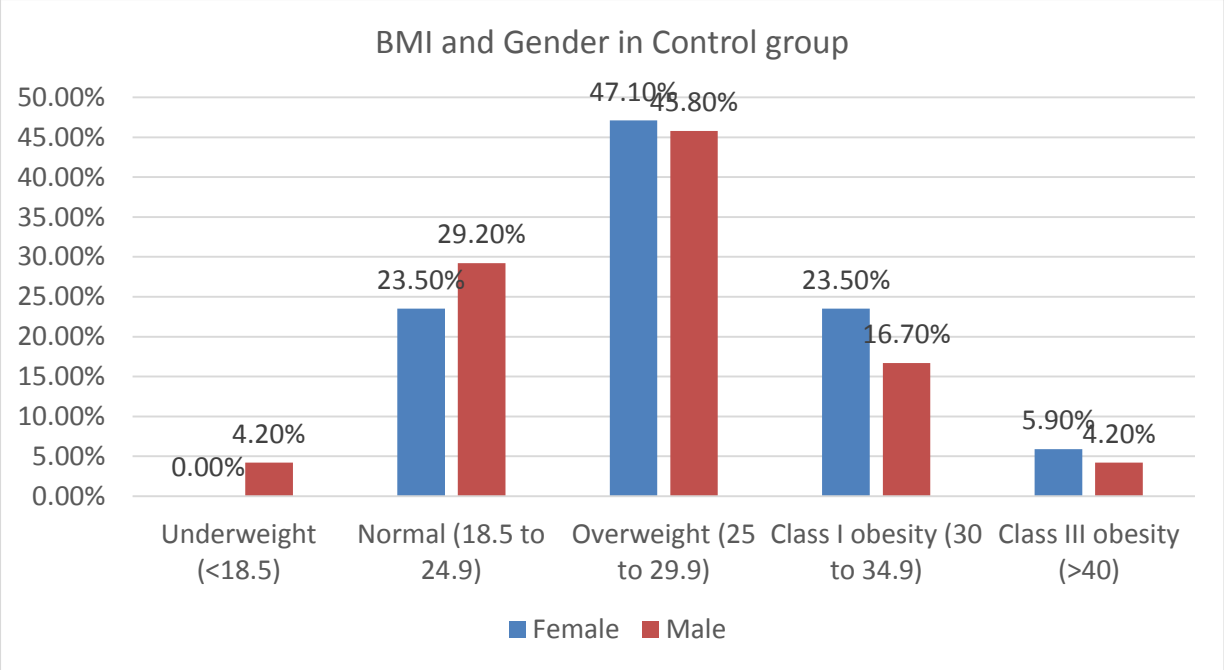
There was no significant association between Gender and BMI in control group.

In Prediabetics group among both female and male genders, majority of them were overweight 47.1% and 45.8%.

There was no significant association between Gender and BMI in Prediabetics group.



Graph 8: Bar diagram showing Comparison between BMI and Gender in control group



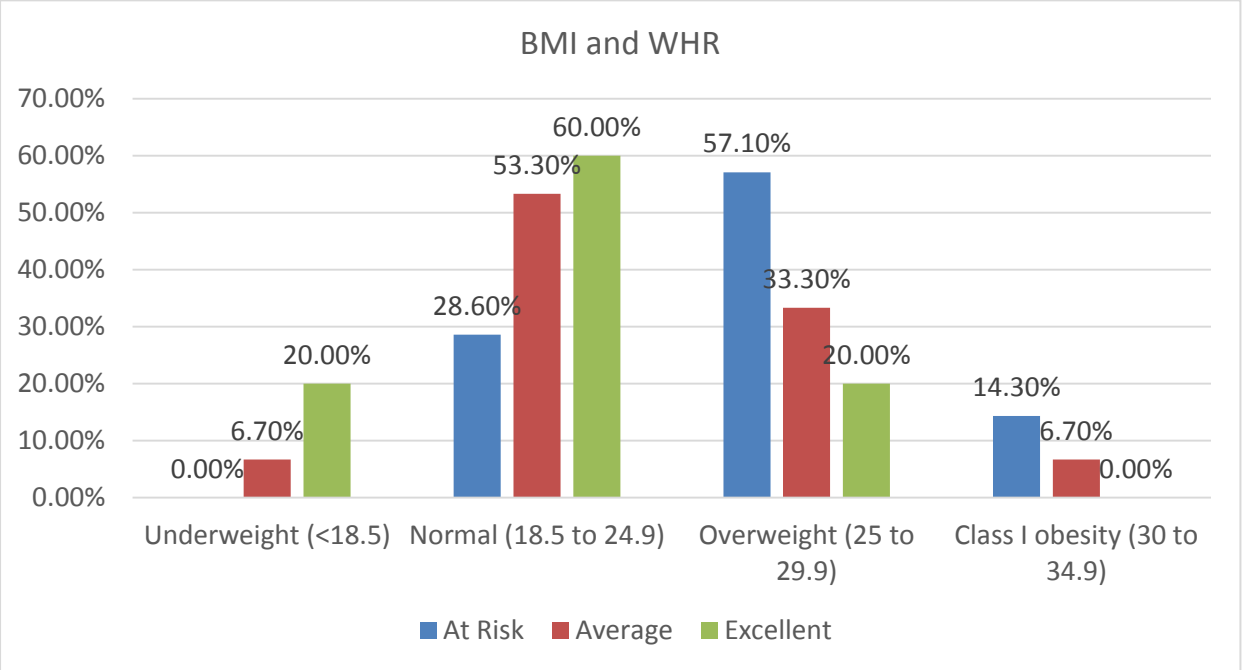
Graph 9: Bar diagram showing Comparison between BMI and Gender in Prediabetics group

Table 9: Comparison between BMI and WHR in control groups

		Group					
		Control					
		WHR					
		At Risk		Average		Excellent	
		Count	%	Count	%	Count	%
BMI	Underweight (<18.5)	0	0.0%	1	6.7%	1	20.0%
	Normal (18.5 to 24.9)	6	28.6%	8	53.3%	3	60.0%
	Overweight (25 to 29.9)	12	57.1%	5	33.3%	1	20.0%
	Class I obesity (30 to 34.9)	3	14.3%	1	6.7%	0	0.0%

$\chi 2 = 8.108$, df = 6, p = 0.225

In the control group there was no significant association between BMI and WHR.



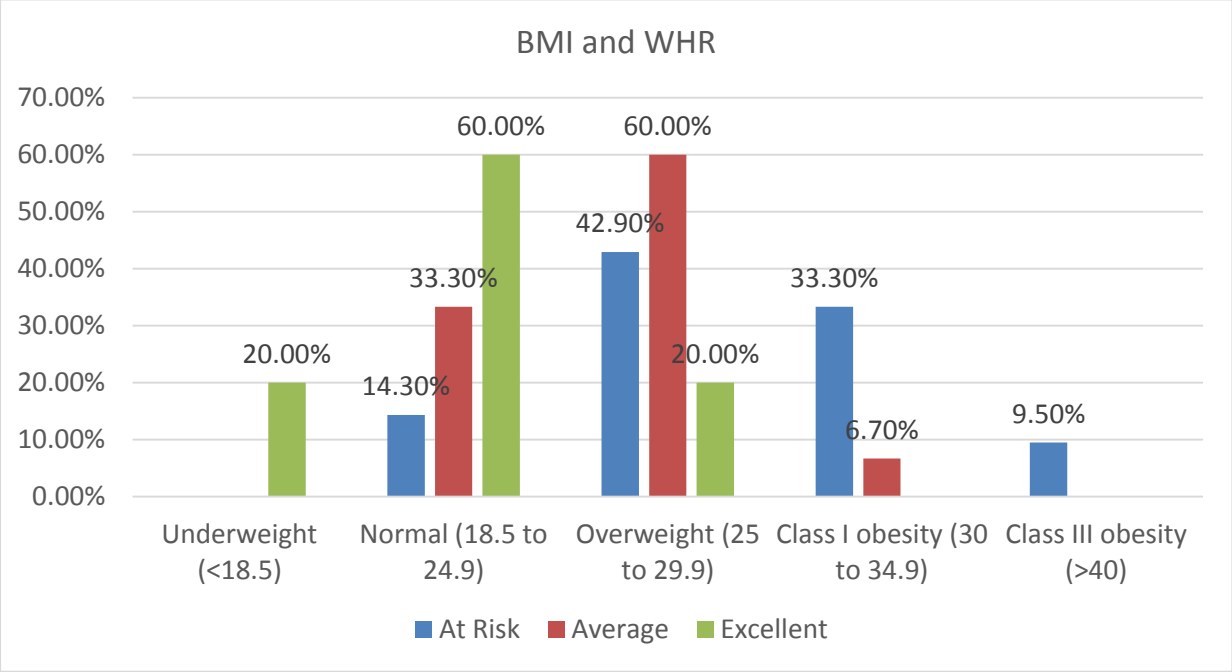
Graph 10: Bar diagram showing Comparison between BMI and WHR in control groups

Table 10: Comparison between BMI and WHR in Prediabetics groups

		Prediabetics					
		WHR					
		At Risk		Average		Excellent	
		Count	%	Count	%	Count	%
BMI	Underweight (<18.5)	0	0.0%	0	0.0%	1	20.0%
	Normal (18.5 to 24.9)	3	14.3%	5	33.3%	3	60.0%
	Overweight (25 to 29.9)	9	42.9%	9	60.0%	1	20.0%
	Class I obesity (30 to 34.9)	7	33.3%	1	6.7%	0	0.0%
	Class III obesity (>40)	2	9.5%	0	0.0%	0	0.0%

$\chi 2 = 18.33$, df = 8, p = 0.019*

In the Prediabetics group significant association was observed between BMI and WHR.



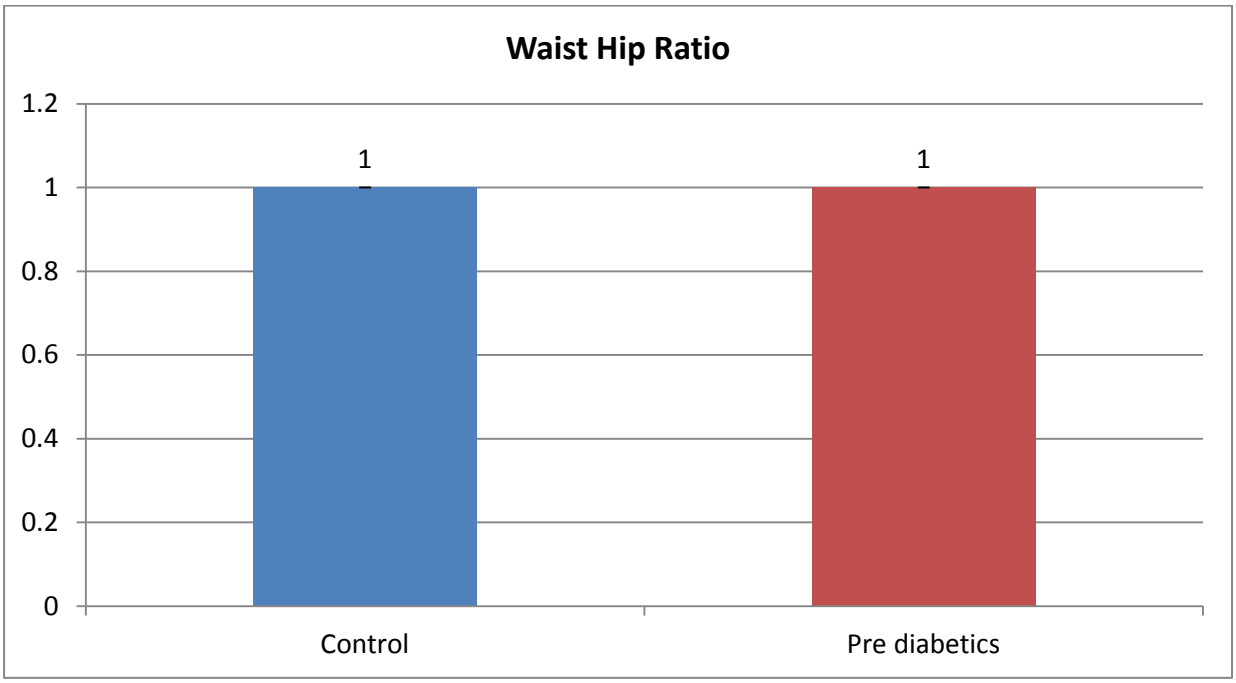
Graph 11: Bar diagram Comparison between BMI and WHR in Prediabetics groups

Table 11: Mean Waist hip ratio comparison between two groups

	Group				P value
	Control		Pre diabetics		
	Mean	SD	Mean	SD	
Waist Hip Ratio	1.0	0.2	1.0	0.2	0.564

Mean waist hip ratio in control and pre diabetic group was 1.0 ± 0.2.

There was no difference between two groups.



