"CORRELATION OF INTERARM SYSTOLIC BLOOD PRESSURE DIFFERENCE TO ANKLE BRACHIAL INDEX (ABI) IN DETECTING PERIPHERAL VASCULAR DISEASE IN TYPE TWO DIABETES MELLITUS PATIENTS – A ONE YEAR CROSS SECTIONAL STUDY IN KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"

REG NO. BG0112002

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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ENDORSEMENT

This is to certify that the dissertation entitled **"CORRELATION OF INTERARM SYSTOLIC BLOOD PRESSURE DIFFERENCE TO ANKLE BRACHIAL INDEX (ABI) IN DETECTING PERIPHERAL VASCULAR DISEASE IN TYPE TWO DIABETES MELLITUS PATIENTS – A ONE YEAR CROSS SECTIONAL STUDY IN KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"** is a bonafide research work done by **CANDIDATE REGISTER NO. BG0112002**.

Dr. V. A. Kothiwale **MD, Ph.D**
Professor and Head,
Department of Medicine,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

Dr. N. S. Mahantshetti **MD**
Principal,
J. N. Medical College,
Nehru Nagar, Belgaum – 10

Date:
Place: Belgaum

LIST OF ABBREVIATIONS USED

AD	-	Anno domini
ADA	-	American Diabetes Association
ALT	-	Alanine transaminase
AST	-	Aspartate aminotransferase
ATP	-	Adenosine triphosphate
BMI	-	Body mass index
CAD	-	Coronary artery disease
CA-UTI	-	Community-acquired urinary tract infection
CDC	-	Centers for Disease Control and Prevention
CKD	-	Chronic kidney disease
CLD	-	Chronic liver disease
CONs	-	Coagulase negative staphylococci
COPD	-	Chronic obstructive pulmonary disease
CT	-	Computed tomography
CVA	-	Cardiovascular accident
DCCT	-	Diabetes Control and Complications Trial
DKA	-	Diabetic ketoacidosis
DM	-	Diabetes mellitus
DNA	-	Deoxyribo nucleic acid
DR	-	Diabetic retinopathy
E. coli	-	Escherachia coli
EC	-	Emphysematous cystitis
EP	-	Emphysematous pyelitis
EPN	-	Emphysematous pyelonephritis

ESBL	-	Extended-spectrum beta-lactamases
ESRD	-	End-stage renal disease
FPG	-	Fasting plasma glucose
g	-	Gram
GAD	-	Glutamic acid decarboxylase
GDM	-	Gestational diabetes mellitus
GIP	-	Glucose-dependent insulinotropic polypeptide
GIPR	-	Gastric inhibitory polypeptide
GLP-1	-	Glucagonlike peptide-1
HbA1c	-	Hemoglobin A1C
HHS	-	Hyperglycemic hyperosmolar state
HIV	-	Human immunodeficiency virus
HLA	-	Human leukocyte antigen
HMGA1	-	High mobility group A1
HNF	-	Hepatocyte nuclear transcription factor
HPF	-	High power field
HTN	-	Hypertension
IA	-	Islet cell antibodies
ICMR	-	Indian Council of Medical Research
IDDM	-	Insulin dependent diabetes mellitus
IDF	-	International Diabetes Federation
IFG	-	Impaired fasting glucose
IGT	-	Impaired glucose tolerance
IGT	-	Impaired glucose tolerance
IHD	-	Ischaemic heart disease

IL	-	Interleukin
INSR	-	Regulator of the insulin receptor gene
IPF	-	Insulin promoter factor
IU/L	-	International units per liter
Kg	-	Kilogram
KUB	-	Kidney, ureter and bladder
m	-	Meter
meq/L	-	Milli equivalent per liter
mg/dl	-	Milligram per deciliter
mmol/l	-	Millimole per liter
MODY	-	Maturity onset diabetes of young
n	-	Total number
NIDDM	-	Non insulin dependent diabetes mellitus
NPH	-	Neutral Protamine Hagedorn
OGTT	-	Oral glucose tolerance test
p	-	Probability
PAD	-	Peripheral arterial disease
PZI	-	First protamine Insulin
RBC	-	Red blood count
RPN	-	Renal papillary necrosis
SD	-	Standard deviation
SNPs	-	Single-nucleotide polymorphisms
TB	-	Tuberculosis
TMP-SMX	-	Trimethoprim-sulphamethoxazole
US	-	United States

UTI	-	Urinary tract infection
WBC	-	White blood count
WHO	-	World Health Organization
WHR	-	Waist hip ratio
XGP	-	Xanthogranulomatous pyelonephritis

ABSTRACT

Background and objectives

The ABI is useful in the diagnosis of both symptomatic and asymptomatic PVD. Interarm systolic blood pressure differences have been studied in patients with various manifestations of vascular disease. The present study was attempt to examine whether interarm differences in SBP and ABI correlate in diagnosing PVD among the patients with type 2 diabetes mellitus.

Methodology

The present cross-sectional study was conducted for a period of one year from January 2013 to December 2013 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 45 patients with type 2 diabetes having duration of ≥ 6 years were studied. All the patients were investigated for ABI and interarm systolic blood pressure difference.

Results

Most of the patients (62.22%) were males and male to female ratio was 1.64:1. 40% of the patients presented with age between 61 to 70 years. The duration of diabetes was between 10 to 15 years in 31.11% of the patients and mean duration was 20.04 ± 6.93 years. Most of the patients (42.22%) were on oral hypoglycaemic agents. The interarm systolic blood pressure difference of ≥10 mm Hg was noted in 37.78% of the patients. In patients with IASBP difference of ≥ 10 mm Hg, all the patients had PVD (100%) and mild and moderate PVD was present in 11.76% and 88.24% of the patients ($p<0.001$). The

mean IASBP difference increased with severity of PVD ($p<0.001$). The linear correlation of ABI and IASBP difference showed strong negative correlation, depicting increase in IASBP difference with decrease in ABI and vice versa ($R=-0.919$; $R^2=0.8447$; $p<0.001$)

Conclusion and interpretation

An IASBPD of ≥ 10 mm Hg prompts physician for signs of peripheral vascular disease.

Keywords

Ankle brachial index; Diabetes mellitus; Interarm systolic blood pressure difference; Peripheral vascular disease;

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion and insulin action or both.[1] Majority of the fall into two broad categories: those having little or no endogenous insulin secretory capacity (IDDM or type 1 DM) and those who retain endogenous insulin secretory capacity but have a combination of resistance to insulin action and an inadequate compensatory insulin secretory response (NIDDM, or Type 2 DM).[1,2]

Diabetes mellitus is a disease of developed countries and one of the endocrine disorders which has reached epidemic proportions worldwide.[3] A report by Centers for Disease Control and Prevention (CDC) estimated that nearly 26 million Americans have diabetes in 2011. Type 2 diabetes mellitus (DM) accounts for more than 90% of the diabetic population world wide.[4] It is a chronic and potentially disabling disease and a major growing threat to global public health.[1]

The chronic hyperglycemia is associated with long term dysfunction, damage and failure of various organs.[1] Lots of complications are associated with DM. Those complications arise chiefly from the disruption of the vascular system which can result in inadequate circulation to the peripheral body.[5] One-third of all diabetic patients have significant peripheral neuropathy and/or peripheral vascular disease (PVD).[6]

Peripheral vascular disease (PVD) is the presence of systemic atherosclerosis in arteries distal to the arch of the aorta. As a result of the atherosclerotic process, patients with PVD develop narrowing of these arteries.[7]

The prevalence of peripheral vascular disease (PVD) ranges from 3 to 10%, rising to 15 to 20% in the elderly.[8,9,10] It has an estimated worldwide prevalence of almost 10%, rising to 15-20% in people over 70 years of age, and it affects around 27 million people in Europe and North America alone. Critical limb ischaemia the most severe manifestation of the disease can lead to limb loss or even death if not treated promptly. Each year, 500-1000 new cases of critical limb ischaemia are diagnosed per million of the population.[8]

One in five people aged 65 to 75 years in the UK has clinical evidence of PVD, although only a quarter are symptomatic.[11] Of patients asymptomatic at baseline, 9 per cent will develop symptoms of intermittent claudication (IC) over five years.[12] The prevalence of IC is 6 per cent in persons with PVD over the age of 60 years.1 However, it is estimated only a quarter of these patients will experience a worsening of symptoms.[9] Forty to 60 per cent of patients with PVD also have coronary artery and cerebral artery disease,[9] and 20 to 30 per cent of those with IC will die within five years, mainly due to cardiovascular events.[13] This is why the most vital goal of PVD treatment is the reduction of the patient's cardiovascular risk.

PVD is primarily caused by atherosclerosis and results in either acute or chronic limb ischaemia. The latter presents as IC, which is defined as pain in the leg muscles on walking.

Atherosclerosis is a complex process involving endothelial dysfunction, thrombosis, platelet activation, lipid disturbances, oxidative stress and genetic factors. Other less common causes of PVD include thrombus formation, emboli and

inflammatory processes resulting in vessel stenosis.[9] In the late stages of the disease, long-term tissue hypoperfusion progresses to critical limb ischaemia.

The differential diagnosis of PVD includes musculoskeletal and neurologic causes. The most common entity that mimics PVD is spinal stenosis. Spinal stenosis can cause compression of the cauda equina, which results in pain that radiates down both legs. The pain occurs with walking (i.e., pseudoclaudication) or prolonged standing and does not subside rapidly with rest. Additional conditions to consider are acute embolism, deep or superficial venous thrombosis, restless legs syndrome, systemic vasculitides, nocturnal leg cramps, muscle or tendon strains, peripheral neuropathy, and arthritides. Patients with PVD have a history of claudication, which manifests as cramp-like muscle pain occurring with exercise and subsiding rapidly with rest. In addition, later in the course of the disease, patients may present with night pain, nonhealing ulcers, and skin color changes.[7]

The ankle–brachial index (ABI), the ratio of the ankle and brachial systolic blood pressures, is often used as a surrogate marker for PVD. An ABI of 1.0 to 1.4 is generally considered normal, whereas an ABI less than 0.9 is abnormal and suggests PVD.[14]

Further, a marked inter arm systolic blood pressure difference have been linked to subclavian stenosis, atherosclerotic plaque, and are most commonly observed in patients with hypertension, diabetes, and chronic renal disease, suggesting interarm differences as a marker of peripheral vascular disease. A small number of studies have shown IASBPD of ≥10 mmHg are associated with an

increased risk for all-cause and cardiovascular disease (CVD) mortality in high risk patients (e.g. hypertension, chronic renal disease).[15]

Although measuring blood pressure at the bilateral brachial is common in medical practice, its clinical significance in patients with peripheral vascular disease has not been fully clarified owing to a paucity of data. The extent of interarm systolic blood pressure difference is not apparent in patients with peripheral vascular disease and is unclear. Accordingly, the present study was aimed to examine whether interarm systolic blood pressure difference (IASBPD) and ABI correlate in diagnosing PVD among the patients with type 2 diabetes mellitus.

OBJECTIVES

The objective of the present study was to explore the association of interarm systolic blood pressure difference (IASBPD) with ankle brachial index (ABI) in detecting PVD in type 2 diabetes mellitus.

REVIEW OF LITERATURE

Diabetes Mellitus

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics and environmental factors. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.[1]

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. DM is the leading cause of end-stage renal disease (ESRD), nontraumatic lower extremity amputations, and adult blindness. DM also predisposes to cardiovascular diseases. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.[1]

History of Diabetes Mellitus

For 2,000 years diabetes has been recognized as a devastating and deadly disease. In the first century A.D. a Greek, Aretaeus, described the destructive nature of the affliction which he named "diabetes" from the Greek word for "siphon."[16]

Eugene J. Leopold in his text Aretaeus the Cappodacian describes Aretaeus' diagnosis "….for fluids do not remain in the body, but use the body only as a channel through which they may flow out. Life lasts only for a time, but not very long. For they urinate with pain and painful is the emaciation. For no essential part

of the drink is absorbed by the body while great masses of the flesh are liquefied into urine".[16]

Physicians in ancient times, like Aretaeus, recognized the symptoms of diabetes but were powerless to effectively treat it. Aretaeus recommended oil of roses, dates, raw quinces, and gruel. And as late as the 17th century, doctors prescribed gelly of viper's flesh, broken red coral, sweet almonds, and fresh flowers of blind nettles.[16]

In the 17th century a London physician, Dr. Thomas Willis, determined whether his patients had diabetes or not by sampling their urine. If it had a sweet taste he would diagnose them with diabetes mellitus- "honeyed" diabetes. This method of monitoring blood sugars went largely unchanged until the 20th century.[16]

In the early 20th century, diabetologists such as Dr. Frederick Allen prescribed low calorie diets-as little as 450 calories per day for his patients. His diet prolonged the life of people with diabetes but kept them weak and suffering from near starvation.[16]

In 1921, in Ontario, Canada, a young surgeon Frederick Banting, and his assistant Charles Best, kept a severely diabetic dog alive for 70 days by injecting it with a murky concoction of canine pancreas extract. With the help of Dr. Collip and Dr. Macleod, Banting and Best administered a more refined extract of insulin to Leonard Thompson, a young boy dying of diabetes. Within 24 hours, Leonard's high blood sugars had dropped to near normal levels.[16]

Since insulin's discovery, medical breakthroughs continued to prolong and ease the lives of people with diabetes. In 1935 Roger Hinsworth discovered there

were two types of diabetes: "insulin sensitive" (type I) and "insulin insensitive" (type II). By differentiating between the two types of diabetes, Hinsworth helped open up new avenues of treatment.[16]

Starting in the late 1930s, new types of pork and beef insulin were created to better manage diabetes. Protamine zinc insulin, a longer acting insulin, was created in 1936. In 1938 NPH insulin was marketed, and in 1952 Lente, containing high levels of zinc which promotes a longer duration of action was invented.[16]

In the 1950s, oral medications-sulfonylureas were developed for people with T2 DM.[16]

The HbA1c test was devised in 1979 in order to create a more precise blood sugar measurement. With the A1c, hemoglobin, the oxygen-carrying pigment in red blood cells, is used to track glucose changes over a period of four months, the life span of the cell. Hemoglobin links with the glucose in blood; the more glucose present, the greater amount of hemoglobin linked with glucose.[16]