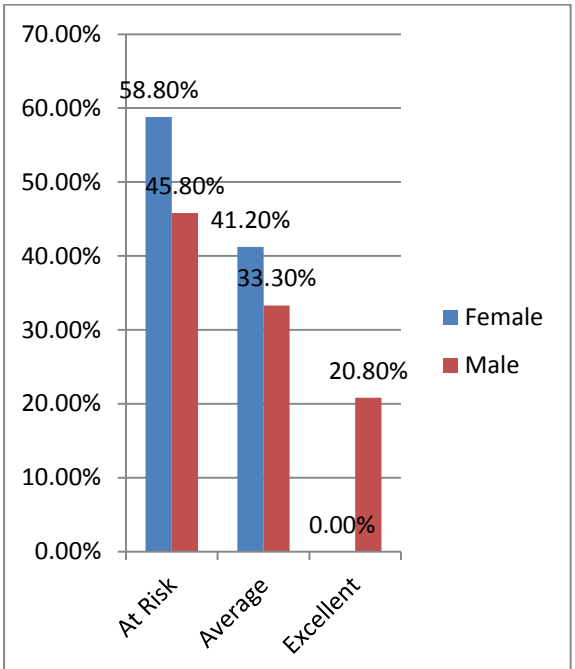
Graph 12: Bar diagram showing Mean Waist hip ratio comparison between two groups

Table 12: Waist hip ratio grading comparison between two groups

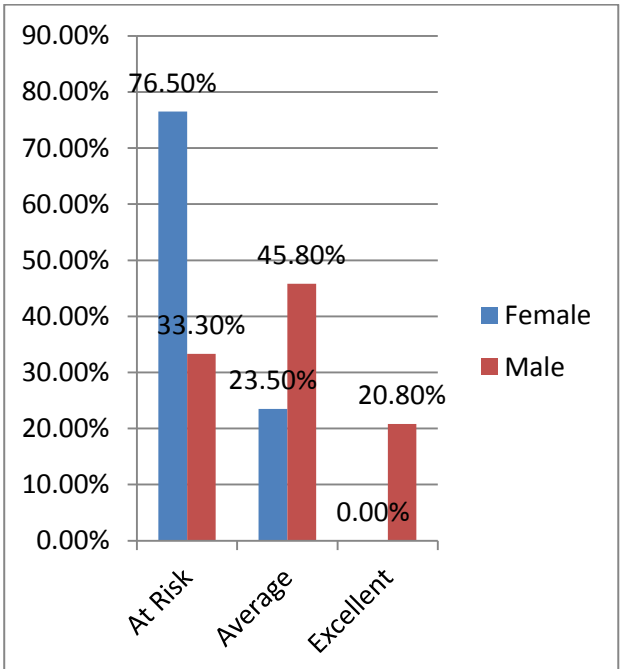
		Group							
		Control				Pre diabetics			
		Gender				Gender			
		Female		Male		Female		Male	
		Count	%	Count	%	Count	%	Count	%
Waist Hip ratio	At Risk	10	58.8%	11	45.8%	13	76.5%	8	33.3%
	Average	7	41.2%	8	33.3%	4	23.5%	11	45.8%
	Excellent	0	0.0%	5	20.8%	0	0.0%	5	20.8%
P value		0.133				0.014*			

In the control group among females 58.8% and among males 45.8% were at risk with respect to Waist Hip ratio and among pre diabetics subjects 76.5% of females and 33.3% of males were at risk.

There was no significant difference observed in control group, were as significant difference was observed in pre diabetics group.



Graph 13: Bar diagram showing Waist hip ratio grading comparison in Control group between male and females.



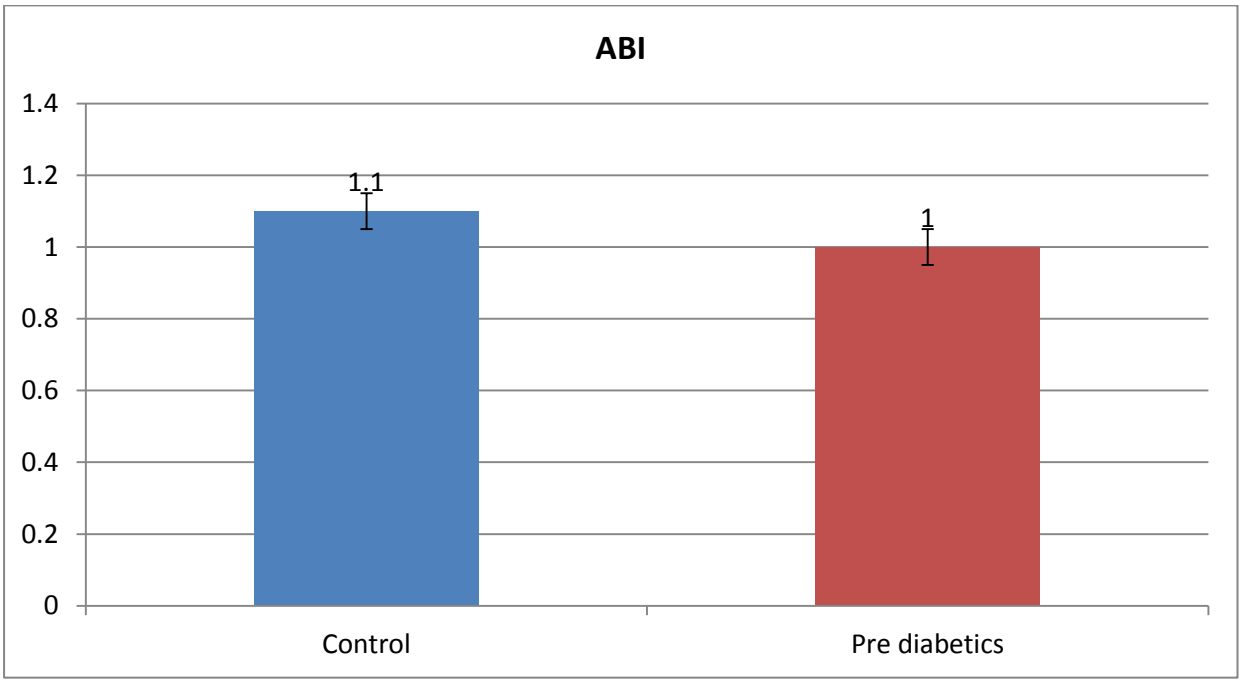
Graph 14: Bar diagram showing Waist hip ratio grading comparison in Pre diabetes group between male and females.

Table 13: Mean ABI comparison between two groups

	Group				P value
	Control		Pre diabetics		
	Mean	SD	Mean	SD	
ABI	1.1	0.1	1.0	0.1	0.120

Mean ABI in control group was 1.1 ± 0.1 and in pre diabetic group was 1.0 ± 0.1.

This difference in mean ABI was statistically significant.



Graph 15: Bar diagram showing Mean ABI comparison between two groups

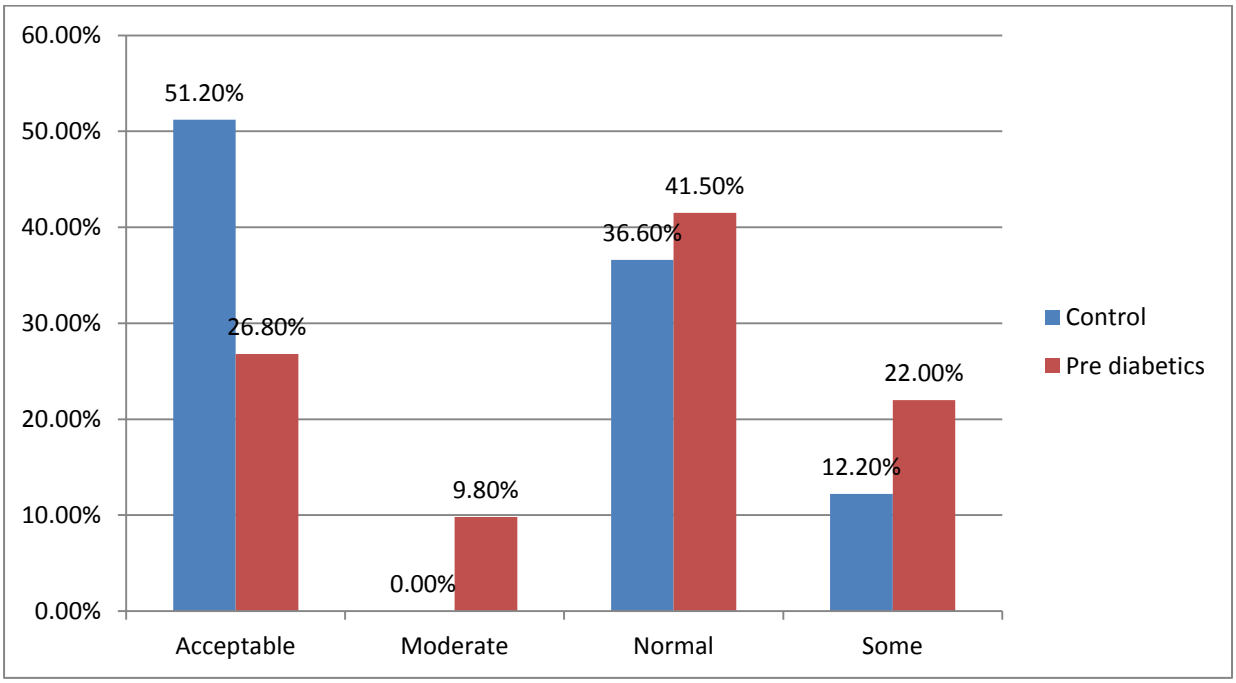
Table 14: ABI grading comparison between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
ABI	Acceptable	21	51.2%	11	26.8%
	Moderate	0	0.0%	4	9.8%
	Normal	15	36.6%	17	41.5%
	Some	5	12.2%	9	22.0%

$\chi 2 = 8.393$, df = 3, p = 0.039*

In control group 51.2% had acceptable ABI, 36.6% had Normal and 12.2% had some ABI grading. In pre diabetic group 26.8% had acceptable, 9.8% had moderate, 41.5% had normal and 22% had some ABI grading.

This difference in ABI grading was statistically significant.



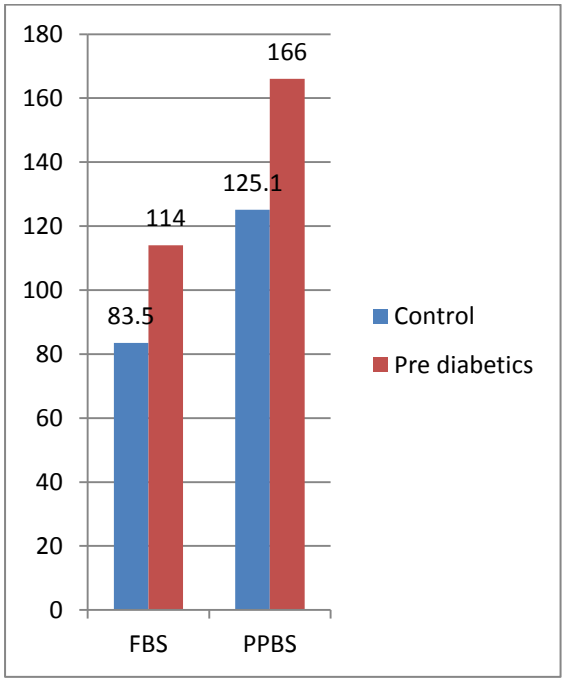
Graph 16: Bar diagram showing ABI grading comparison between two groups

Table 15: Mean Glycemic Profile among subjects in both groups

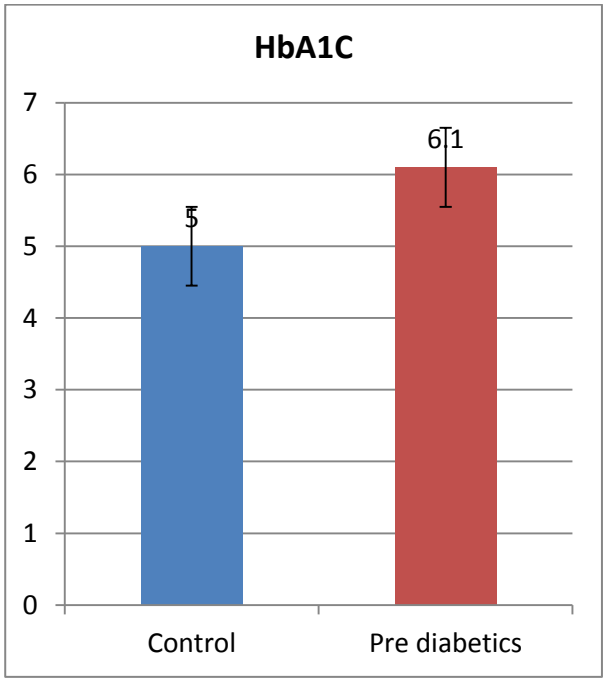
	Group				P value
	Control		Pre diabetics		
	Mean	SD	Mean	SD	
FBS	83.5	11.8	114.0	9.4	<0.001*
PPBS	125.1	19.9	166.0	17.9	<0.001*
HbA1C	5.0	0.3	6.1	0.2	<0.001*

Mean FBS in control group was 83.5 ± 11.8 mg/dl and in pre diabetic group was 114 ± 9.4 mg/dl. Mean PPBS in control group was 125.1 ± 19.9 mg/dl and in pre diabetic group was 166 ± 17.9 mg/dl. Mean HbA1c in control group was 5 ± 0.3 % and in pre diabetic group was 6.1 ± 0.2%.

This difference in mean FBS, PPBS and HbA1c between two groups was statistically significant.