The A1c became a standard measurement for blood sugar control in the comprehensive ten-year study from 1983 to 1993 the Diabetes Control and Complications Trial (DCCT). With the conclusion of the DCCT in 1993, studies showed that people who were able to keep their blood glucose levels as close to normal as possible had less chance of developing complications associated with diabetes.[16]

Before this, many doctors had not put much emphasis on tight control of blood glucose levels. The common belief for decades was that diligent monitoring of blood sugars and intensive insulin therapy had little consequence for people with

diabetes. Since the DCCT's findings, statistics have proven that tight blood glucose control can be extremely beneficial for people with diabetes.[16]

CLASSIFICATION OF DIABETES MELLITUS

DM is classified on the basis of the pathogenic process that leads to hyperglycemia, as opposed to earlier criteria such as age of onset or type of therapy. The two broad categories of DM are designated as[1]

- Type 1
- Type 2

Both types of diabetes are preceded by a phase of abnormal glucose homeostasis as the pathogenic processes progresses. Type 1 diabetes is the result of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the common phenotype of hyperglycemia in type 2 DM and have important potential therapeutic implications now that pharmacologic agents are available to target specific metabolic derangements. Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).[1]

Table 1. Spectrum of glucose homeostasis and diabetes mellitus[1]

Type of diabetes	Normal glucose tolerance (NGT)	Impaired fasting glucose or impaired glucose tolerance	Hyperglycemia: Diabetes mellitus		
			Not insulin required	Insulin required for control	Insulin required for survival
Type 1					
Type 2					
Other Specific types					
Gestational diabetes					
Time (years)					
FPG (mg/dl)	< 100	100-125		≥ 126	
2-h plasma glucose (mg/dl)	< 140	140 – 199		≥ 200	

Etiologic classification of diabetes mellitus[1]

I. Type 1 diabetes (-cell destruction, usually leading to absolute insulin deficiency)

A. Immune-mediated

B. Idiopathic

II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)

III. Other specific types of diabetes

A. Genetic defects of β-cell function characterized by mutations in :

1. Hepatocyte nuclear transcription factor (HNF) 4α maturity onset diabetes of young (MODY) 1
2. Glucokinase (MODY 2)
3. HNF – 1α (MODY 3)
4. Insulin promoter factor (IPF) 1 (MODY 4)
5. HNF – 1β (MODY 5)
6. Neuro D1 (MODY 6)
7. Mitochondrial deoxyribo nucleic acid (DNA)
8. Sub units of adenosine triphosphate (ATP) – sensitive potassium channel.
9. Proinsulin or insulin conversion

B. Genetic defects in insulin action.

1. Type A insulin resistance
2. Leprechaunism
3. Rabson-Mendenhall syndrome
4. Lipodystrophy syndromes.

C. Diseases of the exocrine pancreas – pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculouspancreatopathy.

D. Endocrinopathies – acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma

E. Drug or chemical induced – Vacor, pentamidine, nicotinic acid, glucocorticoids, thyroid hormone, diazoxide, beta-adrenergic agonists, thiazides, phenytoin, α– interferon, protease inhibitors, clozapine, beta blockers.

F. Infections – congenital rubella, cytomegalovirus, coxsackie.

G. Uncommon forms of immune-mediated diabetes – "stiff-man" syndrome, anti-insulin receptor antibodies.

H. Other genetic syndromes sometimes associated with diabetes – Down's syndrome, Klinefelter's syndrome, Turner's syndrome, Wolfram's syndrome, Friedreich's ataxia, Huntington's chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome.

IV. Gestational diabetes mellitus (GDM)

EPIDEMIOLOGY

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 177 million in 2000. Based on current trends, more than 360 million individuals will have diabetes by the year 2030. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly because of increasing obesity and reduced activity levels as countries become more industrialized. This is true in most countries, and 6 of the top 10 countries with the highest rates are in Asia. The prevalence of type 2 DM and its harbinger, IGT, is highest in certain Pacific islands, intermediate in countries such as India and the United States, and relatively low in Russia. This variability is likely due to genetic, behavioral, and environmental factors.[1]

In India it is estimated that presently 19.4 million individuals are affected by this deadly disease, which is likely to go up to 57.2 million by the year 2025.[17]

The prevalence of diabetes is four to six fold lower in rural areas, which is probably attributed to a conventional lifestyle which has beneficial effect on glucose tolerance (IGT). National Urban Diabetes Survey done in six cities, found age standardized prevalence rates of 12% for diabetes; with a slight male preponderance and 14% for impaired glucose tolerance. Subjects under the age of 40 years, had a prevalence of five percent for DM and 13% prevalence of impaired glucose tolerance.[18]

Epidemiologic determinants and risk factors of type 2 diabetes[19]

Genetic Factors

- Genetic markers
- Family history
- "Thrifty gene(s)"

Demographic characteristics

- Sex
- Age
- Ethnicity

Behavioral and lifestyle-related risk factors

- Obesity (including distribution of obesity and duration)
- Physical inactivity

- Diet
- Stress

Metabolic determinants and intermediate-risk categories of type 2 diabetes

- Impaired glucose tolerance
- Insulin resistance
- Pregnancy-related determinants
    - Parity
    - Gestational diabetes
    - Diabetes in offspring of women with diabetes during pregnancy
    - Intrauterine malnutrition or overnutrition

DIAGNOSIS OF DIABETES

Criteria for the Diagnosis of Diabetes Mellitus[1]

- Symptoms of diabetes plus random blood glucose concentration more than or equal to 11.1 mmol/L (200 mg/dL)[a] *or*
- Fasting plasma glucose more than or equal to 7.0 mmol/L (126 mg/dL)[b] *or*
- Two-hour plasma glucose more than or equal to 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test[c]

[a]Random is defined as without regard to time since the last meal.

[b]Fasting is defined as no caloric intake for at least 8 h.

[c]The test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water; not recommended for routine clinical use.

In the absence of unequivocal hyperglycemia and acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day.[1]

Glucose tolerance is classified into three categories based on the FPG:

1. FPG less than 5.6 mmol/L (100 mg/dL) is considered normal;
2. FPG equal to 5.6–6.9 mmol/L (100–125 mg/dL) is defined as IFG; and
3. FPG more than or equal to 7.0 mmol/L (126 mg/dL) warrants the diagnosis of DM.

Oral glucose tolerance test

The test uses the following procedures.

- It first employs an FPG test.
- A blood test is then taken two hours after drinking a 75 g anhydrous glucose solution.

Based on the OGTT, IGT is defined as plasma glucose levels between 7.8 and 11.1 mmol/L (140 and 199 mg/dL). Diabetes is defined when plasma glucose is more than 11.1 mmol/L (200 mg/dL), 2 h after a 75 g oral glucose load.[1]

The current criteria, for the diagnosis of DM emphasize that the FPG is the most reliable and convenient test for identifying DM, in asymptomatic individuals. A random plasma glucose concentration more than or equal to 11.1 mmol/L (200 mg/dL) accompanied by classic symptoms of DM (polyuria, polydipsia, weight loss) is sufficient for the diagnosis of DM.[1]

Hemoglobin A1C (HbA1c) was advocated as a diagnostic test for DM. Though there is a strong correlation between elevations in the plasma glucose and the A1C, the relationship between the FPG and the A1C in individuals with normal glucose tolerance or mild glucose intolerance is less clear, and thus the use of the A1C is not currently recommended to diagnose diabetes.[1]

PATHOPHYSIOLOGY

Insulin biosynthesis

Insulin is produced in the beta cells of the pancreatic islets. It is initially synthesized as preproinsulin. Subsequent proteolytic processing removes the amino terminal signal peptide, giving rise to proinsulin. Cleavage of an internal 31-residue fragment from proinsulin generates the C peptide and the A (21 amino acids) and B (30 amino acids) chains of insulin, which are connected by disulfide bonds. The mature insulin molecule and C peptide are stored together and co-secreted from secretory granules in the beta cells.[1]

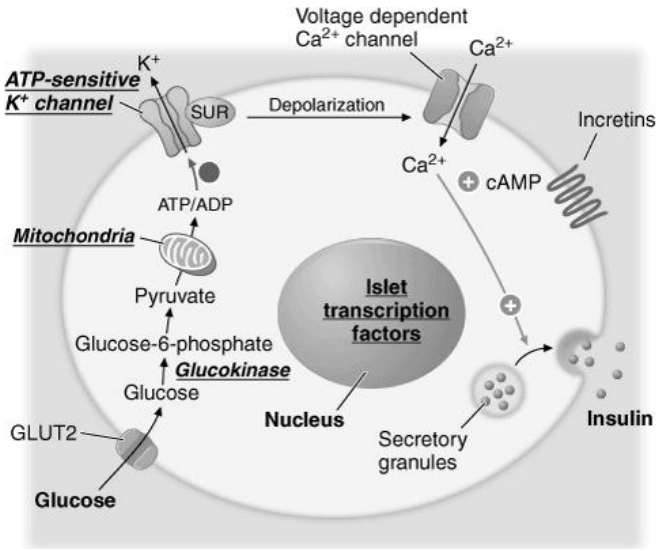


Figure 1. Diabetes and abnormalities in glucose-stimulated insulin secretion[1]

Glucose and other nutrients regulate insulin secretion by the pancreatic beta cell. Glucose is transported by the GLUT2 glucose transporter; subsequent glucose metabolism by the beta cell alters ion channel activity, leading to insulin secretion. The SUR receptor is the binding site for drugs that act as insulin secretagogues. Mutations in the events or proteins underlined are a cause of maturity onset diabetes of the young (MODY) or other forms of diabetes.[1]

Secretion

Glucose is the key regulator of insulin secretion by the pancreatic beta cell, although amino acids, ketones, various nutrients, gastrointestinal peptides, and neurotransmitters also influence insulin secretion. Glucose levels > 3.9 mmol/L (70 mg/dL) stimulate insulin synthesis, primarily by enhancing protein translation and processing. Glucose stimulation of insulin secretion begins with its transport into the beta cell by the GLUT2 glucose transporter. Glucose phosphorylation by glucokinase is the rate-limiting step that controls glucose-regulated insulin secretion. Further metabolism of glucose-6-phosphate via glycolysis generates ATP, which inhibits the activity of an ATP-sensitive K^+ channel. This channel consists of two separate proteins: one is the binding site for certain oral hypoglycemics (e.g., sulfonylureas, meglitinides); the other is an inwardly rectifying K^+ channel protein. Inhibition of this K^+ channel induces beta cell membrane depolarization, which opens voltage-dependent calcium channels, and stimulates insulin secretion. Insulin secretory profiles reveal a pulsatile pattern of hormone release, with small secretory bursts occurring about every 10 min.[1]

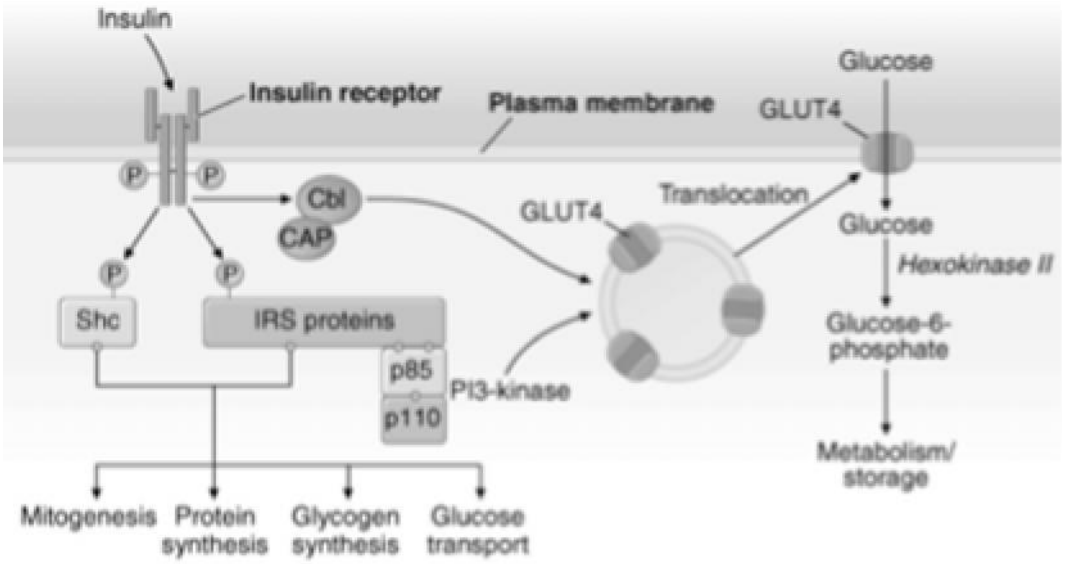


Figure. 2. Insulin signal transduction pathway in skeletal muscle[1]

The insulin receptor has intrinsic tyrosine kinase activity and interacts with insulin receptor substrates (IRS and Shc) proteins. A number of "docking" proteins bind to these cellular proteins and initiate the metabolic actions of insulin [GrB-2, SOS, SHP-2, p65, p110, and phosphatidylinositol-3'-kinase (PI-3-kinase)]. Insulin increases glucose transport through PI-3-kinase and the Cbl pathway, which promotes the translocation of intracellular vesicles containing GLUT4 glucose transporter to the plasma membrane.[1]

Action

Once insulin is secreted into the portal venous system, about 50% is degraded by the liver. Unextracted insulin enters the systemic circulation where it binds to receptors in target sites. Insulin binding to its receptor stimulates intrinsic tyrosine kinase activity, leading to receptor autophosphorylation and the recruitment of intracellular signaling molecules, such as insulin receptor substrates (IRS). IRS and other adaptor proteins initiate a complex cascade of phosphorylation and

dephosphorylation reactions, resulting in the widespread metabolic and mitogenic effects of insulin.[1]

Glucose homeostasis reflects a balance between hepatic glucose production and peripheral glucose uptake and utilization. Insulin is the most important regulator of this metabolic equilibrium, but neural input, metabolic signals, and other hormones result in integrated control of glucose supply and utilization. In the fasting state, low insulin levels increase glucose production by promoting hepatic gluconeogenesis and glycogenolysis and reduce glucose uptake in insulin-sensitive tissues, thereby promoting mobilization of stored precursors such as amino acids and free fatty acids. Glucagon, secreted by pancreatic alpha cells when blood glucose or insulin levels are low, stimulates glycogenolysis and gluconeogenesis by the liver and renal medulla. Postprandially, the glucose load elicits a rise in insulin and fall in glucagon, leading to a reversal of these processes.[1]