Graph 17: Bar diagram showing Mean FBS and PPBS comparison between two groups



Graph 18 : Bar diagram showing mean HbA1c comparison between two groups

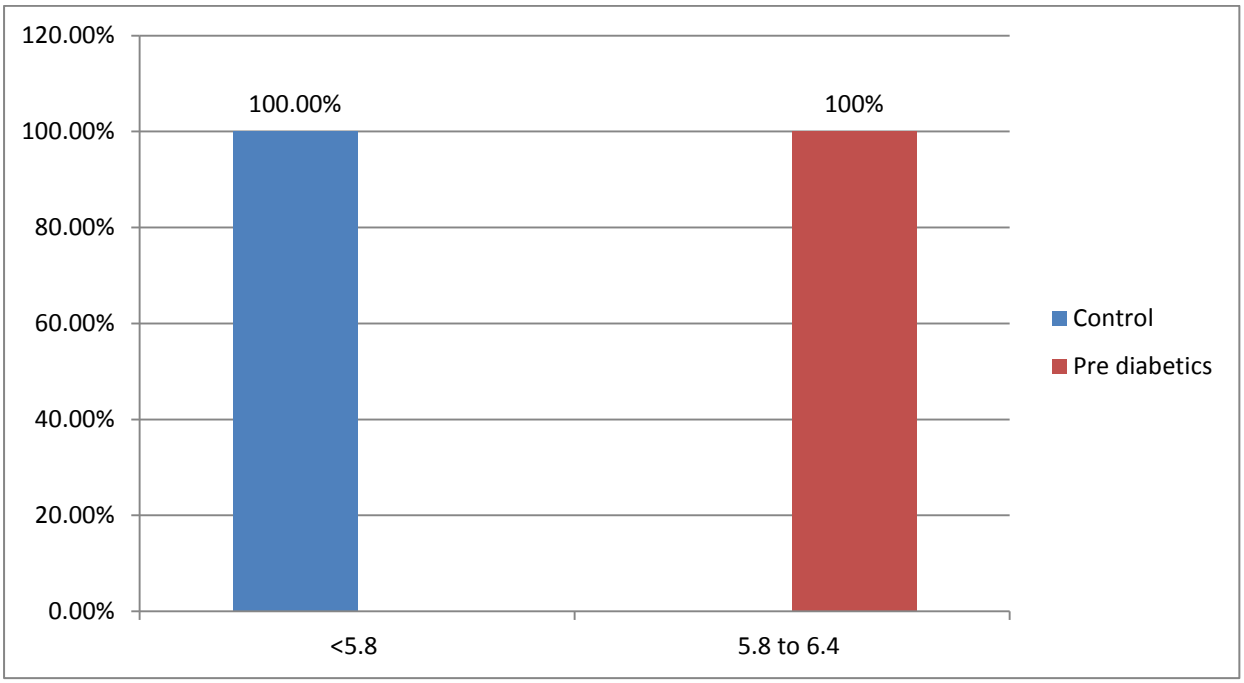
Table 16: HbA1c classification in both groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
HbA1c	<5.6	41	100.0%	4	0%
	5.7 to 6.5	0	0.0%	41	100%

$\chi 2 = 67.42$, df = 1, p <0.001*

In control group all the subjects had HbA1c <5.6 and in all the subjects in pre diabetic group had HbA1c 5.7 to 6.5.

This difference was significant between two groups.

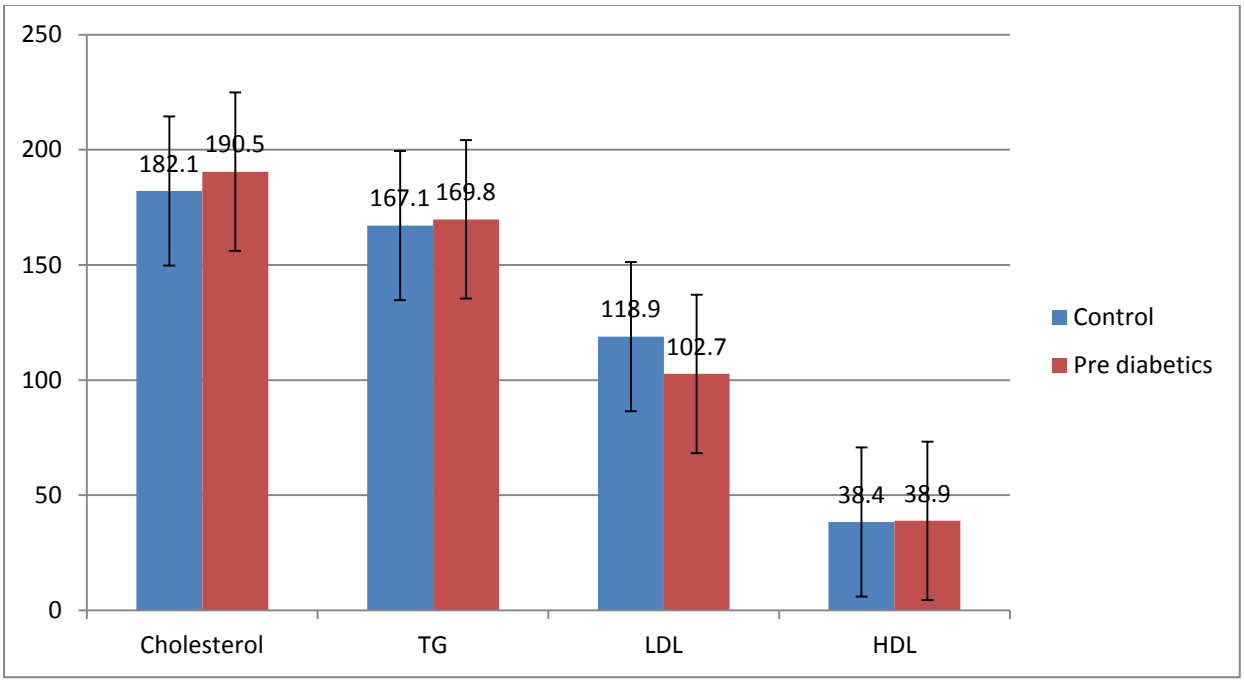


Graph 19: Bar diagram showing HbA1c classification in both groups

Table 17: Mean Lipid profile parameters in both the groups

	Group				P value
	Control		Pre diabetics		
	Mean	SD	Mean	SD	
Cholesterol	182.1	48.0	190.5	58.4	0.476
TG	167.1	43.7	169.8	64.3	0.826
LDL	118.9	33.8	102.7	40.8	0.054
HDL	38.4	7.6	38.9	13.8	0.835

In the study there was no significant difference in mean Total cholesterol, Triglyceride, LDL and HDL levels between two groups.



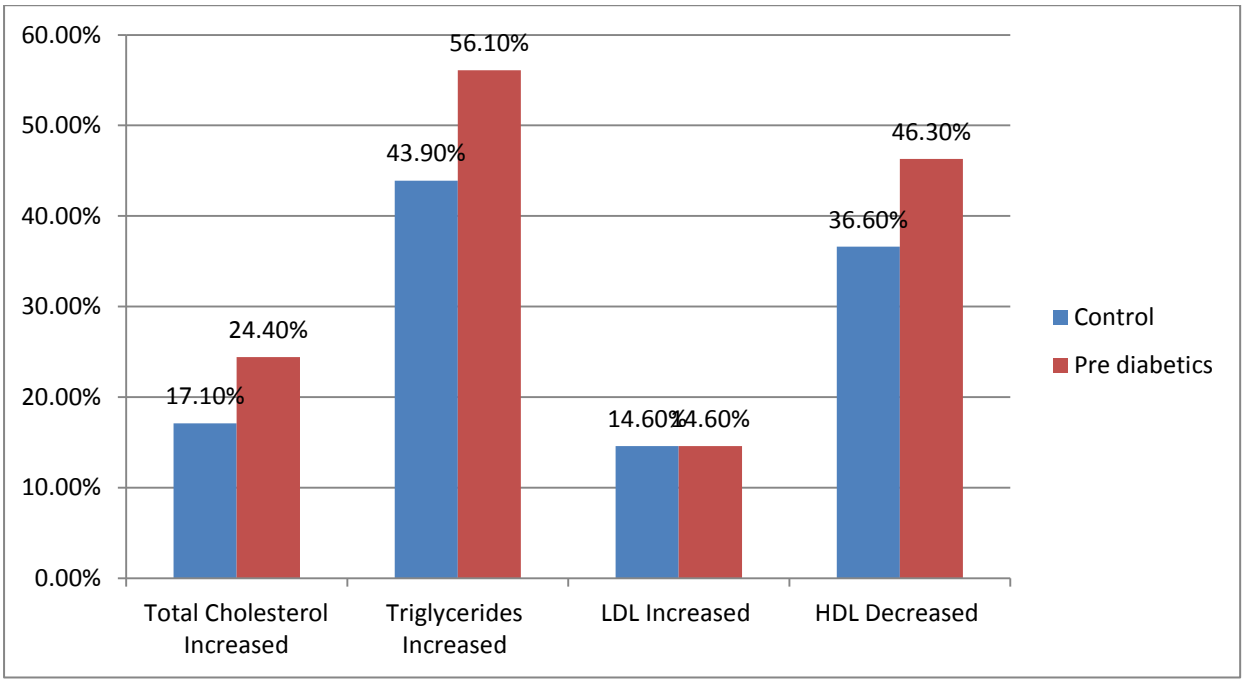
Graph 20: Bar diagram showing Mean Lipid profile parameters in both the groups

Table 18: Classification of Lipid profile parameters between two groups

		Group				P value
		Control		Pre diabetics		
		Count	%	Count	%	
Total Cholesterol	Normal	34	82.9%	31	75.6%	0.414
	Increased	7	17.1%	10	24.4%	
Triglycerides	Normal	23	56.1%	18	43.9%	0.269
	Increased	18	43.9%	23	56.1%	
LDL	Normal	35	85.4%	35	85.4%	1.000
	Increased	6	14.6%	6	14.6%	
HDL	Reduced	15	36.6%	19	46.3%	0.024*
	Normal	25	61.0%	15	36.6%	
	Increased	1	2.4%	7	17.1%	

In the study there was no significant difference in Total cholesterol, Triglyceride and LDL grading between two groups. Were as in control group 36.6% had reduced HDL and in Pre diabetics 46.3% had reduced HDL.

This difference in HDL levels between two groups was statistically significant.



Graph 21: Bar diagram showing abnormal lipid profile pattern between two groups

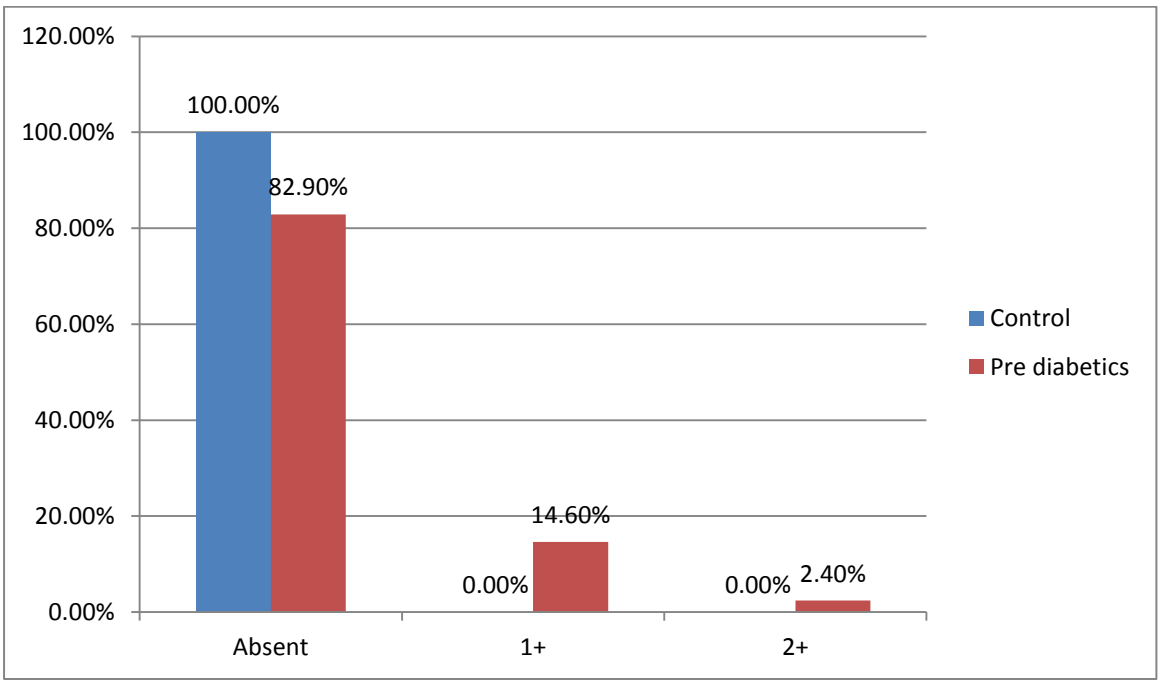
Table 19: Albuminuria findings comparison between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
Albuminuria	Absent	41	100.0%	34	82.9%
	1+	0	0.0%	6	14.6%
	2+	0	0.0%	1	2.4%

$\chi 2 = 7.653$, df = 2, p = 0.022*

In the control group none of the subjects had albuminuria, were as in pre diabetic group 14.6% had 1+ albuminuria and 2.4% had 2+ albuminuria.

This difference in albuminuria between two groups was statistically significant.



Graph 22: Bar diagram showing Albuminuria findings comparison between two groups

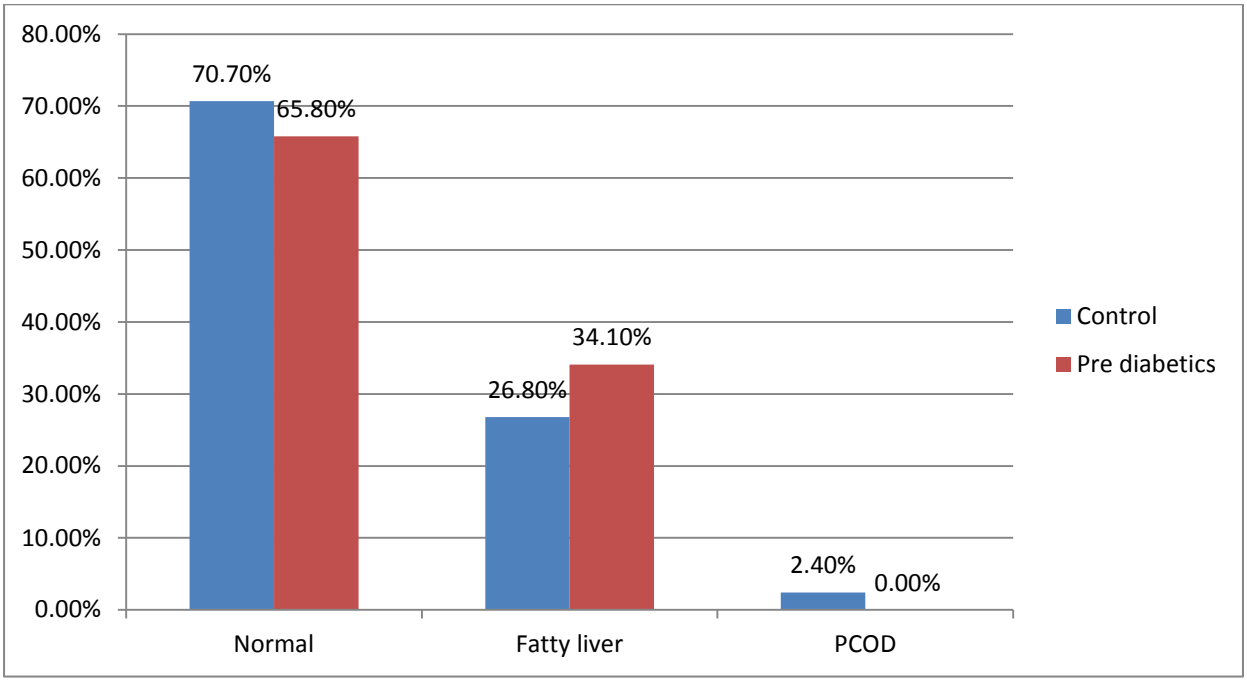
Table 20: USG abdomen findings comparison between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
USG abdomen	Normal	29	70.7%	26	63.4%
	Fatty liver	11	26.8%	14	34.1%
	PCOD	1	2.4%	0	0.0%

$\chi 2 = 2.524$, df = 3, p = 0.471

In Control group 26.8% had fatty liver and in pre diabetic group 34.1% had fatty liver. 2.4% of pre diabetics had grade 1 Splenomegaly and 2.4% of control had PCOD on USG.

There was no significant difference in USG findings between two groups.



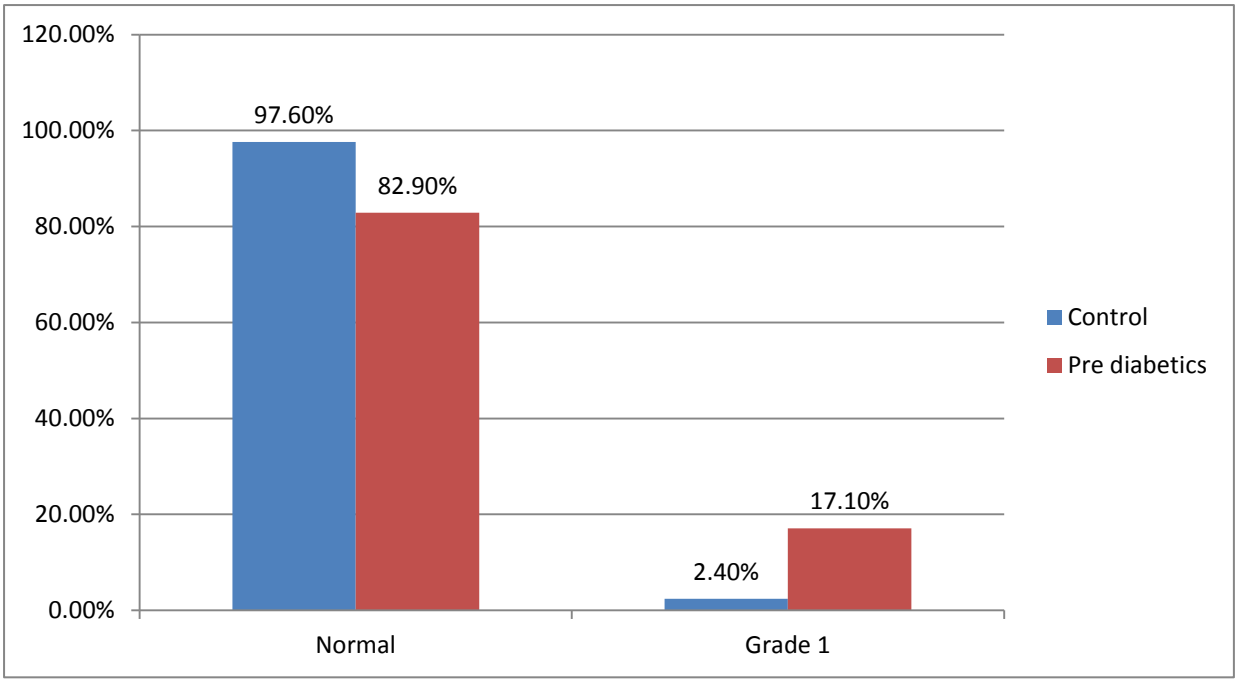
Graph 23: Bar diagram showing USG abdomen findings comparison between two groups

Table 21: CIMT findings comparison between two groups

		Group			
		Control		Pre diabetics	
		Count	%	Count	%
CIMT	Normal	40	97.6%	34	82.9%
	Grade 1*	1	2.4%	7	17.1%

χ 2 = 4.986, df = 1, p = 0.026*

In the control group 2.4% had Grade 1 CIMT and in pre diabetic group 17.1% had Grade 1 CIMT. This difference in CIMT findings between two groups was statistically significant. Odds ratio for pre diabetics for CIMT was 8.235 (1 – 70.31). i.e. pre diabetics are at 8 times higher risk of developing abnormal CIMT than controls.



Graph 24: Bar diagram showing CIMT findings comparison between two groups

Table 22: Association between ABI and CIMT in two groups

		Group							
		Control				Prediabetics			
		CIMT				CIMT			
		Grade 1		Normal		Grade 1		Normal	
		Count	%	Count	%	Count	%	Count	%
ABI	Acceptable	0	0.0%	21	52.5%	1	14.3%	10	29.4%
	Moderate	0	0.0%	0	0.0%	2	28.6%	2	5.9%
	Normal	1	100.0%	14	35.0%	0	0.0%	17	50.0%
	Some	0	0.0%	5	12.5%	4	57.1%	5	14.7%
P value		0.411				0.008*			

In Control subjects who had Grade 1 CIMT, all of them had Normal ABI.
In subjects with normal CIMT, 52.5% had acceptable, 35% had normal and 12.5% had some ABI grade respectively. There was no significant association between CIMT and ABI in control group.

In Prediabetics subjects who had Grade 1 CIMT, 14.3% had acceptable, 28.6% had moderate and 57.1% had some ABI grade. In subjects with normal CIMT, 29.4% had acceptable, 5.9% had moderate, 50% had normal and 14.7% had some ABI grade respectively.

There was significant association between ABI grade and CIMT grade in Prediabetics group.

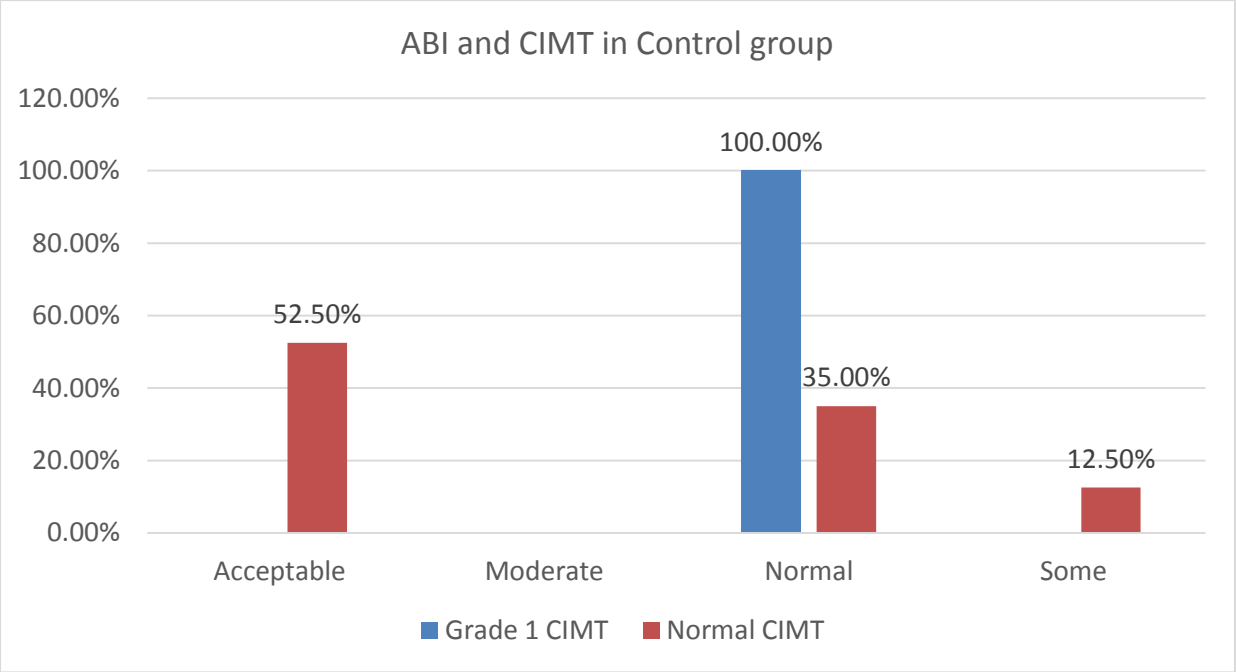


Figure 1: Bar diagram showing Association between ABI and CIMT in control group

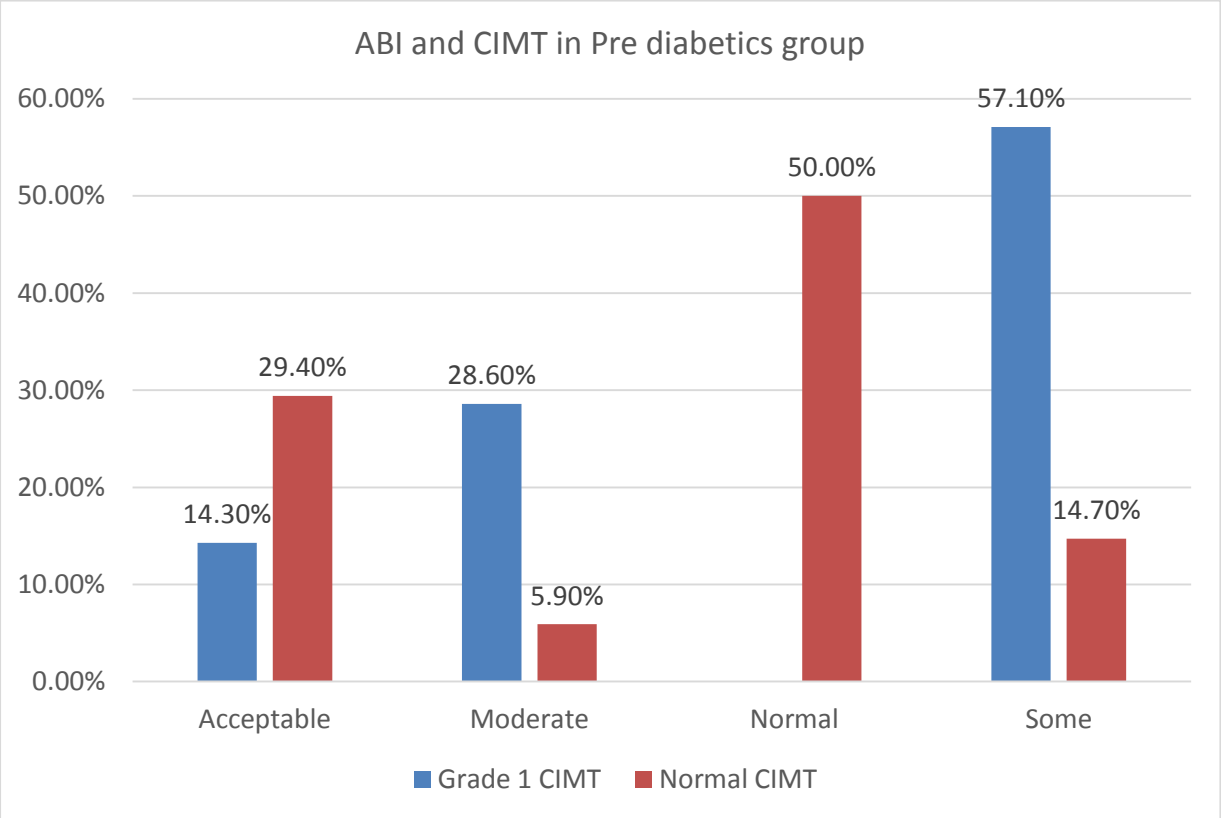


Figure 2: Bar diagram showing Association between ABI and CIMT in Prediabetics group