Type 2 Diabetes mellitus

Insulin resistance and abnormal insulin secretion are central to the development of type 2 DM. Although the primary defect is controversial, most studies support the view that insulin resistance precedes an insulin secretory defect but that diabetes develops only when insulin secretion becomes inadequate.[1]

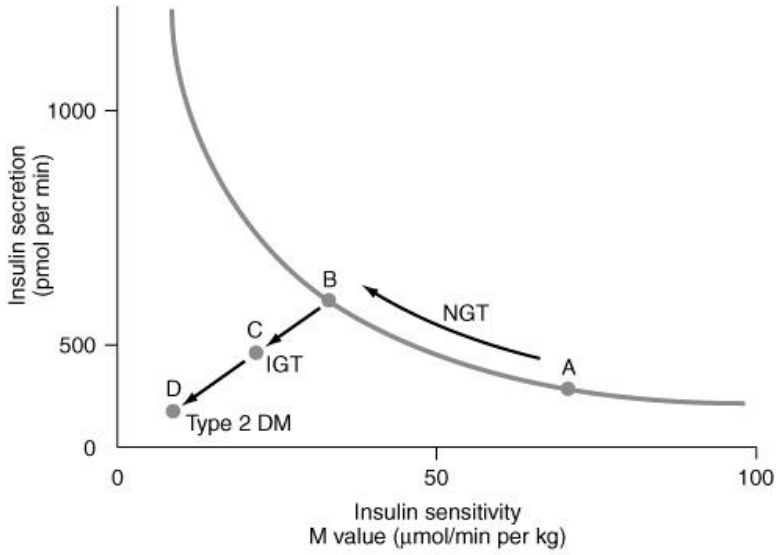


Figure 3. Metabolic changes during the development of type 2 diabetes mellitus[1]

Insulin secretion and insulin sensitivity are related, and as an individual becomes more insulin resistant (by moving from point A to point B), insulin secretion increases. A failure to compensate by increasing the insulin secretion results initially in impaired glucose tolerance (IGT; point C) and ultimately in type 2 DM (point D).[1]

Pathophysiology of type 2 DM

Type 2 DM is characterized by impaired insulin secretion, insulin resistance, excessive hepatic glucose production, and abnormal fat metabolism. Obesity, particularly visceral or central, is very common in type 2 DM. In the early stages of the disorder, glucose tolerance remains near normal, despite insulin resistance, because the pancreatic beta cells compensate by increasing insulin output. As insulin resistance and compensatory hyperinsulinemia progress, the pancreatic islets in certain individuals are unable to sustain the hyperinsulinemic state. IGT,

characterized by elevations in postprandial glucose, then develops. A further decline in insulin secretion and an increase in hepatic glucose production lead to overt diabetes with fasting hyperglycemia. Ultimately, beta cell failure may ensue.[1]

Complications of type 2 diabetes mellitus[1]

Acute

- Diabetic Ketoacidosis
- Hyperglycemic Hyperosmolar State

Chronic

- Microvascular
    - Eye disease
        - Retinopathy (nonproliferative/proliferative)
        - Macular edema
    - Neuropathy
        - Sensory and motor (mono- and polyneuropathy)
        - Autonomic
    - Nephropathy
- Macrovascular
    - Coronary artery disease
    - Peripheral vascular disease
    - Cerebrovascular disease
- Other
    - Gastrointestinal

- Genitourinary
- Dermatologic
- Cataracts
- Glaucoma
- Infectious
- Periodontal disease

Chronic complications

The risk of chronic complications increases as a function of the duration of hyperglycemia; they usually become apparent in the second decade of hyperglycemia. Since type 2 DM often has a long asymptomatic period of hyperglycemia, many individuals with type 2 DM have complications at the time of diagnosis.[1]

The microvascular complications of both type 1 and type 2 DM result from chronic hyperglycemia. Large, randomized clinical trials of individuals with type 1 or type 2 DM have conclusively demonstrated that a reduction in chronic hyperglycemia prevents or delays retinopathy, neuropathy, and nephropathy. Other incompletely defined factors may modulate the development of complications.[1]

Evidence implicating a causative role for chronic hyperglycemia in the development of macrovascular complications is less conclusive. However, coronary heart disease events and mortality are two to four times greater in patients with type 2 DM. These events correlate with fasting and postprandial plasma glucose levels as well as with the A1C. Other factors like dyslipidemia and hypertension also play important roles in macrovascular complications.[1]

Mechanisms of complications

Four prominent theories, which are not mutually exclusive, have been proposed to explain how hyperglycemia might lead to the chronic complications of DM.[1]

One theory is that increased intracellular glucose leads to the formation of advanced glycosylation end products (AGEs) via the nonenzymaticglycosylation of intra- and extracellular proteins. Nonenzymaticglycosylation results from the interaction of glucose with amino groups on proteins. AGEs have been shown to cross-link proteins (e.g., collagen, extracellular matrix proteins), accelerate atherosclerosis, promote glomerular dysfunction, reduce nitric oxide synthesis, induce endothelial dysfunction, and alter extracellular matrix composition and structure. The serum level of AGEs correlates with the level of glycemia, and these products accumulate as glomerular filtration rate declines.[1]

A second theory is based on the observation that hyperglycemia increases glucose metabolism via the sorbitol pathway. Intracellular glucose is predominantly metabolized by phosphorylation and subsequent glycolysis, but when increased, some glucose is converted to sorbitol by the enzyme aldosereductase. Increased sorbitol concentration alters redox potential, increases cellular osmolality, generates reactive oxygen species, and likely leads to other types of cellular dysfunction.[1]

A third hypothesis proposes that hyperglycemia increases the formation of diacylglycerol leading to activation of protein kinase C (PKC). Among other actions, PKC alters the transcription of genes for fibronectin, type IV collagen, contractile proteins, and extracellular matrix proteins in endothelial cells and neurons.[1]

A fourth theory proposes that hyperglycemia increases the flux through the hexosamine pathway, which generates fructose-6-phosphate, a substrate for O-linked glycosylation and proteoglycan production. The hexosamine pathway may alter function by glycosylation of proteins such as endothelial nitric oxide synthase or by changes in gene expression of transforming growth factor β (TGF-β) or plasminogen activator inhibitor-1 (PAI-1).[1]

Growth factors appear to play an important role in DM-related complications, and their production is increased by most of these proposed pathways. Vascular endothelial growth factor A (VEGF-A) is increased locally in diabetic proliferative retinopathy and decreases after laser photocoagulation. TGF- β is increased in diabetic nephropathy and stimulates basement membrane production of collagen and fibronectin by mesangial cells. Other growth factors, such as platelet-derived growth factor, epidermal growth factor, insulin-like growth factor I, growth hormone, basic fibroblast growth factor, and even insulin, have been suggested to play a role in DM-related complications. A possible unifying mechanism is that hyperglycemia leads to increased production of reactive oxygen species or superoxide in the mitochondria; these compounds may activate all four of the pathways described above.[1]

Peripheral vascular disease

Peripheral Vascular Disease of the lower extremity is an important cause of morbidity and affects 10 million people in India.[20] It is a common condition with variable morbidity affecting men and women over the age of 45 years. It is going to be a major health problem in our country as the Indian population is aging.[21]

Atherosclerosis is a generalized disorder and involves medium and large

sized arteries. It is estimated that 74% patients of atherosclerotic coronary artery disease have involvement of some other vascular bed also. 40% patients of coronary artery disease have associated peripheral vascular disease, 14% have carotid artery stenosis and 17% have associated renal artery stenosis.[21]

Therefore it becomes very important for the physicians to know the pathology, clinical presentations and treatment of common vascular disorders. Increasingly, peripheral vascular disease is becoming a focus of involvement for primary care physicians and cardiovascular specialists who must work in partnership. Awareness and interest in peripheral vascular disease is growing in India because of the following reasons:[21]

- Advancing age of the general population, resulting in increase prevalence of the peripheral vascular disease.
- Unwillingness of patients to accept the limitations and associated morbidity of vascular disease when therapeutic options are available.
- The realization that vascular disease in one system should prompt investigation of other areas for coexistent disease.

Epidemiology

Data from the Framingham Heart Study[22] revealed that 20% of symptomatic patients with PAD had diabetes, but this probably greatly underestimates the prevalence, given that many more people with PAD are asymptomatic rather than symptomatic. As well, it has been reported that of those with PAD, over one-half are asymptomatic or have atypical symptoms, about one-third have claudication, and the

remainder have more severe forms of the disease.[23]

The overall prevalence of PVD among Indians is considerably low as compared to the Western patients. Mohan et al have reported the prevalence of PVD in South Indian diabetics to be 3.9%[24] In Western series the prevalence ranges between 22–45%.[26-27] The prevalence of PVD in diabetics increases with age increasing from 3.2% in those below 50 yrs. of age to 33% in those above 80 yrs. of age.[28] The prevalence of PVD in diabetics also increases with the duration of diabetes from 15% to 45% at 10 to 20 years respectively after the diagnosis of diabetes.[29]

In India, the number of diabetic patients above the age of 80 years or with duration of diabetes more than 30 years is extremely low, thus explaining the low prevalence of PVD in diabetics. In the coming years with better disease care, longevity of our diabetics would significantly increase and it will not be surprising to see an increasing prevalence of PVD in Indian diabetics.

Causes of vascular disease[21]

Arterial

- Atherosclerosis
- Thromboangiitis obliterans
- Arteriosclerosis obliterans
- Raynaud's disease
- Acrocynosis
- Erythromelalgia

- Vasculitis
- Takayasu Arteritis

Venous

- Venous thrombosis
- Varicose veins
- AV fistula

Lymphatic

- Lymphoedema
- Lipidemia

Risk factors for Atherosclerotic Vascular Disease

Risk factors for the development of diabetic peripheral vascular disease include genetic predisposition, age, duration of diabetes, smoking, hypertension (systolic or diastolic), hyper cholesterolaemia, hypertriglyceridaemia, hyperglycaemia, truncal obesity, hyperinsulinaemia, proteinuria, dialysis and drugs (eg. Ionotrophic agents, beta blockers).[21]

Of these risk factors, age, duration of diabetes, genetic predisposition and smoking are most important factors.[21]

Conventional[21]

- Smoking
- Diabetes Mellitus
- Hyperlipidemia
- Hypertension

- Obesity
- Syndrome X (Hypertriglyceridemia + Insulin Resistance)

Secondary / Possible[21]

- Angiotensin Converting Enzyme Polymorphism
- Chlamydial infection
- Lp(a)
- Lipid Remnants
- IDL
- Apoprotein B
- Elevated serum fibrinogen level
- Elevated Serum Iron level
- Elevated Serum Uric acid level
- Low Serum Folate level
- Hyperhomocysteinemia
- Hypothyroidism
- Elevated protein C, protein S
- Oxidative Stress (lipid peroxidation)
- Platelet-receptor polymorphism
- von Willebrand disease

Unique features of Peripheral Vascular disease in Indians[21]

- Presentation at younger age (mean age 45 years)
- Increased association of diabetes and presence of typical Diabetic Peripheral

Vascular Disease.

- Takayasu arteritis

Natural history of peripheral vascular disease

In 75% cases peripheral vascular disease is asymptomatic, (manifested by ABI < 0.9). In 25% cases peripheral vascular disease is symptomatic with intermittent claudication, coldness and numbness of feet, weakness of lower limb, dependent rubor, non healing ulcer and gangrene. In patients with intermittent claudication, after 5 years 50% still have stable symptoms, 16% experience worsening of symptoms, 16% require revascularization by surgery / intervention and 4% have major amputation.[30]

There is a strong correlation between the presence of Peripheral Vascular Disease (PVD), Coronary artery disease (CAD) and Cerebrovascular disease (CVD) and mortality. Five years mortality is 30% of which 75% deaths are because of cardiovascular causes. 20% patients have non fatal MI or stroke at 5 years. The mortality from PVD and CVD and CAD is directly related to the severity of PVD. In CAPRIE trial, there was 10.2% increase in relative risk of event rate and mortality for every 0.1 decrease in ABI (P=0.04).[21]

Peripheral Vascular Disease in Diabetes

Diabetes Mellitus is an important risk factor of lower extremity arterial disease (LEAD) in India. Smoking and insulin resistance are frequently present in patients with diabetes and contribute an additional risk for vascular disease. Peripheral Vascular Disease (PVD) in diabetes is complicated by peripheral neuropathy and susceptibility to infection, which leads to foot ulceration, gangrene

and amputation of the affected extremity. Diabetes accounts for ~ 50% of all non traumatic amputations in India.[21]

Mortality is increased in diabetic patients with PVD. Three years survival after an amputation is < 50%. In population based and epidemiology based studies,[21,31,32] it is estimated that 20-30% of diabetic patients over 65 years of age have peripheral arterial disease. Approximately 30% of these diabetic patients with peripheral vascular disease require surgical or percutaneous revascularization. 10% require an amputation of the affected limb within 5-10 years of diagnosis. Progression from intermittent claudication to critical limb ischemia occurs at the rate of 1.4% per year. Five year mortality of diabetic patients with PVD approaches 30%.[21]

Clinical differences in diabetic and non diabetic peripheral vascular disease[21]

	Diabetic	**Non diabetic**
Clinical	More common in younger age; more rapid	Les common in older age; less rapid
Male/Female	M>F	M>>F
Occlusion	Multisegmental	Single segment
Vessel adjacent to occlusion	Involved	Not involved
Collateral vessels	Involved	Usually normal
Lower extremities	Both	Unilateral
Vessels involved	Proximal and distal	Proximal

Pathogenesis

A cluster of factors present in a diabetic leads to the development of peripheral arterial disease (PAD). Some abnormalities in the microcirculation in diabetics are not occlusive but can alter the biology of the foot. There is evidence for thickening of capillary basement membrane,[33] which is key in the exchange of nutrients and metabolic products between the capillary lumen and the interstitium. The chemical structure of the membrane is altered by glycosylation, causing crosslinking of proteins and a decreased in the number of highly charged sulphur groups.[34]

This may explain why molecules such as albumin leak through the capillary membrane in diabetics. There is no impairment in oxygen diffusion. Infact diabetics with foot ulceration have higher levels of transcutaneous pO2 than non diabetics.[35]

Further evaluation of microanatomy reveals more tortuous capillaries in diabetics, appearing as tufts instead of the typical hair pin loops. With ischemia there is less recruitment of new capillaries into the circulation, although per gram there is no difference in capillary concentration.[21]

Atherosclerotic occlusion in diabetes commonly involves tibial and peroneal arteries and spares superficial femoral artery and the arteries of the foot, especially the dorsalis pedis artery.[36-40]

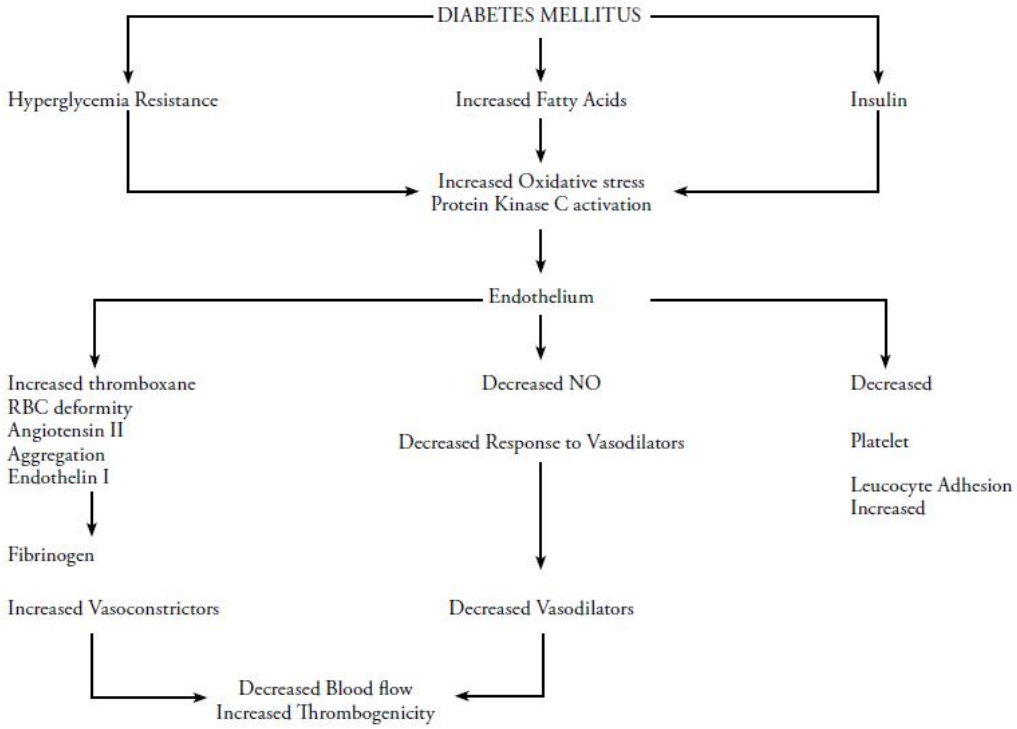


Figure 4. Peripheral arterial disease in diabetes mellitus[21]

Early diagnosis

In routine clinical examination, palpation of peripheral pulses is extremely important. In every diabetic, the ankle brachial systolic index (ABI), should be measured at least once in a year. This is a simple bedside investigation and is quite informative. The ankle/brachial systolic index (ABI) is calculated by dividing the ankle systolic pressure by the brachial pressure. A hand held Doppler ultrasound probe positioned over posterior tibial or dorsalis pedis arteries is most convenient to detect the return of blood flow. Normally, the ABI > 0.9, in claudication, the ABI is 0.5 – 0.8[41] with absolute ankle pressure between 70 and 100 mmHg.

In patients with rest pain ABI is usually < 0.30 with absolute pressure < 50 mmHg.[42,43] Decreased compressibility of blood vessels due to medial calcification

(Monckeberg's Sclerosis), results in falsely elevated systolic pressures. This should be suspected especially when an unusually high ABI > 1.15 is found.[44] Toe pressures can also be measured using a small cuff and is a better clue to the prognosis of primary healing of ischaemic ulcers in foot. The probability of foot ulcer healing, in diabetics, in relation to ABI, is 85%, if ABI is between 0.6 – 0.8, 4.5% if it is between 0.4 – 0.6 and nil if it is < 0.4.[42,43,45]

Other non-invasive diagnostic tests are pulse volume recording and transcutaneous pressure of oxygen measurement (Tcp02) and invasive tests are digital substraction angiography (DSA) and conventional angiography.

Ankle brachial index (ABI)

The ABI is the ratio of the blood pressure in the legs to the blood pressure in the arms. The ABI is calculated by dividing the higher systolic blood pressure in either the dorsalis pedis or posterior tibial arteries by the higher of the two systolic blood pressures in the arms. It can be performed in primary care settings without expensive or elaborate equipment or extensive training or experience.

Method

A Doppler ultrasound blood flow detector, commonly called Doppler Wand or Doppler probe, and a sphygmomanometer (blood pressure cuff) are usually needed. The blood pressure cuff is inflated proximal to the artery in question. Measured by the doppler wand, the inflation continues until the pulse in the artery ceases. The blood pressure cuff is then slowly deflated. When the artery's pulse is re-detected through the doppler probe the pressure in the cuff at that moment indicates the systolic pressure of that artery.

The higher systolic reading of the left and right arm brachial artery is generally used in the assessment. The pressures in each foot's posterior tibial artery and dorsalis pedis artery are measured with the higher of the two values used as the ABI for that leg.

$$ABPI_{Leg} = \frac{P_{Leg}}{P_{Arm}}$$

Where, P_{Leg} is the systolic blood pressure of dorsalis pedis or posterior tibial arteries

P_{Arm} is the highest of the left and right arm brachial systolic blood pressure

Ankle Brachial Index can be used as a non invasive method of assessing sub clinical peripheral atherosclerosis. When compared to angiography, the sensitivity of ABI in detecting peripheral atherosclerosis is 90% and the specificity is 98%.[46] Results of one of the studies states that ABI is the gold standard in screening for atherosclerosis.[47] Organizations such as the American Heart Association and the Society of Interventional Radiology recommend the use of the ABI in the evaluation of asymptomatic atherosclerosis.[47] A study has even recommended that ABI should be incorporated into routine cardiovascular screening methods and that the potential of its inclusion into cardiovascular scoring systems should be examined.[48]

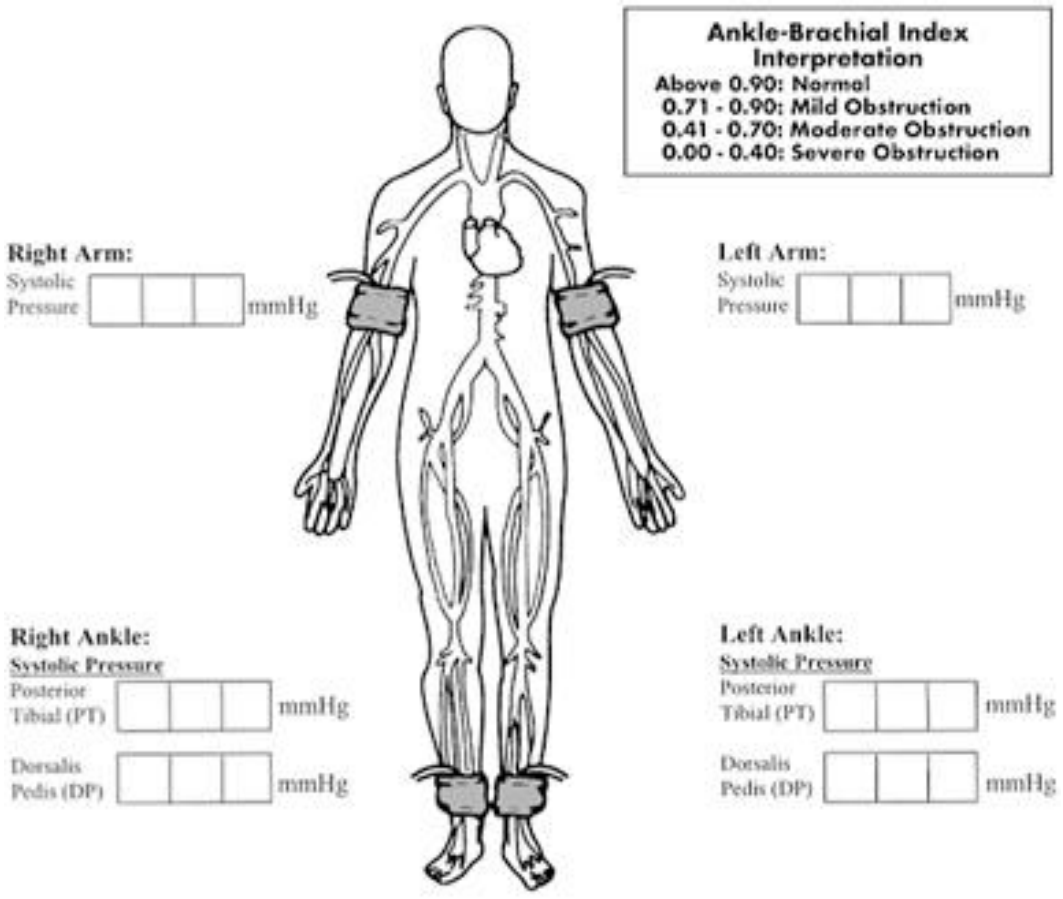


Figure 6. Ankle-Brachial Index (ABI) Worksheet

Interpretation of results

ABI scores should be interpreted as follows:

- Greater than 0.90 = normal
- 0.71 – 0.90 = mild obstruction
- 0.41 – 0.70 = moderate obstruction
- Less than 0.40 = severe obstruction

Interarm systolic blood pressure difference (IASBPD)

A systolic difference in blood pressures between arms is associated with peripheral arterial disease, cerebrovascular disease, and increased cardiovascular and all-cause mortality; these findings are mainly derived from populations at elevated cardiovascular risk.[49]

Studies that have examined the interarm difference in people with diabetes, who are also at elevated cardiovascular risk, report a prevalence of a systolic difference ≥10 mmHg between arms in type 2 diabetes of 9–10%.[49,50] However, the associations of interarm difference in blood pressure with increased cardiovascular and all-cause mortality have not been reported in diabetes.[49]

Failure to recognize an interarm difference in blood pressure may incorrectly classify the majority of subjects with such a difference as having controlled hypertension if the lower reading arm is measured. This can delay the diagnosis or confound the treatment of hypertension, a key component of effective diabetes care, if an interarm difference is not specifically looked for.[49] Guidelines advise measuring both arms during initial assessment of high blood pressure, but this guidance is followed by less than one in five general practitioners in the U.K., perhaps due, in part, to clinical inertia or to a lack of evidence directly relevant to primary care for the importance of measuring both arms.[51]

Confirmation of an interarm difference requires a method of repeated simultaneous measurement, to avoid overestimation of prevalence.[52] This technique, however, may not be practical in routine clinical care. It adds time to the clinical

assessment of subjects in primary care, and we have found it to be a barrier to recruitment in our previous study in diabetes.[49]

Initially, a sequentially measured pair of readings may be sufficient to rule subjects out of further assessment for an interarm difference, but this requires further evaluation.[49] Previous small studies that directly compared sequential and simultaneous measurement techniques have concluded that the reproducibility of an interarm difference measured by different techniques is poor,[53,54] although repeated sequential measures can predict a systolic interarm difference ≥10 mmHg on repeated simultaneous measurement.[55]

Peripheral arterial disease, a recognized risk factor for future cardiovascular events and mortality, has been assumed to be the pathological basis for an interarm difference in blood pressure.[56]

The differences observed may result from more diffuse stiffening in the arteries since structural changes in large arteries as a result of hypertension begin early in the course of the condition and are insidious, whereas symptomatic cardiovascular and peripheral vascular disease are late sequelae of a process of gradual arterial stiffening as a result of damage to the elastic fibers under sustained elevated blood pressure.[57]

Unevenly distributed stiffness could produce a measurable interarm difference; Su et al. have recently shown an association of a systolic difference ≥10 mmHg with elevated brachial-ankle pulse wave velocity, suggesting increased arterial stiffness.[58]

Increased blood pressure variability is a potential confounder of interarm difference and is associated with increased arterial stiffness. Different methods of measurement of blood pressure variability exist; however, the SD of blood pressure measurements is one simple method that correlates independently with mortality differences.[49]

The number of failed attempts to measure pairs of blood pressures brings into question the practicality of repeated simultaneous measures in clinical practice.[49]

Newer sphygmomanometers are equipped with algorithms to detect atrial fibrillation, which was a common reason for failure. However, time was evidently a factor during data collection, and this has been observed before. Machines that measure two (e.g., Microlife WatchBP Office) or four (e.g., Omron Colin VP-1000) limbs are now more readily available and may permit more practical assessment of interarm differences. They are, however, more costly than standard clinical sphygmomanometers. The findings presented suggest that a single pair of measurements that can be feasibly made within routine practice can reliably rule subjects out of the need for further paired measurements; this may be a more practical first approach than resourcing simultaneous bilateral arm measurements for all subjects.[49]

The associations of interarm difference with peripheral arterial disease and with increased cardiovascular mortality suggest that detection of an interarm difference may define a subpopulation at high risk of vascular events.[59] In therapeutic terms, there is no evidence to support any different intervention on

detection of a difference, but in a health service of finite and shrinking resources, this may help to identify subjects who can most benefit from intensive lifestyle interventions.

METHODOLOGY

The present study, was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with type 2 DM during the period of January 2013 to December 2013.

Study design and duration

The study design was a one year cross-sectional study.

Study period

The present study was conducted from January 2013 to December 2013.

Source of Data

Patients presenting with type 2 diabetes mellitus at Department of Medicine KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were included in the study.

Sample size

A total of 45 type 2 diabetic patients were included in the study.

Sampling procedure

The sample size (n) was calculated using the following formula:

$$n = 4\,pq/d^2$$

Where,

n = Sample size

p = Prevalence

q = 100 – p

d = Error

The prevalence (p) of atherosclerosis in asymptomatic diabetic patients was taken as 91.4%.[60] The error (d) was taken as 10% of the prevalence. Hence, by substituting these values in the above given formula a sample size of 38 was obtained. However 45 patients fulfilled the selection criteria and hence were enrolled in the study.