Table 23: Association between CIMT grade and various parameters in Control group

		CIMT				P value
		Abnormal		Normal		
		Count	%	Count	%	
Age	<30 years	0	0.0%	7	17.5%	0.485
	31 to 40 years	1	100.0%	16	40.0%	
	> 40 years	0	0.0%	17	42.5%	
BMI	Underweight (<18.5)	0	0.0%	2	5.0%	0.727
	Normal (18.5 to 24.9)	0	0.0%	17	42.5%	
	Overweight (25 to 29.9)	1	100.0%	17	42.5%	
	Class I obesity (30 to 34.9)	0	0.0%	4	10.0%	
	Class III obesity (>40)	0	0.0%	0	0.0%	
Waist Hip ratio	At Risk	1	100.0%	20	50.0%	0.614
	Average	0	0.0%	15	37.5%	
	Excellent	0	0.0%	5	12.5%	
Total Cholesterol	Normal	1	100.0%	33	82.5%	0.646
	Increased	0	0.0%	7	17.5%	
Triglycerides	Normal	0	0.0%	23	57.5%	0.252
	Increased	1	100.0%	17	42.5%	
LDL	Normal	1	100.0%	34	85.0%	0.675
	Increased	0	0.0%	6	15.0%	
HDL	Reduced	0	0.0%	15	37.5%	0.720
	Normal	1	100.0%	24	60.0%	
	Increased	0	0.0%	1	2.5%	

There was no significant association between CIMT grade and various parameters such as Age, BMI, WHR, TC, TG, LDL and HDL in control group.

Table 24: Association between CIMT grade and various parameters in Prediabetics group

		CIMT				P value
		Abnormal		Normal		
		Count	%	Count	%	
Age	<30 years	1	14.3%	5	14.7%	0.621
	31 to 40 years	2	28.6%	16	47.1%	
	> 40 years	4	57.1%	13	38.2%	
BMI	Underweight (<18.5)	1	14.3%	0	0.0%	0.135
	Normal (18.5 to 24.9)	1	14.3%	10	29.4%	
	Overweight (25 to 29.9)	3	42.9%	16	47.1%	
	Class I obesity (30 to 34.9)	1	14.3%	7	20.6%	
	Class III obesity (>40)	1	14.3%	1	2.9%	
Waist Hip ratio	At Risk	4	57.1%	17	50.0%	0.889
	Average	2	28.6%	13	38.2%	
	Excellent	1	14.3%	4	11.8%	
Total Cholesterol	Normal	6	85.7%	25	73.5%	0.494
	Increased	1	14.3%	9	26.5%	
Triglycerides	Normal	2	28.6%	16	47.1%	0.369
	Increased	5	71.4%	18	52.9%	
LDL	Normal	6	85.7%	29	85.3%	0.977
	Increased	1	14.3%	5	14.7%	
HDL	Reduced	2	28.6%	17	50.0%	0.517
	Normal	3	42.9%	12	35.3%	
	Increased	2	28.6%	5	14.7%	

There was no significant association between CIMT grade and various parameters such as age, BMI, WHR, TC, TG, LDL and HDL in Prediabetics group.

Table 25: Association between ABI grade and various parameters in Control group

		ABI						P value
		Acceptable		Normal		Some		
		Count	%	Count	%	Count	%	
Age	<30 years	2	9.5%	4	26.7%	1	20.0%	0.463
	31 to 40 years	9	42.9%	7	46.7%	1	20.0%	
	> 40 years	10	47.6%	4	26.7%	3	60.0%	
BMI	Underweight (<18.5)	1	4.8%	1	6.7%	0	0.0%	0.308
	Normal (18.5 to 24.9)	10	47.6%	4	26.7%	3	60.0%	
	Overweight (25 to 29.9)	7	33.3%	10	66.7%	1	20.0%	
	Class I obesity (30 to 34.9)	3	14.3%	0	0.0%	1	20.0%	
	Class III obesity (>40)	0	0.0%	0	0.0%	0	0.0%	
WHR	At Risk	10	47.6%	8	53.3%	3	60.0%	0.882
	Average	9	42.9%	5	33.3%	1	20.0%	
	Excellent	2	9.5%	2	13.3%	1	20.0%	
Total Cholesterol	Normal	18	85.7%	13	86.7%	3	60.0%	0.347
	Increased	3	14.3%	2	13.3%	2	40.0%	
Triglycerides	Normal	12	57.1%	8	53.3%	3	60.0%	0.958
	Increased	9	42.9%	7	46.7%	2	40.0%	
LDL	Normal	18	85.7%	13	86.7%	4	80.0%	0.934
	Increased	3	14.3%	2	13.3%	1	20.0%	
HDL	Reduced	7	33.3%	7	46.7%	1	20.0%	0.478
	Normal	14	66.7%	7	46.7%	4	80.0%	
	Increased	0	0.0%	1	6.7%	0	0.0%	

There was no significant association between ASI grade and various parameters such as age, BMI, WHR, TC, TG, LDL and HDL in control group.

Table 26: Association between ABI grade and various parameters in Prediabetic group

		ABI								P value
		Acceptable		Moderate		Normal		Some		
		Count	%	Count	%	Count	%	Count	%	
Age	<30 years	0	0.0%	0	0.0%	4	23.5%	2	22.2%	0.628
	31 to 40 years	5	45.5%	2	50.0%	7	41.2%	4	44.4%	
	> 40 years	6	54.5%	2	50.0%	6	35.3%	3	33.3%	
BMI	Underweight (<18.5)	0	0.0%	1	25.0%	0	0.0%	0	0.0%	0.078
	Normal (18.5 to 24.9)	3	27.3%	1	25.0%	4	23.5%	3	33.3%	
	Overweight (25 to 29.9)	5	45.5%	2	50.0%	10	58.8%	2	22.2%	
	Class I obesity (30 to 34.9)	3	27.3%	0	0.0%	3	17.6%	2	22.2%	
	Class III obesity (>40)	0	0.0%	0	0.0%	0	0.0%	2	22.2%	
WHR	At Risk	9	81.8%	1	25.0%	7	41.2%	4	44.4%	0.200
	Average	1	9.1%	2	50.0%	7	41.2%	5	55.6%	
	Excellent	1	9.1%	1	25.0%	3	17.6%	0	0.0%	
Total Cholesterol	Normal	10	90.9%	3	75.0%	13	76.5%	5	55.6%	0.338
	Increased	1	9.1%	1	25.0%	4	23.5%	4	44.4%	
Triglycerides	Normal	5	45.5%	1	25.0%	11	64.7%	1	11.1%	0.057
	Increased	6	54.5%	3	75.0%	6	35.3%	8	88.9%	
LDL	Normal	10	90.9%	4	100.0%	15	88.2%	6	66.7%	0.310
	Increased	1	9.1%	0	0.0%	2	11.8%	3	33.3%	
HDL	Reduced	5	45.5%	1	25.0%	9	52.9%	4	44.4%	0.960
	Normal	4	36.4%	2	50.0%	5	29.4%	4	44.4%	
	Increased	2	18.2%	1	25.0%	3	17.6%	1	11.1%	

There was no significant association between ABI grade and various parameters such as age, BMI, WHR, TC, TG, LDL and HDL in Prediabetics group.

DISCUSSION

DISCUSSION

BMI (body mass index) and WHR (waist hip ratio):

Mean BMI in control group was 25.5 ± 3.4 and in pre diabetes group was 27.1 ± 5.3. In the Control group 4.9% were underweight, 43.9% were overweight and 9.8% had Class I obesity others (41.4%) where within normal limits. Similarly in Pre diabetics group 2.4% were Underweight, 46.3% were overweight, 19.5% were Class I Obese and 4.9% were class III obese rest (29.3%) were within normal limit. There was no significant difference in BMI classification between two groups.

In Control group among female gender, majority of them were overweight (52.9%) and among males majority of them had normal BMI (54.2%). In Prediabetics group among both female and male genders, majority of them were overweight 47.1% and 45.8%.

Mean waist hip ratio in control and pre diabetic group was 1.0 ± 0.2. In the control group among females 58.8% and among males 45.8% were at risk with respect to Waist Hip ratio and among pre diabetics subjects 76.5% of females and 33.3% of males were at risk. There was no significant difference observed in control group, were as significant difference was observed in pre diabetics group.

In Dewan S. Alam et al. Both overweight and abdominal obesity contribute to the hidden public health threat of undiagnosed diabetes and pre-diabetes. Awareness raising and screening of high risk groups combined with a tailored approach are essential for halting the epidemic of diabetes and pre-diabetes.

LIPID PROFILE:

Total cholesterol in control and prediabetes was 182.1±48mg/dl and 190.5±58.4mg/dl, triglycerides in control 167.1±43.7mg/dl and prediabetes 169.8±64.5mg/dl, LDL levels in control 118.9±33.8mg/dl and prediabetes 102.7±40.8mg/dl. HDL in control and prediabetes was 38.4±7.6, 38.9+13.8 respectively

In Subodh Kansal et al[100]. Mean value of total cholesterol for cases (184.75 ± 46.02 mg/dL) was more than controls (170.99 ± 38.27 mg/dL). mean value of LDL for case (120.39 ± 38.34 mg/dL) was more than controls (99.84 ± 29.57 mg/dL) mean value of HDL for male case (36.12 ± 6.44 mg/ dL) was lower than male controls (41.16 ± 6.58 mg/dL). Mean value of triglyceride for case (139.5 ± 47.24 mg/dL) was higher than controls (106.81 ± 61.97 mg/dL).

Similarly in Williams et al. studied data from National Health and Nutrition Examination Survey done in 1999-2000(NHANES). The mean total cholesterol of the Prediabetic subjects was higher (174.2mg/dl) than the controls (157.5mg/dl).

In Kumar M et al[101]. mean LDL cholesterol was significantly higher in prediabetes subjects than controls (116.95 mg/dL of cases vs. 95.62 mg/dL of control) triglycerides-high density lipoprotein cholesterol concentration (TG/HDL) ratio was higher in prediabetes subject than in controls (4.30 of cases vs. 2.77 of controls).

CIMT:

In the control group 2.4% had abnormal CIMT and in pre diabetic group 17.1% had abnormal CIMT. This difference in CIMT findings between two groups was statistically significant. Odds ratio for pre diabetics for CIMT was 8.235 (1 – 70.31). I.e. pre diabetics are at 8 times higher risk of developing grade 1 CIMT than controls.

There was no significant association between abnormal CIMT and various parameters such as Age, BMI, WHR, TC, TG, LDL and HDL in Prediabetes group, but increasingly abnormal CMIT was seen with increasing age, obesity, abnormal lipid profile.

In Altin et al [102]Both CIMT and EFT(epicardial fat thickness) was significantly greater in patients with prediabetes compared with controls (0.81 ± 0.20 mm vs 0.68 ± 0.16 mm,P< .001 and 7.0 ± 2.0 mm vs 5.6 ± 1.6 mm,P< .001, respectively). This difference was mainly attributed to patients with IGT. Age, waist circumference, and 2-hour glucose independently predicted CIMT, while 2-hour glucose was the only independent predictor of EFT in multivariate analysis among other relevant parameters for CIMT and EFT.

In Parildar H et al[103]. CIMT were statistically higher among Prediabetics compared to control group. There was a positive, significant correlation between left, right, maximum CIMT and fasting blood glucose, HbA1c, Hs-CRP levels and BMI. CIMT was also positively correlated with BMI. Obesity is an important risk factor for cardio metabolic disorders.

In Sengul et al[104]. The EFT (Echocardiographic epicardial fat thickness) and CIMT were also increased significantly in patients with MetS compared to controls (7.2 ± 2 mm vs. 5.7 ± 1.9 mm; P = 0.001, 0.74 ± 0.1 mm vs. 0.59 ± 0.1 mm; P < 0.01, respectively). The waist circumference, total and LDL-cholesterol, fasting glucose, triglycerides, systolic and diastolic blood pressure levels, hs-CRP, and homeostasis model assessment index for insulin resistance (HOMA-IR) were significantly increased in patients with Metabolic syndrome.

ABI:

In Control subjects who had abnormal CIMT, had Normal ABI. In subjects with normal CIMT, 52.5% had acceptable, 35% had normal and 12.5% had some ABI grade respectively. There was no significant association between abnormal CIMT and ABI in control group.

In Prediabetics subjects who had Grade 1 CIMT, 14.3% had acceptable, 28.6% had moderate and 57.1% had some ABI grade. In subjects with normal CIMT, 29.4% had acceptable, 5.9% had moderate, 50% had normal and 14.7% had some ABI grade respectively.

There was significant association between ABI grade and CIMT grade in Prediabetics group.

In Kasliwal RR et al[105]. Presence of significant correlation between carotid intima-media thickness and brachial-ankle pulse wave velocity in patients with coronary artery disease but absence of the same in individuals without major atherosclerotic vascular disease suggests that the correlation between carotid intima-media thickness and brachial-ankle pulse wave velocity becomes stronger with increasing extent of atherosclerosis.

In Doobay et al[106]. The sensitivity and specificity of a low ankle-brachial index to predict incident coronary heart diseases were 16.5% and 92.7%, for incident stroke were 16.0% and

92.2%, and for cardiovascular mortality were 41.0% and 87.9%, respectively. The corresponding positive likelihood ratios were 2.53 (95% CI, 1.45 to 4.40) for coronary heart disease, 2.45 (95% CI, 1.76 to 3.41) for stroke, and 5.61 (95% CI, 3.45 to 9.13) for cardiovascular death. The specificity of a low ankle-brachial index to predict future cardiovascular outcomes is high, but its sensitivity is low. The ankle-brachial index should become part of the vascular risk assessment among selected individuals.

Leng GC et al [107.] Baseline 90 (5.7%) of subjects had an ankle brachial pressure index < or = 0.7, 288 (18.2%) had an index < or = 0.9, and 566 (35.6%) < or = 1.0. After five years subjects with an index < or = 0.9 at baseline had an increased risk of non-fatal myocardial infarction (relative risk 1.38, 95% confidence interval 0.88 to 2.16), stroke (1.98, 1.05 to 3.77), cardiovascular death (1.85, 1.15 to 2.97), and all-cause mortality (1.58, 1.14 to 2.18) after adjustment for age, sex, coronary disease, and diabetes at baseline. The ability to predict subsequent events was greatly increased by combining the index with other risk factors--for example, hypertensive smokers with normal cholesterol concentrations had a positive predictive value of 25.0%, increasing to 43.8% in subjects with a low index and decreasing to 15.6% in those with a normal index.

The ankle brachial pressure index is a good predictor of subsequent cardiovascular events, and improves on predictions by conventional risk factors alone. It is simple and accurate and could be included in routine screening of cardiovascular status.

SUMMARY

SUMMARY

This study was conducted in R. L. Jalappa hospital and research centre Tamaka, Kolar,
82 patients were studied out of which 41 Prediabetic, 41 with normal glycemic control, age and gender matched. 58.5% were males and 41.5% were females in both group.

Mean age of subjects in controls was 38.5 ± 7.4 years and in Pre diabetes was 38.8 ± 7.1 years.

In control group 31.7% and in pre diabetes group 46.3% had family history of diabetes.
Mean BMI in control group was 25.5 ± 3.4 and in pre diabetes group was 27.1 ± 5.3. In the Control group 4.9% were underweight, 43.9% were overweight and 9.8% had Class I obesity. Similarly in Pre diabetics group 2.4% were Underweight, 46.3% were overweight, 19.5% were Class I Obese and 4.9% were class III obese.

In Control group among female gender, majority of them were overweight (52.9%) and among males majority of them had normal BMI (54.2%).
In the control group among females 58.8% and among males 45.8% were at risk with respect to Waist Hip ratio and among pre diabetics subjects 76.5% of females and 33.3% of males were at risk.

Total cholesterol in control and prediabetes was 182.1±48mg/dl and 190.5±58.4mg/dl, triglycerides in control 167.1±43.7mg/dl and prediabetes 169.8±64.5mg/dl, LDL levels in control 118.9±33.8mg/dl and prediabetes 102.7±40.8mg/dl. HDL in control and prediabetes was 38.4±7.6, 38.9+13.8 respectively

Were as in control group 36.6% had reduced HDL and in Pre diabetics 46.3% had reduced HDL.

In the control group none of the subjects had albuminuria, were as in pre diabetic group 14.6% had 1+ albuminuria and 2.4% had 2+ albuminuria.

In control group 51.2% had acceptable ABI, 36.6% had Normal and 12.2% had some ABI grading. In pre diabetic group 26.8% had acceptable, 9.8% had moderate, 41.5% had normal and 22% had some ABI grading.

In the control group 2.4% had abnormal CIMT and in pre diabetic group 17.1% had abnormal CIMT.

This difference in CIMT findings between two groups was statistically significant. Odds ratio for pre diabetics for CIMT was 8.235. I.e. pre diabetics are at 8 times higher risk of developing abnormal CIMT than controls. In Control subjects who had abnormal CIMT, all of them had Normal ABI. In subjects with normal CIMT, 52.5% had acceptable, 35% had normal and 12.5% had some ABI grade respectively.

In Prediabetic subjects who had abnormal CIMT, 14.3% had acceptable, 28.6% had moderate and 57.1% had some ABI grade. In subjects with normal CIMT, 29.4% had acceptable, 5.9% had moderate, 50% had normal and 14.7% had some ABI grade respectively. There was significant association between ABI grade and CIMT grade in Prediabetic group.

Since measurement of CIMT and ABI is non-invasive, it may prove to be a useful tool both in diagnosing potential problems, but also in monitoring treatment and their outcomes specially in Prediabetes.

In a word use of the concept of Prediabetes can be useful tool for intervention to prevent both macrovascular and microvascular disease in clinical and public health spheres.

Considering the conflicting outcomes of different studies it is suggested that further research is required in larger number of patients to find out the interrelationship and contribution of various risk factors for atherosclerosis in prediabetes patients.

Thus we can conclude that CIMT and ABI in prediabetes should be included as a routine investigation due to its non-invasive nature and its utility in detecting atherosclerosis at subclinical stage which will finally help in cardiovascular risk reduction in Prediabetes.

Lifestyle modification should be adopted to prevent the conversion of Prediabetes into Type 2 Diabetes Mellitus

CONCLUSION

CONCLUSION

It is a comparative study comprising of 82 patients out of which 41 are prediabetes study group and 41 normoglycemic control group.

CIMT and ABI which are non-invasive marker of atherosclerosis is abnormal in Prediabetic study group when compared to normoglycemic control group.

Dyslipidaemia was a feature in Prediabetic group with increased triglycerides levels, HDL where significantly reduced in Prediabetic group.

BMI. TGL, Total cholesterol level, family history of diabetes were recognised as risk factor for Prediabetes.

Through our study we can summarise that CIMT and ABI being a non-invasive marker of subclinical atherosclerosis should be routinely used to diagnose potential problems and treatment outcomes in patient diagnosed with prediabetes and lifestyle modification should be adopted to prevent the conversion of Prediabetes into Type 2 Diabetes Mellitus.

BIBLIOGRAPHY

BIBILOGRAPHY

1. Alvin c.powers. Harrisons Principles of internal medicine 18th edition chapter 344 pg 2968 Diabetes mellitus peter Libby, chapter 241 pg1983 The pathogenesis, prevention, and treatment of atherosclerosis peter Libby.
2. Abbott RD, Donahue RP, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA. 1988;260(23):3456-60.
3. Sibal L, Aldibbiat A, Agarwal SC, et al.Circulating endothelial progenitor cells, endothelial function, carotid intima-media thickness and circulating markers of endothelial dysfunction in people with type 1 diabetes without macrovascular disease or microalbuminuria. Diabetologia. 2009;52(8):1464-73.
4. Kahn SE, Prigeon RL, McCulloch DK, et al.Quantification of the relationship between insulin sensitivity and beta-cell function in human subjects:Evidence for a hyperbolic function. Diabetes. 1993;42(11):1663-72.
5. Sacca L,Orofino G,Petrone A,Vigorito C.Differential roles of splanchnic and peripheral tissues in the pathogenesis of impaired glucose tolerance.J Clin Invest. 1984;73(6): 1683–1687.
6. Epidemiology of Diabetes Interventions and Complications (EDIC) research group Effect of intensive diabetes treatment on carotid artery wall thickness in the epidemiology of diabetes interventions and complications. Diabetes. 1999;48(2):383-90.
7. Djaberi R, Schuijf JD, De Koning EJ, et al. Usefulness of carotid intima media thickness in patient with diabetes mellitus as predictor of coronary artery disease.Am J Cardiol.2009;104(8):1041-1046.

8. Bernard S, Serusclat A, Targe F, et al. Incremental Predictive Value of Carotid Ultrasonography in the Assessment of Coronary Risk in a Cohort of Asymptomatic Type 2 Diabetic Subjects. Diabetes Care. 2005;28 (5): 1158-1162.
9. Folsom AR, Kronmal RA, Detrano RC, et al. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA).Arch Intern Med. 2008;168(12):1333-9.
10. Cao JJ, Arnold AM , Manolio TA ,et al. Association of Carotid Artery Intima-Media Thickness, Plaques, and C-Reactive Protein With Future Cardiovascular Disease and All-Cause Mortality :The Cardiovascular Health Study. Circulation. 2007;116(1):32-38.
11. Hodis HN, Mack WJ, LaBree L, Selzer RH, et al. The role of carotid arterial intima-media thickness in predicting clinical coronary events. Ann Intern Med. 1998;128(4):262-9.
12. Alberti KG.Screening and diagnosis of prediabetes: where are we headed? Diabetes Obes Metab. 2007;9 Suppl 1:12-6.
13. World health organization. WHO Expert committee on Diabetes Mellitus second report. World Health Organ Tech Reo Ser 1980;646:1-80.
14. American Diabetes Association Diagnosis and classification of diabetes mellitus. Diabetes Care 2005;28 Suppl 1:s37-42.
15. World Health Organization. Definition and Diagnosis of diabetes Mellitus and Intermediate Hyperglycemia: Report of a WHO/IDF consultation. Geneva: World Health Organization, 2006.

16. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;3 suppl 1:S62-9.
17. Tirosh A, Shai I,Tekes-Manova D,Pereg D,et al.The Israeli Diabetes Research Group: Normal Fasting Plasma Glucose Levels and Type 2 Diabetes in Young Men.N Engl J Med 2005; 353:1454-1462.
18. Dinneen SF, Maldonado D 3rd, Leibson CL, Klee GG, Li H, Melton LJ 3rd, Rizza RA. Effects of changing diagnostic criteria on the risk of developing diabetes. Diabetes Care. 1998;21(9):1408-13.
19. Meigs JB, Muller DC, Nathan DM, Blake DR, Andres R. The natural history of progression from normal glucose tolerance to type 2 diabetes in the Baltimore Longitudinal Study of Aging. Diabetes. 2003;52(6):1475-84.
20. Dinneen S, Gerich J, Rizza R. Carbohydrate metabolism in non-insulin-dependent diabetes mellitus. N Engl J Med. 1992;327(10):707-13.
21. National Diabetes Data Group. Classification and Diagnosis of Diabetes Mellitus and Other Categories of Glucose Intolerance. Diabetes 1979; 28(12): 1039-1057.
22. Cowie CC, Rust KF, Ford ES, Eberhardt MS, Byrd-Holt DD, et al. Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. Diabetes Care. 2009;32(2):287-94.
23. The DECODE Study Group. Age- and Sex-Specific Prevalence of Diabetes and Impaired Glucose Regulation in 13 European Cohorts. Diabetes Care 2003; 26(1): 61-69.
24. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM,et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.

25. Ferrannini E, Gastaldelli A, Iozzo P. Pathophysiology of prediabetes. Med Clin North Am. 2011;95(2):327-39.
26. Gerstein HC, Santaguida P, Raina P, Morrison KM, Balion C, et al. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies.Diabetes Res Clin Pract. 2007;78(3):305-12.
27. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, et al. Impaired Fasting Glucose and Impaired Glucose Tolerance. Diabetes Care 2007; 30(3): 753-759.
28. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2002; 25: s5-s20.
29. Harris M, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998;21(4):518-24.
30. The International Expert Committee. International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes. Diabetes Care. 2009; 32(7): 1327-1334.
31. Ackermann RT, Cheng YJ, Williamson DF, Gregg EW. Identifying adults at high risk for diabetes and cardiovascular disease using hemoglobin A1c National Health and Nutrition Examination Survey 2005-2006. Am J Prev Med. 2011;40(1):11-7.
32. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement (erratum in: Circulation 2005;112:e297–8). Circulation 2005;112:2735–52.

33. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120:1640 –5.
34. Deng Y, Scherer PE. Adipokines as novel biomarkers and regulators of the metabolic syndrome. Ann N Y Acad Sci 2010;1212:E1–19.
35. Reaven GM. Insulin resistance, the insulin resistance syndrome, and cardiovascular disease. Panminerva Med 2005;47:201–10.
36. Hanley AJ, Wagenknecht LE, D'Agostino RB Jr., Zinman B, Haffner SM. Identification of subjects with insulin resistance and beta-cell dysfunction using alternative definitions of the metabolic syndrome.Diabetes 2003;52:2740 –7.
37. Bianchi C, Miccoli R, Bonadonna RC, et al., for the GENFIEV Investigators. Metabolic syndrome in subjects at high risk for type 2 diabetes: the genetic, physiopathology and evolution of type 2 diabetes (GENFIEV) study. Nutr Metab Cardiovasc Dis 2011;21:699 –705.
38. Zidek W, Schrader J, Lüders S, et al. First-line antihypertensive treatment in patients with pre-diabetes: rationale, design and baseline results of the ADaPT investigation. Cardiovasc Diabetol 2008;7:22.
39. Alexander CM, Landsman PB, Teutsch SM, Haffner SM. NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. Diabetes. 2003;52(5):1210-4.