Selection criteria

Inclusion Criteria

- Patients with type 2 diabetes mellitus with illness duration greater than six years.

Exclusion Criteria

- Trauma, Surgery or amputation involving the lower limb.
- Leg ulcers.
- Deep vein thrombosis.
- Filariasis or lower limb swelling due to other causes which would impair Doppler image quality.
- Hemiparesis, limb abnormality or significant limb injury .
- History of vascular surgery
- Known atrial fibrillation (reduced accuracy of automated blood pressure measurements.

- Patients on lipid lowering drugs.

Ethical clearance

Prior to the commencement, the study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belgaum.

Informed consent

During the study period, all patients presenting with diabetes mellitus and fulfilling the selection criteria were included in the study after obtaining a written informed consent (Annexure–I).

Data collection

Patients were interviewed and relevant history was obtained. Further the patients were subjected to clinical examination and the findings were recorded on a predesigned and pretested proforma (Annexure-II).

Investigations

Patients were subjected to fasting blood sugar levels.

Outcome variables

Ankle brachial index

Ankle brachial index was determined as the ratio of ankle systolic blood pressure to the brachial systolic blood pressure, with both determined using a hand held Doppler. The higher of left and right brachial pressures was used for the calculation of the ABI.

Interarm systolic blood pressure difference

Blood pressure was measured simultaneously in both arms with two automated sphygmomanometers using a previously piloted protocol.[55] In brief, this involved the participant sitting quietly for 5 minutes. Two pairs of bilateral blood pressure measurements were then obtained by simultaneous activation of two automated sphygmomanometers, the cuffs were then swapped to the contralateral arms, and two further pairs of blood pressure readings obtained. Mean systolic and diastolic pressures were calculated for each arm (for each individual) and subtracted to derive inter-arm systolic and diastolic blood pressure differences.

Statistical methods

The data obtained was coded and entered into the Microsoft Excel Spreadsheet (Annexure III). The categorical data was expressed in terms of rates, ratios and percentages. The prevalence of inter-arm differences greater than 10 mmHg was derived using simple descriptive statistics. To explore differences in characteristics between males and females with or without an inter-arm difference, Chi square or Fisher's exact test were used. The correlation between ABI and IASBP difference was done using correlation co-efficient and means IASBP differences with different ABI grades were compared using analysis of variance. A ‘p’ value (probability value) of less than or equal to 0.050 at 95% confidence interval was considered as statistically significant.

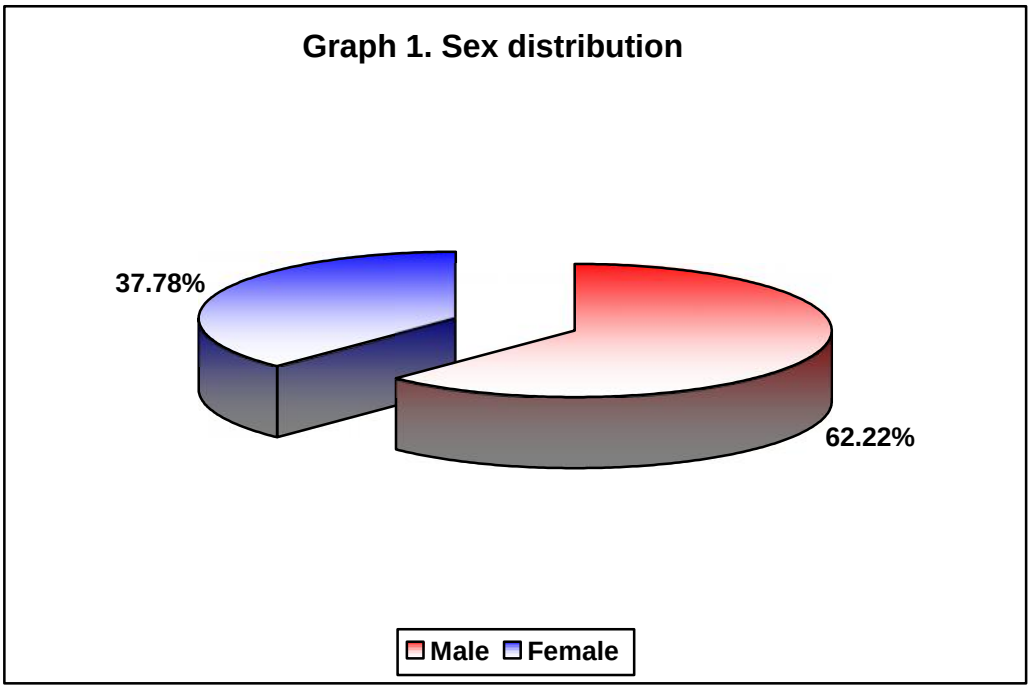
RESULTS

This one year cross-sectional study was conducted from January 2013 to December 2013 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 45 patients presenting with type 2 diabetes with a duration of six years or more were studied.

Data obtained was analysed and the final results and interpretation are tabulated as below.

Table 1. Sex distribution

Sex	Distribution (n=45)	
	Number	**Percentage**
Male	28	62.22
Female	17	37.78
Total	**45**	**100.00**

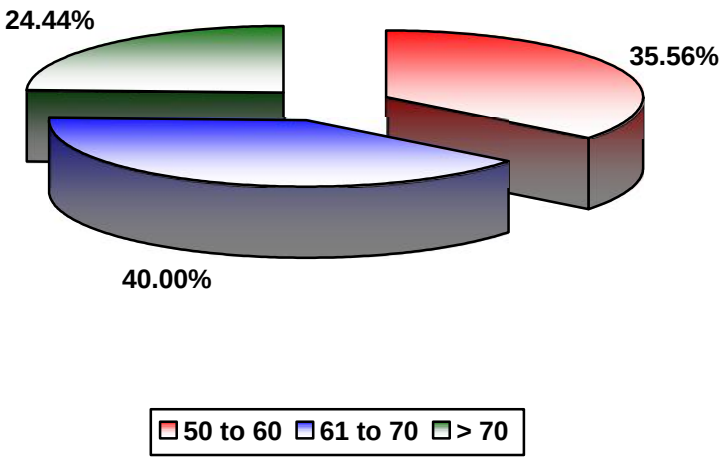


In the present study 62.22% o of the patients were males and 37.78% were females. The male to female ratio was 1.64:1.

Table 2. Age distribution

Age group (Years)	Distribution (n=45)	
	Number	**Percentage**
50 to 60	16	35.56
61 to 70	18	40.00
> 70	11	24.44
Total	**45**	**100.00**

Graph 2. Age distribution



In this study 40% of the patients presented with age between 61 to 70 years.

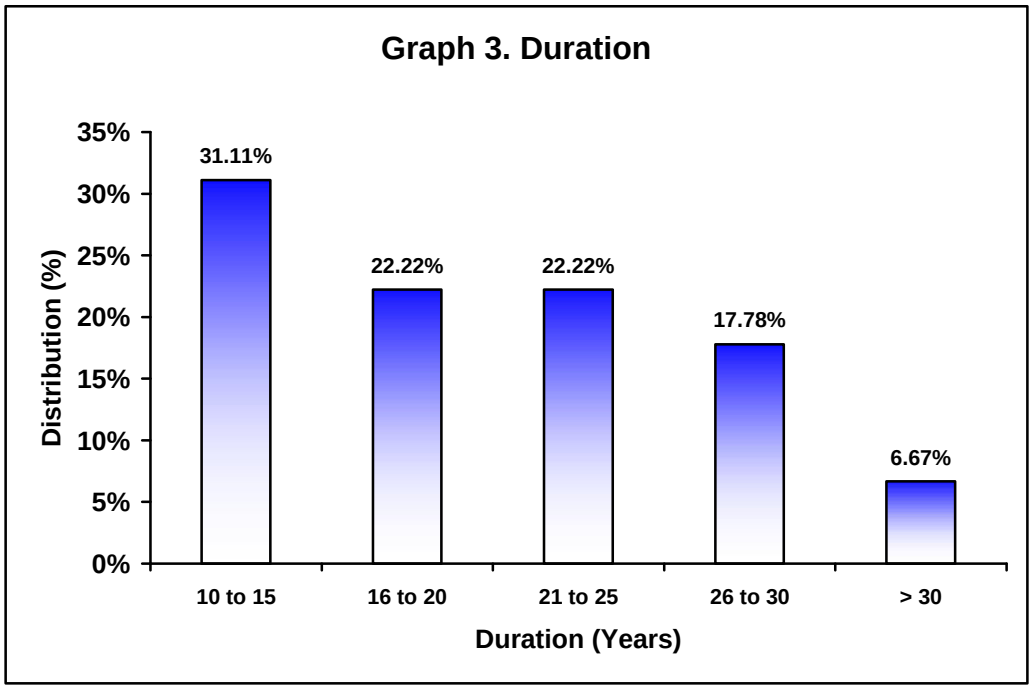
Table 3. Mean age

Sex	Patients	Distribution (n=45)		
		Mean	**SD**	**Range**
Male	28	65.1	9.01	50-80
Female	17	65.2	7.62	51-82
Overall	**45**	**65.1**	**8.07**	50-82

Table3 shows mean age of the study population as well as the mean age in males and females.

Table 4. Duration

Duration (Years)	Distribution (n=45)	
	Number	Percentage
10 to 15	14	31.11
16 to 20	10	22.22
21 to 25	10	22.22
26 to 30	8	17.78
> 30	3	6.67
Total	**45**	**100.00**



In this study most of the patients presented with duration between 10 to 15 years (31.11%). The duration among the other patients is as depicted in table 4 and graph 3.

Table 5. Mean duration

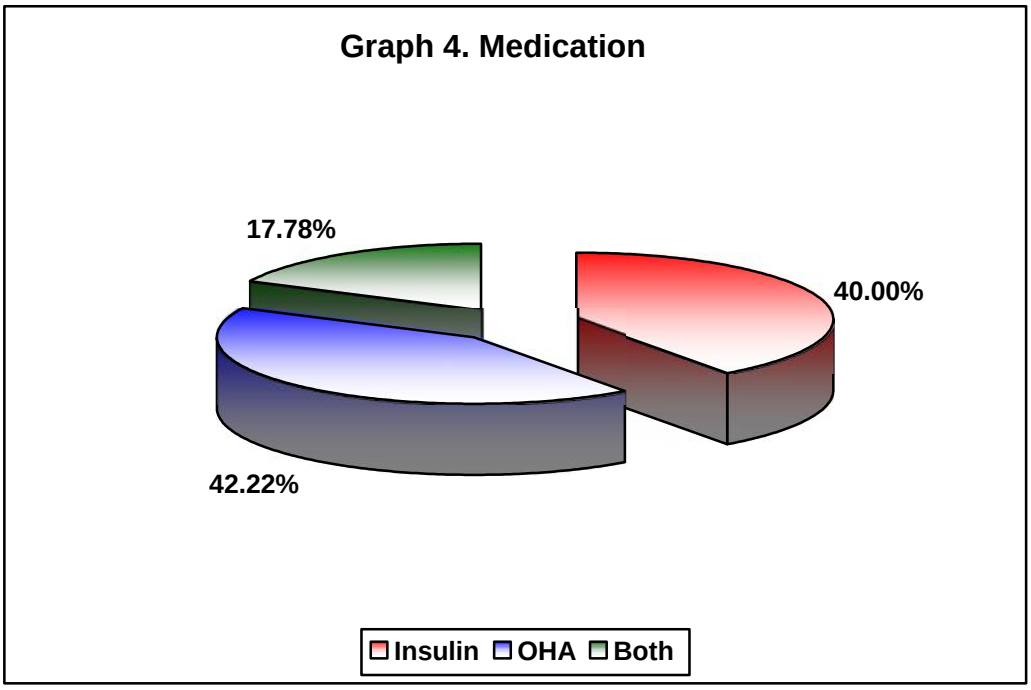
Sex	Patients	Distribution (n=45)		
		Mean	**SD**	**Range**
Male	28	19.8	7.72	10-37
Female	17	20.9	6.51	10-38
Overall	**45**	**20.4**	**6.93**	10-38

In the present study the mean duration of diabetes was 20.04 ± 6.93 years.

The mean duration of diabetes in males and females is as shown in table 5.

Table 6. Medication

Medication	Distribution (n=45)	
	Number	Percentage
Insulin	18	40.00
OHA	19	42.22
Both	8	17.78
Total	**45**	**100.00**

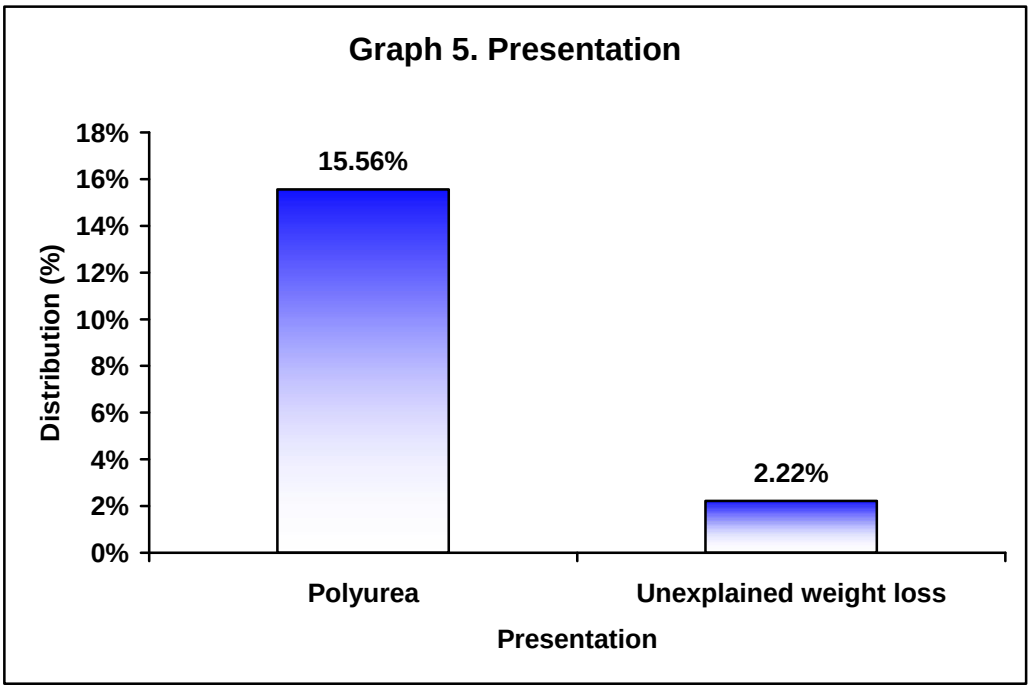


In this study 42.22% and 40% of the patients were on oral hypoglycaemic agents and insulin respectively.