40. Kannel WB, McGee DL. Diabetes and Glucose Tolerance as Risk Factors for Cardiovascular Disease: The Framingham Study.Diabetes Care 1979; 2(2): 120-126.
41. Turner RC,Millns H,Stratton IM,Matthews DR. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom prospective diabetes study (UKPDS: 23). BMJ. 1998; 316(7134): 823–828.
42. Sharma M,Ganguly NK. Premature Coronary Artery Disease in Indians and its Associated Risk Factors. Vasc Health Risk Manag. 2005; 1(3): 217–225.
43. Enas EA. Coronary artery disease epidemic in Indians: a cause for alarm and call for action. J Indian Med Assoc. 2000;98(11):694-5.
44. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M,et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study.Lancet. 2004;364(9438):937-52.
45. Liviakis L, Pogue B, Paramsothy P, Bourne A, Gill EA. Carotid intima-media thickness for the practicing lipidologist. J Clin Lipidol. 2010;4(1):24-35.
46. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging.Circulation. 1986;74(6):1399-406.
47. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease.Arterioscler Thromb 1991;11:1245-9.
48. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. J Am Soc Echocardiogr. 2008;21(2):93-111.

49. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, et al. Mannheim carotid intima-media thickness and plaque consensus (2004-2006-2011). Cerebrovasc Dis. 2012;34(4):290-6.
50. Ballantyne CM. Clinical Lipidology:A companion to Braunwald's heart disease. 1st ed. Saunders Elsevier Publication;2008. P. 608.
51. Jacoby DS, Mohler,ER, Rader DJ. Noninvasive atherosclerosis imaging for predicting cardiovascular events and assessing therapeutic interventions Curr Atheroscler Rep (2004) 6: 20.
52. Hansa G, Bhargava K, Bansal M, Tandon S, Kasliwal RR. Carotid intima-media thickness and coronary artery disease: an Indian perspective. Asian Cardiovasc Thorac Ann. 2003;11(3):217-21.
53. O'Leary DH, Bots ML. Imaging of atherosclerosis: carotid intima-media thickness. Eur Heart J. 2010;31(14):1682-9.
54. Crouse JR 3rd, Tang R, Espeland MA, Terry JG, Morgan T, Mercuri M. Associations of extracranial carotid atherosclerosis progression with coronary status and risk factors in patients with and without coronary artery disease. Circulation. 2002;106(16):2061-6.
55. Lorenz MW, von Kegler S, Steinmetz H, Markus HS, Sitzer M. Carotid intima-media thickening indicates a higher vascular risk across a wide age range: prospective data from the Carotid Atherosclerosis Progression Study (CAPS). Stroke. 2006;37(1):87-92.
56. Kablak-Ziembicka A, Tracz W, Przewlocki T, Pieniazek P, Sokolowski A, Konieczynska M. Association of increased carotid intima-media thickness with the extent of coronary artery disease.Heart.2004; 90:1286-90.

57. Crouse JR 3rd, Raichlen JS, Riley WA, Evans GW, Palmer MK, O'Leary DH, et al. Effect of rosuvastatin on progression of carotid intima-media thickness in low-risk individuals with subclinical atherosclerosis: the METEOR Trial. JAMA. 2007;297(12):1344-53.
58. Cobble M, Bale B. Carotid intima-media thickness: knowledge and application to everyday practice. Postgrad Med. 2010;122(1):10-8.
59. Karason K, Wikstrand J, Sjöström L, Wendelhag I. Weight loss and progression of early atherosclerosis in the carotid artery: a four-year controlled study of obese subjects. Int J Obes Relat Metab Disord. 1999;23(9):948-56.
60. Wu H, Dwyer KM, Fan Z, Shircore A, Fan J, Dwyer JH. Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study. Am J Clin Nutr. 2003;78(6):1085-91.
61. Nordstrom CK, Dwyer KM, Merz CN, Shircore A, Dwyer JH. Leisure time physical activity and early atherosclerosis: the Los Angeles Atherosclerosis Study .Am J Med. 2003;115(1):19-25.
62. Sibal L, Agarwal SC,Home PD. Carotid intima-media thickness as a surrogate marker of cardiovascular disease in diabetes. Diabetes Metab Syndr Obes. 2011; 4: 23–34.
63. Lakka TA, Laukkanen JA, Rauramaa R, Salonen R, Lakka HM, Kaplan GA, Salonen JT. Cardiorespiratory fitness and the progression of carotid atherosclerosis in middle-aged men. Ann Intern Med. 2001;134(1):12-20.
64. Gepner AD, Korcarz CE, Aeschlimann SE, LeCaire TJ, Palta M, Tzou WS, Stein JH. Validation of a carotid intima-media thickness border detection program for use in an office setting. J Am Soc Echocardiogr. 2006;19(2):223-8.

65. Iglesias del Sol A,Bots ML,Grobbee DE, Hofman A, Witteman JCM.Carotid intima-media thickness at different sites: relation to incident myocardial infarction:The Rotterdam Study.Eur Heart J 2002;23:934-40.
66. Joshi SR. Indian Diabetes Risk Score. J Assoc Physicians India. 2005;53:755-7.
67. Joshi SR. Sub clinical diabetes--vascular threat to Asian Indians. J Assoc Physicians India. 2003;51:756-7.
68. Gerstein HC, Miller HC, Byington RP, Goff DC, Bigger T, et al. Effects of Intensive Glucose Lowering in Type 2 Diabetes.N Engl. J Med.2008;2545-99.
69. Rema M, Mohan V, Deepa R, Ravikumar R. Association of carotid intima-media thickness and arterial stiffness with diabetic retinopathy: the Chennai Urban Rural Epidemiology Study (CURES-2). Diabetes Care. 2004;27(8):1962-7.
70. Modi N, Kapoor A, Kumar S, Tewari S, Garg N, Sinha N. Utility of carotid intimal medial thickness as a screening tool for evaluation of coronary artery disease in pre-transplant end stage renal disease.J Postgrad Med. 2006;52(4):266-70.
71. Mahajan V, Handa R, Kumar U, Sharma S, Gulati G, Pandey RM, Lakshmy R. Assessment of atherosclerosis by carotid intimomedial thickness in patients with rheumatoid arthritis. Assoc Physicians India. 2008;56:587-90.
72. Madhuri V, Chandra S, Jabbar A. Age associated increase in intima media thickness in adults. Indian J Physiol Pharmacol. 2010;54(4):371-5.
73. Kasliwal RR, Bansal M, Gupta H, Agrawal S. Association of carotid intima-media thickness with left main coronary artery disease. Indian Heart J. 2007;59(1):50-5.
74. Kurihara o,Takano m, Yamamoto m,Shirakabe m,Kimata n,et al. Impact of Prediabetic Status on Coronary Atherosclerosis: A multivessel angioscopic study. Diabetes Care 36:729–733, 2013.

75. Andrea L.C. Schneider, Rita R. Kalyani, Sherita Golden, Sally C et al Diabetes Care May 2016, 39 (5) 772-779.
76. Winsor T. Influence of arterial disease on the systolic blood pressure gradients of the extremity. Am J Med Sci. 1950;220:117–126.
77. Smith FB, Lee AJ, Price JF, van Wijk MC, Fowkes FG. Changes in ankle brachial index in symptomatic and asymptomatic subjects in the general population. J Vasc Surg. 2003;38:1323–1330.
78. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, Browner D. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med. 1992;326:381–386.
79. McDermott MM, Guralnik JM, Tian L, Liu K, Ferrucci L, Liao Y, Sharma L, Criqui MH. Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year follow-up: the WALCS (Walking and Leg Circulation Study). J Am Coll Cardiol. 2009;53:1056 –1062.
80. Ankle Brachial Index Collaboration, Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, et al . Ankle brachial index combined with Framingham risk score to predict cardiovascular events and mortality: a meta-analysis. JAMA. 2008;300:197–208.
81. Safar ME, Protogerou AD, Blacher J. Statins, central blood pressure, and blood pressure amplification. Circulation. 2009;119:9 –12.
82. Tsamis A, Stergiopulos N. Arterial remodeling in response to hypertension using a constituent-based model. Am J Physiol Heart Circ Physiol. 2007;293:H3130–H3139.

83. Humphrey JD. Mechanisms of arterial remodeling in hypertension: coupled roles of wall shear and intramural stress. Hypertension. 2008; 52:195–200.
84. Katz S, Globerman A, Avitzour M, Dolfin T. The ankle-brachial index in normal neonates and infants is significantly lower than in older children and adults. J Pediatr Surg. 1997;32:269 –271.
85. Zheng ZJ, Rosamond WD, Chambless LE, Nieto FJ, Barnes RW,Hutchinson RG, Tyroler HA, Heiss G; ARIC Investigators. Lower extremity arterial disease assessed by ankle-brachial index in a middle-aged population of African Americans and whites: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Prev Med. 2005; 29(suppl 1):42– 49.
86. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999 –2000. Circulation. 2004;110: 738–743.
87. Newman AB, Siscovick DS, Manolio TA, Polak J, Fried LP, Borhani NO, Wolfson SK. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study: Cardiovascular Heart Study (CHS) Collaborative Research Group. Circulation. 1993;88:837– 845.
88. Allison MA, Criqui MH, McClelland RL, Scott JM, McDermott MM,Liu K, et al. The effect of novel cardiovascular risk factors on the ethnic-specific odds for peripheral arterial disease in the Multi-Ethnic Study of Atherosclerosis (MESA). J Am Coll Cardiol. 2006;48:1190 –1197.

89. Zheng ZJ, Sharrett AR, Chambless LE, Rosamond WD, Nieto FJ, Sheps DS, Dobs A, Evans GW, Heiss G. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. Atherosclerosis. 1997;131:115–125.
90. Newman AB, Shemanski L, Manolio TA, Cushman M, Mittelmark M, Polak JF, Powe NR, Siscovick D. Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study: the Cardiovascular Health Study Group. Arterioscler Thromb Vasc Biol. 1999;19:538 –545.
91. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al . Peripheral arterial disease detection,awareness, and treatment in primary care. JAMA. 2001;286:1317–1324.
92. Leng GC, Fowkes FG, Lee AJ, Dunbar J, Housley E, Ruckley CV. Use of ankle brachial pressure index to predict cardiovascular events and death: a cohort study. BMJ. 1996;313:1440 –1444.
93. Hooi JD, Kester AD, Stoffers HE, Rinkens PE, Knottnerus JA, van Ree JW. Asymptomatic peripheral arterial occlusive disease predicted cardiovascular morbidity and mortality in a 7-year follow-up study. J Clin Epidemiol. 2004;57:294 –300.
94. Ogren M, Hedblad B, Isacsson SO, Janzon L, Jungquist G, Lindell SE. Non-invasively detected carotid stenosis and ischaemic heart disease in men with leg arteriosclerosis. Lancet. 1993;342:1138 –1141.
95. van der Meer IM, Bots ML, Hofman A, del Sol AI, van der Kuip DA, Witteman JC. Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. Circulation. 2004;109:1089 –1094.

96. Weatherley BD, Nelson JJ, Heiss G, Chambless LE, Sharrett AR, Nieto FJ, Folsom AR, Rosamond WD. The association of the ankle-brachial index with incident coronary heart disease: the Atherosclerosis Risk in Communities (ARIC) study, 1987–2001. BMC Cardiovasc Disord. 2007:3.
97. Kornitzer M, Dramaix M, Sobolski J, Degre S, De Backer G. Ankle/arm pressure index in asymptomatic middle-aged males: an independent predictor of ten-year coronary heart disease mortality. Angiology. 1995; 46:211–219.
98. Abbott RD, Petrovitch H, Rodriguez BL, Yano K, Schatz IJ, Popper JS, Masaki KH, Ross GW, Curb JD. Ankle/brachial blood pressure in men 70 years of age and the risk of coronary heart disease. Am J Cardiol. 2000;86:280 –284.
99. Resnick HE, Lindsay RS, McDermott MM, Devereux RB, Jones KL, Fabsitz RR, Howard BV. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. Circulation. 2004;109:733–739.
100. Subodh Kansal, TK Kamble. Lipid Profile in Prediabetes.JAPI. 2016; 64
101. Kumar M, Singh PS, Zafar KS, et al. A study of lipid profile in prediabetes. J. Evid. Based Med. Healthc. 2016; 3(44), 2208-2212.
102. Altin C, Sade LE, Gezmis E, Ozen N, Duzceker O, Bozbas H, Eroglu S, Muderrisoglu H. Assessment of Subclinical Atherosclerosis by Carotid Intima-Media Thickness and Epicardial Adipose Tissue Thickness in Prediabetes. Angiology. 2016 Apr 10.
103. Parildar H,Gulmez O,Cigerli O,Unal AD,et al . Carotid Artery Intima Media Thickness and HsCRP; Predictors for Atherosclerosis in Prediabetic Patients? Pak J Med Sci. 2013; 29(2): 495–499.
104. Sengul C, Cevik C, Ozveren O, Oduncu V, Sunbul A, Akgun T, Can MM, Semiz E, Dindar I.Echocardiographic epicardial fat thickness is associated with carotid intima-

media thickness in patients with metabolic syndrome. . Echocardiography. 2011 Sep;28(8):853-8.