Table 7. Presentation

Presentation	Distribution (n=45)	
	Number	**Percentage**
Polyurea	7	15.56
Unexplained weight loss	1	2.22

Multiple presentations hence total not shown

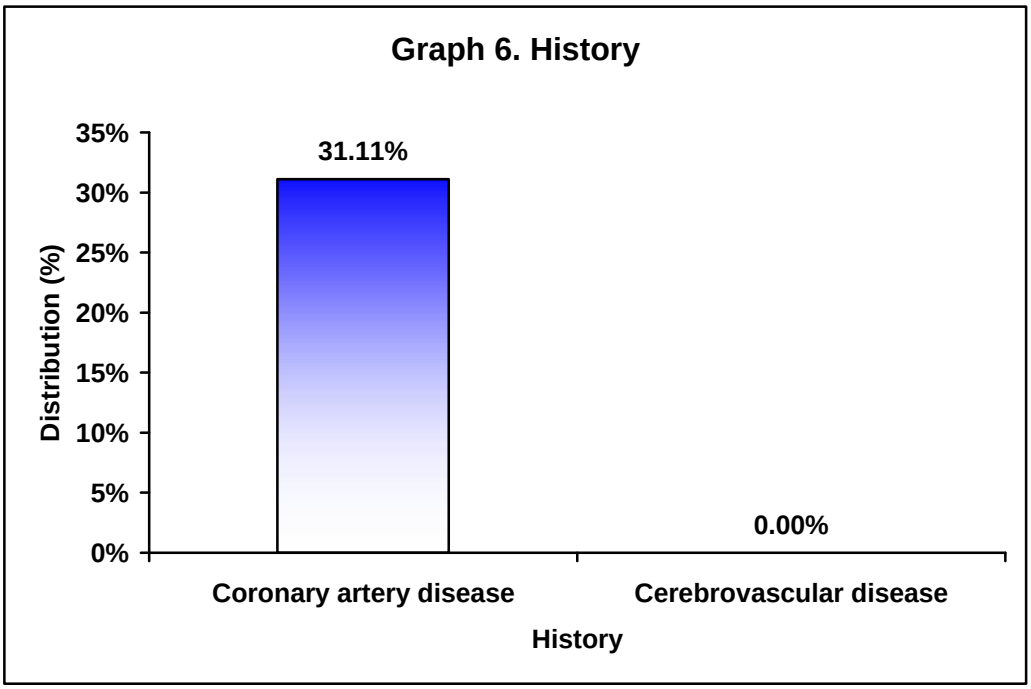


In the present study 15.56% and 2.25% of the patients presented with polyurea and unexplained weight loss.

Table 8. History

History	Distribution (n=45)	
	Number	**Percentage**
Coronary artery disease	14	31.11
Cerebrovascular disease	0	0.00

Multiple presentations hence total not shown

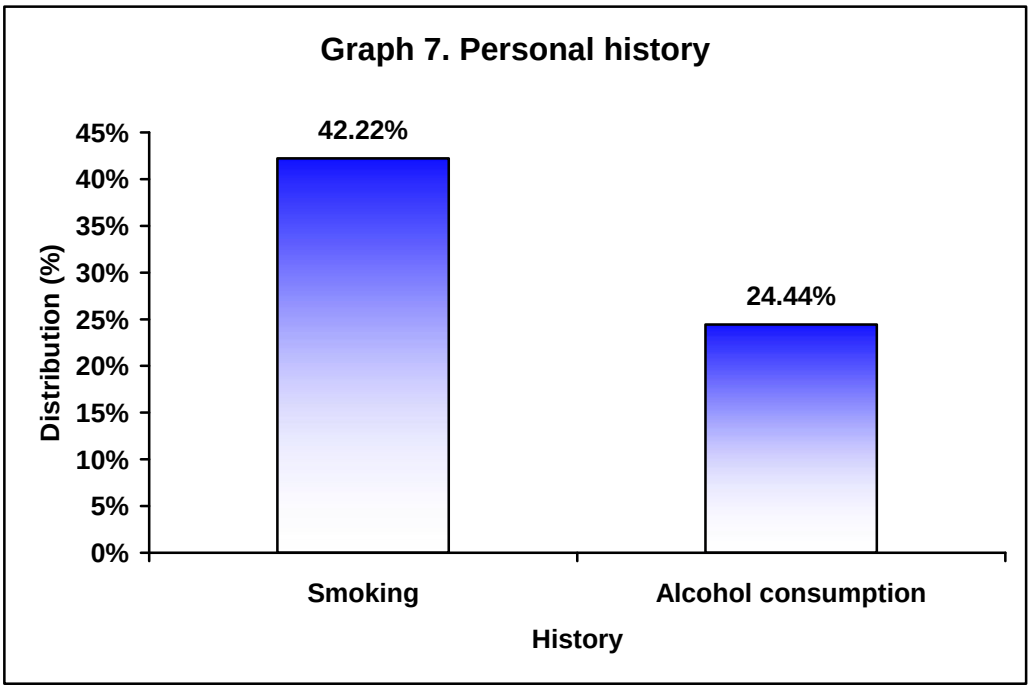


In this study 31.11% of the patients reported history of coronary artery disease.

Table 9. Personal history

History	Distribution (n=45)	
	Number	**Percentage**
Smoking	19	42.22
Alcohol consumption	11	24.44

Multiple presentations hence total not shown



In the present study personal history of smoking and alcohol consumption was noted in 42.22% and 24.44% of the patients.

Table 10. Clinical examination findings

Variables		Distribution (n=45)	
		Mean	**SD**
Pulse rate (/Minute)		74.44	6.11
Respiratory rate (/Minute)		17.49	0.66
Blood pressure Standing	Systolic	133.02	9.43
	Diastolic	83.16	7.99
Blood pressure supine	Systolic	129.82	9.51
	Diastolic	79.96	8.65

Table 10 shows mean vitals that is, mean pulse rate, respiratory rate, blood pressure (on standing and supine positions).

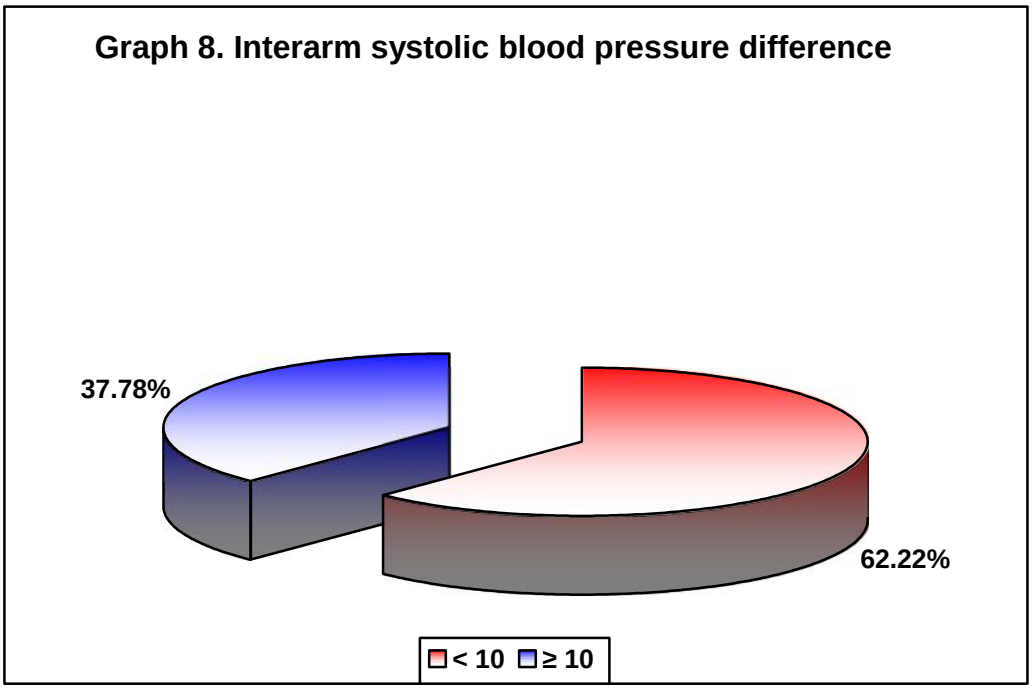
Table 11. Interarm systolic blood pressure

Reading	Side	SBP (mm Hg) (n=45)	
		Mean	**SD**
Reading 1	Right arm	133.51	10.89
	Left Arm	125.24	9.34
Reading 2	Right arm	133.20	9.32
	Left Arm	125.38	9.08
Reading 3	Right arm	133.02	9.51
	Left Arm	125.31	9.06
Mean difference	Right arm	133.04	9.41
	Left Arm	125.33	9.14

Table 11 shows mean interarm systolic blood pressure at first, second and third reading and the mean interarm systolic blood pressure difference.

Table 12. Interarm systolic blood pressure difference

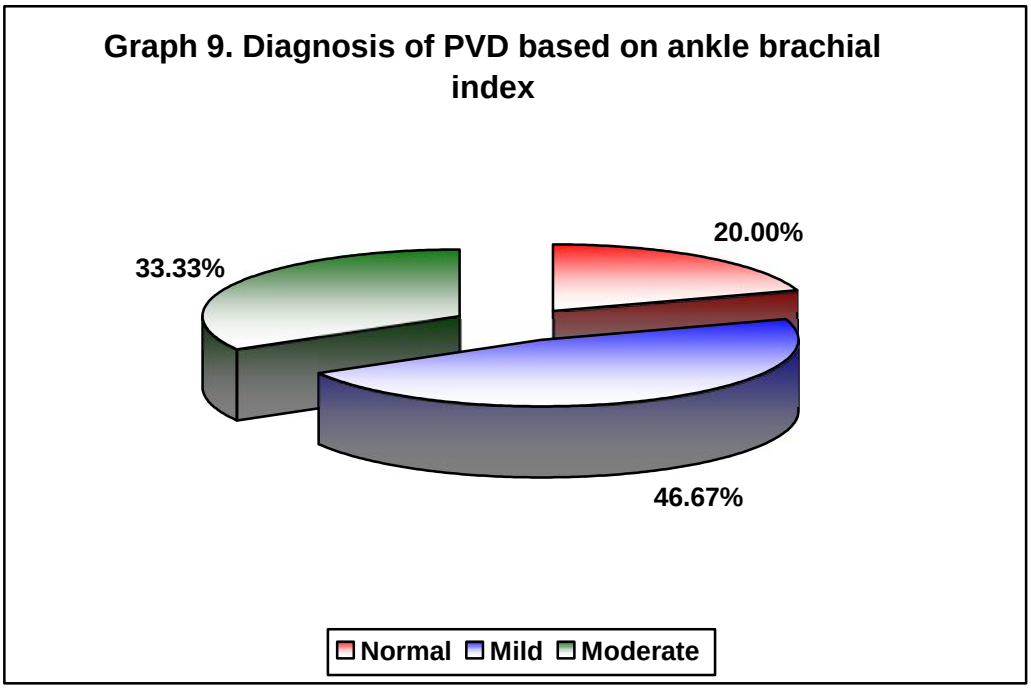
IASBP difference (mm Hg)	Distribution (n=45)	
	Number	**Percentage**
< 10	28	62.22
≥ 10	17	37.78
Total	**45**	**100.00**



In the present study interarm systolic blood pressure difference of ≥10 mm Hg was noted in 37.78% of the patients.

Table 13. Diagnosis of PVD based on ankle brachial index

ABI	Distribution (n=45)	
	Number	**Percentage**
Normal (>0.90)	9	20.00
Mild (0.71-0.90)	21	46.67
Moderate (0.41-0.70)	15	33.33
Total	**45**	**100.00**



In this study based on ABI most of the patients (46.67%) had mild and 33.33% had moderate peripheral vascular disease.

Table 14. Correlation of IASBP with ABI

IASBP difference (mm Hg)	ABI							
	Normal (>0.90)		Mild (0.71-0.90)		Moderate (0.41-0.70)		Total	
	No.	%	No.	%	No.	%	No.	%
< 10	9	32.14	19	67.86	0	0.00	28	100.00
≥ 10	0	0.00	2	11.76	15	88.24	17	100.00
Total	**9**	**20.00**	**21**	**46.67**	**15**	**33.33**	**45**	**100.00**

p < 0.001

In the present study 17 patients had IASBP difference ≥ 10 mm Hg. Of these all the patients had PVD (100%) and 2 (11.76%) had mild PVD while 15 (88.24%) had moderate PVD based on ABI. This difference was statistically significant ($p<0.001$).

Table 15. Correlation of IASBP with ABI in males

IASBP difference (mm Hg)	ABI Normal (>0.90)		Mild (0.71-0.90)		Moderate (0.41-0.70)		Total	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
< 10	2	20.00	8	80.00	0	0.00	10	100.00
≥ 10	0	0.00	0	0.00	7	100.00	7	100.00
Total	**2**	**11.76**	**8**	**47.06**	**7**	**41.18**	**17**	**100.00**

p < 0.001

In the present study 7 males had IASBP difference of ≥ 10 mm Hg and all of them were diagnosed to have moderate PVD (100%) based on ABI. This difference was statistically significant ($p<0.001$).

Table 16. Correlation of IASBP with ABI in females

IASBP difference (mm Hg)	ABI							
	Normal (>0.90)		Mild (0.71-0.90)		Moderate (0.41-0.70)		Total	
	No.	%	No.	%	No.	%	No.	%
< 10	7	38.89	11	61.11	0	0.00	18	100.00
≥ 10	0	0.00	2	20.00	8	80.00	10	100.00
Total	**7**	**25.00**	**13**	**46.43**	**8**	**28.57**	**28**	**100.00**

p < 0.001

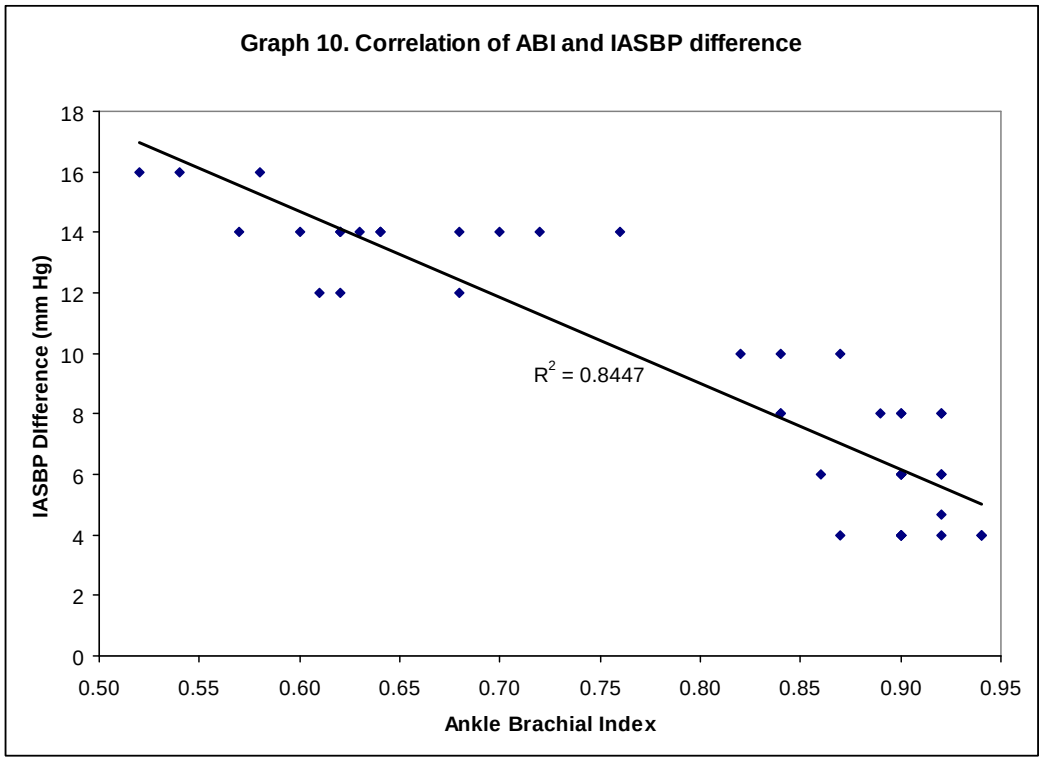
In the present study 10 females had IASBP difference of ≥ 10 mm Hg. Of these 2 (20%) had mild and 8 (80%) them were diagnosed to have moderate PVD based on ABI. This difference was statistically significant (p<0.001).

Table 17. Comparison of mean IASBP difference and severity of PVD

ABI	Patients	Mean IASBP Difference	
		Mean	SD
Normal (>0.90)	9	5.43	1.65
Mild (0.71-0.90)	21	9.20	3.16
Moderate (0.41-0.70)	15	14.00	1.33

F=82.08; **p<0.001**

Table 17 shows comparison of mean IASBP difference with severity of PVD. It was observed that, as the PVD severity increased the mean IASBP difference increased. The mean IASBP values differed significantly in all the grades PVD based on ABI ($p<0.001$).



Graph 10 shows linear correlation of ABI and IASBP difference. There was a strong negative correlation, depicting increase in IASBP difference with decrease in ABI and vice versa ($R=-0.919$; $R^2=0.8447$; $p<0.001$)

DISCUSSION

Peripheral vascular disease is a major macrovascular complication of diabetes mellitus. Because of the unique involvement of distal pattern of vessels and invariable association with neuropathy, peripheral vascular disease in diabetics presents late, having already developed limb threating ischaemia.[61]

The main reasons to diagnose PVD in diabetic individuals are to initiate therapies that decrease the risk of atherothrombotic events, improve quality of life, and decrease disability. A diagnosis of PVD indicates the presence of systemic atherosclerosis that confers additional cardiovascular risk to the patient with diabetes, and gives further impetus to aggressively manage vascular risk factors in this high-risk group.

Although physical examination provides important information, additional non-invasive testing is necessary to ensure the diagnosis. The ABI is a reproducible and reasonably accurate measurement for the detection of PVD. The ABI is defined as the ratio of the ankle systolic blood pressure divided by the brachial systolic blood pressure, and is normally between 1.00 and 1.40.[62] In PVD, the ankle systolic blood pressure is less than the brachial systolic blood pressure, and the ABI is reduced to <1.00; PVD is defined as an ABI <0.90. Lower ABI values indicate more severe PAD and a higher risk of cardiovascular events.[63]

The ADA consensus statement recommends that a screening ABI be performed in all diabetic individuals >50 years of age. If normal (0.91 to 1.40), the

test should be repeated every five years. A screening ABI should be performed in any patient with or with out symptoms of PVD.[64]

In the primary care setting, Mohler et al.[65] assessed perceptions of the ABI among 886 clinicians; most believed the ABI was useful in the diagnosis of both symptomatic (96%) and asymptomatic (89%) PVD.

However, ankle-brachial index determinations may be of limited value in some patients with diabetes, because calcification of the tibial arteries may render them non-compressible, resulting in unusually high ABI values (>1.40). Under these conditions, the ABI cannot distinguish patients who have arterial occlusion from those who do not, making the ABI unreliable. However, an elevated ABI is still predictive of an increased risk of cardiovascular events, and other non-invasive vascular tests should be considered to make the diagnosis of PVD.[63]

Interarm systolic blood pressure differences have been studied in patients with various manifestations of vascular disease. It has been found to correlate with classic and novel cardiovascular risk factors and may be predictive of cardiovascular events. Nevertheless, data on the epidemiology of interarm systolic blood pressure difference are relatively scarce.[66] This prompted us to examine whether interarm differences in SBP and ABI correlate in diagnosing PVD among the patients with type 2 diabetes mellitus.

The present cross-sectional study was conducted for a period of one year from January 2013 to December 2013 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 45

patients with type 2 diabetes having duration of ≥ 6 years were studied. All the patients were investigated for ABI and interarm systolic blood pressure difference.

Peripheral vascular disease (PVD) is one of the macrovascular complications of type 2 diabetes mellitus. In the present study ABI revealed 80% of the patients with peripheral vascular disease. The severity of mild grade was noted in 46.67% of the patients and moderate in 33.33% of the patients. In the remaining that is 20% of the patients the ABI was > 0.90 suggesting no evidence of PVD. There is significant difference in the reported prevalence of PVD. A hospital-based, cross-sectional study[67] from New Delhi in order to assess PVD in type 2 diabetics, reported evidence of PVD in 14.3% using ankle brachial index. Recently another study[61] from Punjab reported prevalence of peripheral vascular disease in type 2 diabetes mellitus measured by ankle-brachial pressure index as 33%.

The higher prevalence of peripheral vascular disease observed in the present study compared to study from New Delhi and Punjab may be due to the higher duration of diabetes that is, most of the patients presented with duration between 10 to 15 years (31.11%) and the mean duration was 20.40 ± 6.93 years while the Study[67] from New Delhi reported mean duration of 8 years. The history of coronary artery disease was present in 31.11% of the patients in this study and higher rate of smoking was observed that is 42.22% which are risk factors significantly associated with PVD.

In this study the mean interarm systolic blood pressure difference was obtained though three readings of both arms. The mean systolic blood pressure in right arm was noted as 133.04 ± 9.41 mm Hg and in left the same was recorded as

125.33 ± 9.14 mm Hg. Further interarm systolic blood pressure difference of ≥10 mm Hg was present in 17 patients that is 37.78%. Among these, all the patients were diagnosed to have PVD (100%) on ankle brachial index. The severity of PVD was moderate in majority of the patients that is 88.24% and the remaining 2 patients that is 11.76% had mild PVD. Of the 28 patients with interarm systolic blood pressure difference of < 10 mm Hg, 19 (67.86%) had mild PVD and 9 (32.14%) patient were not diagnosed to have PVD based on ABI. These differences observed were statistically significant ($p<0.001$). These findings suggest that interarm systolic blood pressure difference of ≥10 mm Hg is significantly predicts peripheral vascular disease.

A cross sectional study[68] to measure prevalence of an inter-arm blood pressure difference in patients with type 2 diabetes on a total of 101 participants, authors observed a systolic inter-arm difference ≥10 mmHg was observed in 10% of patients with diabetes. However the authors did not assess the presence of peripheral vascular disease.

In the present study male preponderance was noted that is, 62.22% were males and 37.78% were females with male to female ratio of 1.64:1. But ABI findings revealed PVD in 21 females and 15 males suggesting higher incidence of PVD among females. Similar findings were reported in a study[61,67] from New Delhi and Punjab where authors reported higher prevalence of PVD among females.

In the present study the interarm systolic blood pressure difference of ≥10 mm Hg was noted in 7 males and 10 females. Of the 10 females with IASBP difference of ≥ 10 mm Hg, 2 (20%) had mild and 8 (80%) had moderate PVD based

on ABI. Further, of the 7 males with IASBP difference of ≥ 10 mm Hg, all of them (100%) were diagnosed to have moderate PVD based on ABI. This difference was statistically significant ($p<0.001$). These findings show that, interarm systolic blood pressure difference of ≥10 mm Hg significantly predicts peripheral vascular disease in males as well as females. However data exploring the mean IASBP difference in males and females is scarce and hence could not be commented upon.

In this study the mean interarm systolic blood pressure difference in patients with moderate PVD were found to be significantly high (14.00 ± 1.33 mm Hg) compared to mild (9.20 ± 3.16 mm Hg) and normal (5.43 ± 1.65 mm Hg) ($p<0.001$). The linear correlation of mean IASBP difference with ABI showed strong negative correlation, depicting significant increase in IASBP difference with decrease in ABI and vice versa ($R=-0.919$; $R^2=0.8447$; $p<0.001$) These findings again predict that patients with PVD are likely to have higher mean interarm systolic blood pressure difference and the same increases with severity of the peripheral vascular disease. The inverse correlations between the magnitudes of the IADs and the ABPI in this study support the hypothesis that the IAD is a proxy marker for PVD in this population.

Similar findings were reported in a cross sectional study by Clark CE et al[55] in 2007 in a hypertensive primary care population.

A recent cross-sectional retrospective study[69] of 206 Japanese patients with type 2 diabetes aged 49–76 years assessed whether the IAD could be a marker for subclinical atherosclerosis in patients with type 2 diabetes who are at high risk of

cardiovascular disease (CVD). Study concluded that, the IAD could be a novel risk marker for subclinical atherosclerosis in patients with type 2 diabetes.

A cross-sectional study[55] to establish the prevalence of an inter-arm blood pressure difference (IAD) and explore its association with other indicators of peripheral vascular disease (PVD) in a hypertensive primary care population reported negative correlation between systolic (Pearson's correlation coefficient - 0.378; P = 0.01) and diastolic (Pearson's correlation coefficient - 0.225; P = 0.05) magnitudes of IAD with ABPI. Authors concluded that, magnitude of the IAD is inversely correlated with ABPI, supporting the hypotheses that IADs are causally linked to PVD, and that IAD is a useful marker for the presence of PVD. These findings are in strong agreement with these studies.

Overall the present study showed that, interarm systolic blood pressure (BP) difference is often encountered in patients with type 2 diabetes and associated with peripheral vascular disease. However this study had certain limitations. As the selection criteria of the patients directed us to recruit patients with duration of more than six years the prevalence of disease was very high which would have created the bias in study results. Further the other comorbid conditions such as hypertension and thyroid profile were not considered. Hence further studies with case control design after the adjustment of these confounding variables would explore the role of interarm systolic blood pressure difference in the diagnosis of peripheral vascular disease.

CONCLUSION

Overall the present study showed that, interarm systolic blood pressure difference (IASBPD) is often encountered in patients with type 2 diabetes and associated with peripheral vascular disease.

There was a strong association and correlation of interarm systolic blood pressure difference with ankle brachial index for the detection of detection of PVD in type 2 diabetes mellitus.

Hence, IASBPD can be used as simple, bedside, non-invasive method of detection of PVD in patients with type 2 diabetes mellitus. Consequently, detection of an IASBPD of ≥ 10 mm Hg should prompt the clinician to screen subjects for other signs of vascular disease and target them for aggressive cardiovascular risk factor modification.

SUMMARY

Peripheral vascular disease is a major macrovascular complication of diabetes mellitus. The ABI is useful in the diagnosis of both symptomatic and asymptomatic PVD. Interarm systolic blood pressure differences have been studied in patients with various manifestations of vascular disease. The present study was attempt to examine whether interarm differences in SBP and ABI correlate in diagnosing PVD among the patients with type 2 diabetes mellitus.

The present cross-sectional study was conducted for a period of one year from January 2013 to December 2013 in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 45 patients with type 2 diabetes having duration of ≥ 6 years were studied. All the patients were investigated for ABI and interarm systolic blood pressure difference.

Most of the patients (62.22%) were males and male to female ratio was 1.64:1. 40% of the patients presented with age between 61 to 70 years. The duration of diabetes was between 10 to 15 years in 31.11% of the patients and mean duration was 20.04 ± 6.93 years. Most of the patients (42.22%) were on oral hypoglycaemic agents. The history of coronary artery disease was present in 31.11% of the patients. The interarm systolic blood pressure difference of ≥10 mm Hg was noted in 37.78% of the patients. Based on ABI most of the patients (46.67%) had mild and 33.33% had moderate peripheral vascular disease. IASBP difference ≥ 10 mm Hg was noted in 17 patients and of these, all the patients had PVD (100%). Mild PVD was noted in 11.76% and moderate in 88.24% ($p<0.001$). Comparison of mean IASBP difference with severity of PVD showed an increasing trend in the mean values with severity of

disease that is, as the PVD severity increased the mean IASBP difference increased and mean IASBP values differed significantly in all the grades of PVD based on ABI ($p<0.001$). The linear correlation of ABI and IASBP difference showed strong negative correlation, depicting increase in IASBP difference with decrease in ABI and vice versa ($R=-0.919$; $R^2=0.8447$; $p<0.001$)

An IASBPD of ≥ 10 mm Hg prompts physician for signs of peripheral vascular disease.