105. Kasliwal RR, Bansal M, Bhargava K, Gupta H, Tandon S, Agrawal V. Carotid intima-media thickness and brachial-ankle pulse wave velocity in patients with and without coronary artery disease.Indian Heart J. 2004;56(2):117-22.

106. Doobay AV, Anand SS. Sensitivity and specificity of the ankle-brachial index to predict future cardiovascular outcomes: a systematic review. Arterioscler Thromb Vasc Biol. 2005;25(7):1463-9.

107. Leng GC, Fowkes FG, Lee AJ, Dunbar J, Housley E, Ruckley CV. Use of ankle brachial pressure index to predict cardiovascular events and death: a cohort study. BMJ. 1996;313(7070):1440-4.

108. Grant EG, Benson CB, Moneta GL, et al. Carotid artery stenosis: grayscale and Doppler ultrasound diagnosis--Society of Radiologists in Ultrasound consensus conference. Ultrasound Q. 2003 Dec. 19(4):190-8.

ANNEXURE

PROFORMA FOR DATA COLLECTION

NAME: IP NO:

AGE:

SEX:

ADDRESS:

OCCUPATION:

DETAILED HISTORY:

ANTHROPOMETRIC MEASUREMENT:

HEIGHT: WEIGHT:

BODY MASS INDEX:

HIP WAIST RATIO:

GENERAL PHYSICAL EXAMINATION:

PULSE:

BLOOD PRESSURE:

ANKLE BRACIAL INDEX:

SYSTEMIC EXAMINATION:

CARDIOVASCULAR EXAMINATION:

RESPIRATORY EXAMINATION:

PER ABDOMINAL EXAMINATION:

CENTRAL NERVOUS SYSTEM EXAMINATION:

LABORATORY DATA:

1. FASTING PLASMA GLUCOSE:
2. POST PRANDAL PLASMA GLUCOSE:
3. GLYCOSYLATED HEAMOGLOBIN (HBA1C):
4. FASTING LIPID PROFILE:
5. RENAL FUNCTION TESTS:
6. URINE FOR ALBUMINURIA:
7. OTHER TESTS:
8. ECG
9. USG ABDOMEN
10. CIMT MEASUREMENT USING B MODE USG

Master chart of control group- non diabetics

Sl No	hopital number	Age	Sex	BMI	W/H	ABI	FBS	PPBS	HbA1C	Chol	TG	LDL	HDL	albuminuria	ECG	USG abdomen	CIMT	family history of diabetes
1	229073	40	f	27.6	0.94	1.07	88	91	5	177	94	113	45	absent	normal	normal	normal	Absent
2	170950	42	f	31.6	1.08	0.88	75	143	5.2	175	165	105	33	absent	normal	normal	normal	Present
3	230790	26	f	24.4	0.84	0.91	78	104	4.8	249	169	178	37	absent	normal	normal	normal	Present
4	229043	36	m	22	0.82	0.91	71	79	4.8	210	140	137	45	absent	normal	normal	normal	Absent
5	234280	46	f	28.4	0.8	1.03	98	122	5.2	155	145	76	50	absent	normal	fatty liver	normal	Absent
6	231243	45	f	30.9	0.85	1	83	125	5.6	190	228	105	39	absent	normal	fatty liver	normal	Present
7	203028	39	m	27.5	0.8	1.107	78	131	5	124	186	102	41	absent	normal	normal	normal	Present
8	234140	33	m	31.9	1.8	1	88	128	5.5	133	211	90	43	absent	normal	fatty liver	normal	Absent
9	212611	49	m	24.7	1.2	1.01	90	121	5.2	154	156	97	36	absent	normal	normal	normal	Absent
10	181774	38	m	23.7	0.9	1.01	96	134	5.4	198	167	81	45	absent	normal	normal	normal	Absent
11	197189	45	m	23.2	0.9	1	70	124	5.3	156	155	149	40	absent	normal	normal	normal	Absent
12	218621	46	m	24.6	1	0.94	82	98	5	132	178	122	50	absent	normal	normal	normal	Present
13	201894	40	m	26.5	1.4	1.1	80	128	5.1	154	189	123	46	absent	normal	normal	grade 1	Absent
14	212153	30	m	24.4	0.9	1	80	128	5	176	100	92	40	absent	normal	normal	normal	Absent
15	214174	39	m	27.5	1.1	1.003	66	126	4.6	124	186	102	34	absent	normal	fatty liver	normal	Absent
16	219032	38	m	26.6	1.1	1.06	98	134	5.3	143	122	98	28	absent	normal	normal	normal	Absent
17	201496	22	m	22.3	0.9	1.04	80	114	4.2	176	175	96	40	absent	normal	normal	normal	Absent
18	148534	42	m	28.6	1.1	1.015	94	136	5.4	165	146	93	33	absent	normal	normal	normal	Present
19	204812	38	f	24.3	1.4	1.01	78	114	4.1	142	126	78	40	absent	normal	fatty liver	normal	Absent
20	216681	45	f	32.8	1.5	1	78	134	5.2	350	149	198	25	absent	normal	fatty liver	normal	Absent
21	168104	34	m	24.8	1.3	1.01	90	132	5	146	148	119	36	absent	normal	normal	normal	Present
22	187162	49	m	21.8	0.7	1.04	48	136	4.6	145	177	104	34	absent	normal	normal	normal	Absent

23	186135	45	m	24.5	1.1	1.07	94	136	5.5	187	185	146	26	absent	normal	normal	normal	Absent
24	203241	48	m	17.5	0.7	1	63	98	5	188	173	140	50	absent	normal	normal	normal	Absent
25	203216	37	f	22.8	0.8	1.03	90	136	4.4	164	124	78	42	absent	normal	normal	normal	Absent
26	216403	45	f	25.3	1.2	1.03	90	120	5.1	196	228	106	39	absent	normal	normal	normal	Absent
27	237041	35	f	26.42	1.2	1.03	90	136	5.2	252	159	181	31	absent	normal	fatty liver	normal	Present
28	217032	34	m	23.7	0.9	1.01	96	138	5.5	124	187	92	31	absent	normal	normal	normal	Present
29	216486	45	f	25.3	0.85	1	100	127	4.9	251	198	170	30	absent	normal	fatty liver	normal	Absent
30	227125	38	m	27.8	1	1.04	80	128	5	189	137	79	41	absent	normal	normal	normal	Absent
31	223478	23	f	25.5	1.1	1.06	92	130	4.6	148	166	80	34	absent	normal	pcod	normal	Present
32	249586	34	f	27.9	1.2	1.07	88	104	5	248	98	176	32	absent	normal	normal	normal	Absent
33	200916	44	m	20.1	0.85	1.3	74	134	5.2	143	133	126	64	absent	normal	normal	normal	Present
34	209505	48	m	21.5	0.94	1.2	79	156	5	178	187	123	28	absent	normal	normal	normal	Absent
35	235610	36	f	17.9	0.75	1.2	98	124	4.8	178	135	75	32	absent	normal	normal	normal	Absent
36	112291	30	F	24.4	1	1.3	65	166	5.3	155	127	134	44	absent	normal	normal	normal	Present
37	93133	44	F	29.4	1.2	0.9	96	174	5	240	307	139	40	absent	normal	fatty liver	normal	Present
38	236452	26	M	25.5	0.9	1.1	90	132	4.8	147	113	119	35	absent	normal	normal	normal	Absent
39	309393	33	m	28.1	0.94	1.2	64	98	5.1	208	196	129	39	absent	normal	normal	normal	Absent
40	302631	45	f	26.4	0.84	1.2	88	76	4.9	215	223	130	40	absent	normal	fatty liver	normal	Absent
41	97739	26	m	27.2	1.1	1.4	98	134	5.2	280	264	193	36	absent	normal	fatty liver	normal	Absent

Master chart of study group- Prediabetic

Sl NO	hospital number	Age	Sex	BMI	W/H	ABI	FBS	PPBS	HbA1C	Chol	TG	LDL	HDL	albuminuria	ECG	USG abdomen	CIMT	family history of diabetes
1	67777	39	M	24.8	0.91	0.9	102	152	5.8	87	210	36	19	absent	normal	Normal	normal	Absent
2	179515	33	M	25.7	0.86	1.21	128	168	6.4	161	73	83	63	1+	normal	Normal	normal	Absent
3	180403	49	M	20.9	0.98	0.97	114	152	6.1	161	73	83	63	absent	T wave inversion in 2 3 avf	Normal	grade 1	Absent
4	180773	38	M	28.3	0.88	1.14	128	168	6.3	228	210	36	20	2+	normal	fatty liver	normal	Absent
5	179890	45	M	30.4	0.92	0.9	110	186	6.1	368	210	56	26	absent	normal	fatty liver	normal	Absent
6	169062	46	M	26.4	0.93	0.84	118	167	6.6	287	210	86	20	absent	normal	Normal	normal	Present
7	174099	30	M	22.9	0.83	1.2	122	198	6.4	124	106	58	44	absent	normal	fatty liver	normal	Present
8	177116	40	M	28.01	0.92	1.07	112	186	6.4	280	210	120	24	absent	normal	fatty liver	normal	Present
9	179900	39	M	22.83	0.88	1.12	120	144	5.7	161	73	83	63	1+	normal	Normal	normal	Absent
10	180904	38	M	22.4	0.93	0.8	128	196	6.3	200	180	110	40	1+	normal	fatty liver	normal	Absent
11	177891	22	M	22.7	0.84	1.09	91	142	6.1	151	70	83	63	absent	normal	Normal	normal	present
12	168505	42	M	15	0.75	0.7	114	168	5.9	164	70	83	63	1+	sinus tachycardia	grade 1 mdico renal disease splenomegaly /Normal	grade 1	absent
13	144534	38	F	21.6	0.93	0.9	114	167	6	160	70	80	60	absent	normal	Normal	normal	absent
14	163883	45	F	31.6	0.92	1.03	128	184	6.4	173	79	104	53	absent	normal	fatty liver	normal	absent
15	61608	45	F	26.7	0.88	1.1	120	147	6.2	186	86	114	48	absent	normal	fatty liver	normal	present
16	180273	34	m	25.6	0.81	1.11	104	166	6	164	82	73	34	1+	normal	Normal	normal	present
17	229408	49	m	27.5	0.94	1.07	126	179	6.2	182	178	96	50	absent	normal	Normal	normal	absent
18	229401	45	m	34.1	1.2	1.04	102	148	6	200	268	80	66	absent	normal	Normal	normal	present
19	234691	48	m	27.6	0.9	0.89	118	190	6.1	205	277	106	44	absent	T wave inversion in 2 3 avf	Normal	grade 1	present
20	180908	37	f	30.03	0.92	1.07	104	146	5.8	196	158	129	35	absent	normal	Normal	normal	absent

21	234642	26	f	41.8	1.71	0.9	111	180	6.2	239	233	151	42	absent	normal	fatty liver	normal	present
22	229871	45	f	29.6	0.85	1.1	101	187	6.2	190	228	105	39	absent	normal	fatty liver	normal	present
23	235778	35	f	20.1	0.78	0.9	109	177	6.3	251	198	172	40	absent	normal	normal	normal	present
24	231486	34	m	25.6	0.9	0.9	128	186	6	159	205	91	27	absent	normal	fatty liver	grade 1	absent
25	227484	45	f	31.6	1.1	1.1	124	189	6.3	83	123	34	24	absent	normal	normal	normal	absent
26	229284	38	m	27.5	1.1	1	118	194	6.3	182	263	97	32	absent	normal	fatty liver	normal	absent
27	231127	23	f	25.1	0.84	1.2	112	138	5.7	195	155	130	34	absent	normal	normal	normal	absent
28	227484	34	f	26.5	0.96	0.95	114	156	5.7	83	123	34	24	absent	normal	normal	normal	present
29	226874	36	m	26.5	0.96	1.02	101	150	5.8	183	178	110	38	absent	normal	normal	normal	absent
30	219376	46	f	23.9	0.8	1.02	117	180	5.9	173	136	93	27	absent	normal	normal	normal	absent
31	200926	40	f	26.5	1.5	1.04	104	156	5.8	145	176	80	32	absent	normal	normal	normal	absent
32	237899	42	f	28.3	1.1	1.04	106	160	6.1	186	166	116	36	absent	normal	normal	normal	present
33	254574	26	m	42.5	1.7	0.9	117	151	6.2	160	238	97	32	1+	normal	fatty liver	grade 1	present
34	276955	40	m	25.1	0.95	0.8	110	140	5.9	145	184	131	36	absent	normal	normal	grade 1	present
35	2311010	33	m	20	0.74	1.04	123	186	5.8	291	210	222	36	absent	normal	normal	normal	absent
36	229043	30	f	21	0.9	1.2	96	144	5.9	191	160	152	40	absent	normal	normal	normal	absent
37	229073	36	f	28.4	1.2	1.1	112	157	5.7	150	170	104	27	absent	normal	fatty liver	normal	absent
38	229023	48	m	33.4	1.1	1.2	113	146	6.4	300	280	185	22	absent	normal	fatty liver	normal	present
39	131608	45	f	33	1.01	1	116	162	5.8	192	198	107	32	absent	normal	normal	normal	present
40	1019929	44	m	31	1.2	0.94	119	151	5.8	240	251	170	45	absent	normal	normal	grade 1	present
41	236452	44	f	28	1	1.1	121	162	6.2	236	194	132	32	absent	normal	normal	normal	present