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ANNEXURE I – CONSENT FORM

"CORRELATON OF INTERARM SYSTOLIC BLOOD PRESSURE DIFFERENCE TO ANKLE BRACHIAL INDEX (ABI) IN DETECTING PERIPHERAL VASCULAR DISEASE IN TYPE TWO DIABETES MELLITUS PATIENTS"

Objective and purpose of the study:

This research is intended to explore the association of the IASBPD with the ABPI as the non invasive method of detection of PVD in type 2 diabetes mellitus. The Principal investigator of the study is Dr. **** ****** under the guidance of Dr. **** *****.

Procedure:

If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations.

Alternatives

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part now, you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study you will receive the standard treatment for patients with your condition.

Voluntary participation / withdrawal

Your participation in this study is entirely voluntary and you may withdraw from the study at any time.

Privacy and Confidentiality

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy

Does not apply to this research

Financial incentives for participation

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

If you have any questions about your right as a participant you may call

Dr. **** ******,
Investigator,
PG in General Medicine,
Jawaharlal Nehru Medical College,
Belgaum
Contact No: ***** ******

Dr. ***** ******,
Chairman, Ethical Committee for
Human Research,
Jawaharlal Nehru Medical College,
Belgaum
Contact No: ****** *** Ext: *****

Dr. ****** *******,
Professor,
Department of Medicine,
Jawaharlal Nehru Medical College,
Belgaum
Contact No: ***** *****

Consent Statement

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, and has been explained to me in my vernacular language and had had all my questions answered. I will be given a copy of this consent form.

Signature / Left thumb print of the participant or legally authorized representative

Name of the Participant: _____

Signature / Thumb print _____

Impression of the participant

Name of the legally _____

Authorized representative / guardian

Signature / Thumb print _____

Name of the witness _____

Signature / Thumb print _____

Investigators name _____

and signature

Date: Place:

Dr. ****** *******,
Professor,
Department of Medicine,
Jawaharlal Nehru Medical College,
Belgaum
Contact No: ***** ***** Ext: *****

Dr. ****** *****,
Investigator,
PG in General Medicine,
Jawaharlal Nehru Medical College,
Belgaum
Contact No: ***** ******

ANNEXURE II – PROFORMA

"CORRELATION OF INTER ARM SYSTOLIC BLOOD PRESSURE DIFFERENCE TO ANKLE BRACHIAL INDEX(ABI) IN DETECTING PERIPHERAL VASCULAR DISEASE IN TYPE TWO DIABETES MELLITUS PATIENTS"

1) SL.NO:

2)NAME:

3) AGE:

4) SEX:

5) OCCUPATION:

6) RELIGION:

7) I.P.NO./O.P.NO.:

8) ADDRESS:

9) DATE OF ADMISSION:

10) DATE OF DISCHRGE:

HISTORY:

PRESENTING COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

SIGNIFICANT PAST HISTORY:

Coronary artery disease-

Cerebrovascular disease-

DIABETIC HISTORY:

Polyuria-

Polydipsia-

Polyphagia-

Unexplained weight loss-

Duration of Diabetes:

Age of onset of Diabetes-

Family history of Diabetes-

Treatment history of Diabetes:

Drug name-

Dosage-

Frequency-

Duration of Treatment-

Other Drug (If any)

Significant personal history:

Significant Family history:

GENERAL PHYSICAL EXAMINATION:

VITAL SIGNS:

Pulse- Temp- Respiratory Rate-

Blood pressure: Supine position-

Standing position-

Right arm systolic BP Left arm systolic BP

1)

2)

3)

Mean:

INTER ARM SYSTOLIC BLOOD PRESSURE DIFFERENCE:

SYSTEMIC EXAMINATION:

Respiratory system-

Cardiovascular system-

Per abdominal examination-

Central nervous system-

INVESTIGATIONS:

Fasting blood sugar-

Ankle brachial index-

Special investigations if any

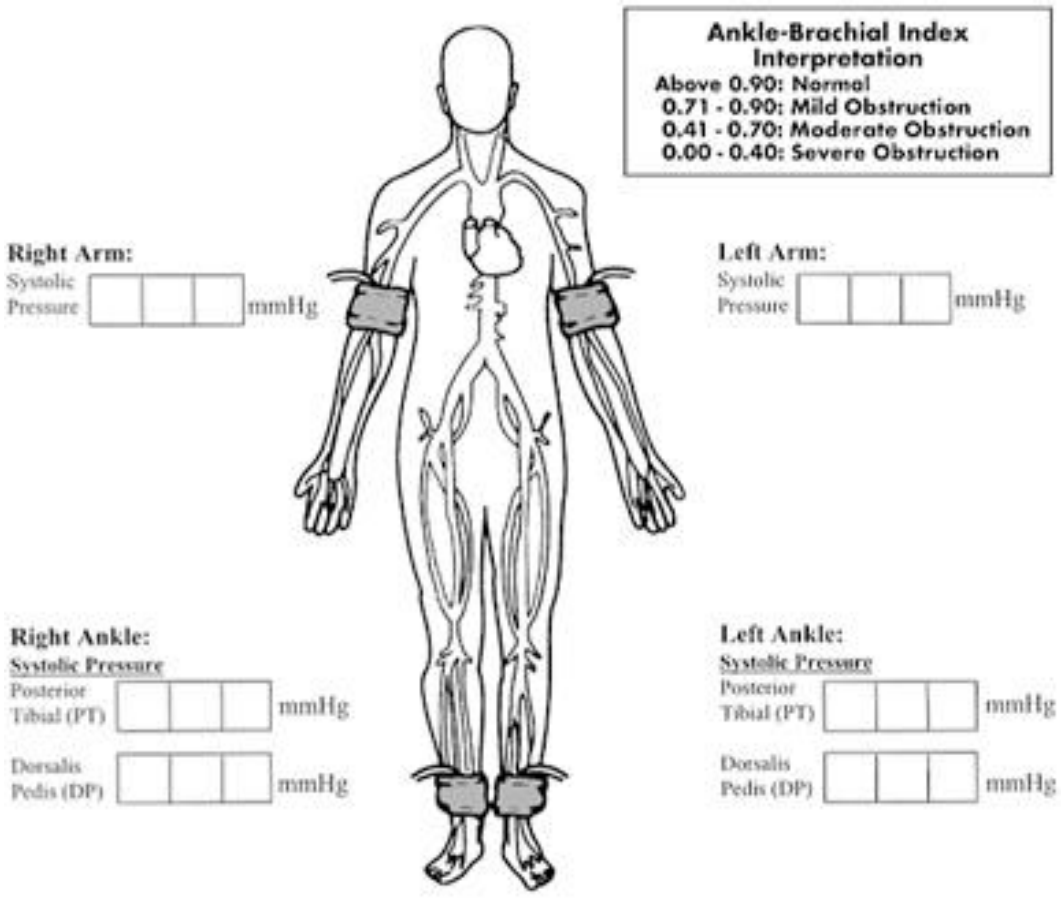

Figure. Ankle-Brachial Index (ABI) Worksheet

Interpretation of results

ABI scores should be interpreted as follows:

- Greater than 0.90 = normal
- 0.71 – 0.90 = mild obstruction
- 0.41 – 0.70 = moderate obstruction
- Less than 0.40 = severe obstruction

ANNEXURE III – KEY TO MASTER CHART

-	-	Absent
+	-	Present
BSL	-	Blood sugar levels
BTH	-	Both
F	-	Female
IASBP	-	Interarm systolic blood pressure
INS	-	Insulin
M	-	Male
mm Hg	-	Millimeters of mercury
OHA	-	Oral hyperglycaemic agent

ANNEXURE III - MASTER CHART

Serial Number	In / out patient number	Age (Years)	Sex	Diabetic history					History		Family history of diabetes	Personal history		General physical examination						Investigation													
																BP (mm Hg)				BSL	IASBP difference (mm Hg) (Readings)												
																Supine		Standing			1		2		3		Mean					
				Age of onset (Years)	Duration (Years)	Medication	Polyuria	Unexplained weight loss	Coronary artery disease	Cerebrovascular diseae		Smoking	Alcohol consumption	Pulse rate (/Minute)	Respiratory rate (/Minute)	Systolic	Diastolic	Systolic	Diastolic	Fasting (mg/dL)	Right Arm	Left Arm	Right Arm	Left Arm	Right Arm	Left Arm	Right Arm	Left Arm	Difference (mm Hg)	Lower limb SBP (mm Hg)	Ankle brachial index			
1	425345	63	M	51	12	OHA	+	-	+	-	+	+	-	78	16	124	90	120	90	134	124	110	126	110	122	110	124	110	14	76	0.62			
2	475292	60	M	43	17	OHA	-	-	-	-	-	-	-	74	18	116	90	110	90	168	116	106	116	106	116	106	116	106	10	96	0.82			
3	475366	82	M	54	28	INS	+	-	-	-	-	+	+	60	18	122	80	120	60	137	122	114	122	114	122	114	122	114	8	110	0.92			
4	475426	60	F	48	12	INS	-	-	-	-	-	-	-	66	18	130	94	120	90	150	130	122	130	122	130	122	130	122	8	116	0.89			
5	475850	51	M	40	11	OHA	+	-	+	-	+	+	-	78	17	126	96	126	90	174	126	118	126	118	126	118	126	118	8	106	0.84			
6	464200	70	F	41	29	INS	-	-	-	-	-	-	-	74	18	128	94	126	94	134	128	140	128	140	128	140	128	140	12	86	0.61			
7	465131	54	M	39	15	OHA	+	-	-	-	-	-	-	69	17	126	80	120	80	120	126	122	128	122	126	122	127	122	5	116	0.92			
8	481059	65	M	51	14	OHA	-	-	-	-	-	+	+	64	18	130	70	146	70	110	130	116	130	116	130	116	130	116	14	82	0.63			
9	476488	63	M	50	13	OHA	+	+	+	-	+	-	-	76	18	140	70	140	70	120	140	134	140	134	140	134	140	134	6	130	0.92			
10	479833	60	M	46	14	OHA	+	-	-	-	-	-	+	78	18	110	80	110	80	147	110	116	110	116	110	116	110	116	6	100	0.86			
11	511997	70	M	44	26	INS	-	-	-	-	-	+	+	74	18	130	82	130	80	152	130	110	130	116	130	116	130	114	16	76	0.58			
12	489748	80	F	43	37	BTH	+	-	+	-	+	-	-	68	17	126	70	120	70	186	126	140	126	140	126	140	126	140	14	80	0.57			
13	509143	76	M	38	38	INS	-	-	-	-	-	+	-	74	18	146	80	140	80	140	146	132	146	132	146	132	146	132	14	88	0.60			
14	513159	58	M	41	17	INS	-	-	-	-	-	-	-	80	18	124	80	120	80	168	120	116	124	116	128	116	124	116	8	112	0.90			
15	508422	57	F	42	15	INS	-	-	+	-	-	-	-	72	18	130	70	126	70	116	130	122	130	120	130	124	130	122	8	110	0.84			

ANNEXURE III - MASTER CHART

Serial Number	In / out patient number	Age (Years)	Sex	Diabetic history					History		Family history of diabetes	Personal history		General physical examination						Investigation													
																BP (mm Hg)				BSL	IASBP difference (mm Hg) (Readings)												
																Supine		Standing			1		2		3		Mean					
				Age of onset (Years)	Duration (Years)	Medication	Polyuria	Unexplained weight loss	Coronary artery disease	Cerebrovascular diseae		Smoking	Alcohol consumption	Pulse rate (/Minute)	Respiratory rate (/Minute)	Systolic	Diastolic	Systolic	Diastolic	Fasting (mg/dL)	Right Arm	Left Arm	Right Arm	Left Arm	Right Arm	Left Arm	Right Arm	Left Arm	Difference (mm Hg)	Lower limb SBP (mm Hg)	Ankle brachial index			
16	477134	67	M	40	27	BTH	-	-	-	-	+	+	+	68	18	130	74	130	70	130	130	116	132	116	128	116	130	116	14	98	0.76			
17	477151	56	M	39	17	INS	-	-	-	-	-	-	-	74	17	136	76	130	70	160	136	130	134	130	138	130	136	130	6	126	0.92			
18	513057	59	M	39	20	BTH	-	-	-	-	-	+	+	72	16	140	80	136	76	170	140	136	140	136	140	136	140	136	4	130	0.94			
19	477684	62	M	41	21	INS	-	-	-	-	+	-	-	80	18	140	90	140	90	110	140	138	140	136	140	134	140	136	4	128	0.92			
20	488772	70	F	52	18	OHA	-	-	+	-	+	-	-	82	18	140	92	140	90	180	140	128	140	130	140	126	140	128	12	96	0.68			
21	469238	72	M	47	25	INS	-	-	-	-	-	+	+	89	17	136	78	130	78	187	134	120	128	124	136	122	136	122	14	98	0.72			
22	513076	80	F	53	27	INS	-	-	-	-	-	-	-	70	17	140	70	136	68	167	140	130	140	130	140	130	140	130	10	118	0.84			
23	469407	70	F	57	13	OHA	-	-	+	-	-	-	-	68	16	150	80	140	70	166	150	134	148	134	152	134	150	134	16	82	0.54			
24	476500	62	M	42	20	INS	-	-	-	-	-	-	-	70	17	136	90	130	80	182	136	132	136	130	136	134	136	132	4	122	0.90			
25	504254	65	M	44	21	INS	-	-	-	-	-	+	+	74	18	130	94	130	90	169	130	126	130	126	130	126	130	126	4	126	0.90			
26	480762	68	F	43	25	BTH	-	-	+	-	+	-	-	74	18	150	90	140	80	181	150	136	150	136	150	136	150	136	14	94	0.62			
27	513046	60	F	44	16	OHA	-	-	-	-	+	-	-	74	18	140	92	134	90	140	140	136	140	136	140	136	140	136	4	132	0.94			
28	513148	66	M	40	26	INS	-	-	+	-	-	+	-	70	17	124	80	120	76	134	122	116	126	116	124	116	124	116	8	112	0.90			
29	480818	58	F	45	13	OHA	-	-	-	-	-	-	-	68	18	140	88	140	80	160	140	130	142	130	136	130	140	130	10	122	0.87			
30	464344	63	M	42	21	BTH	-	-	+	-	-	+	-	70	18	132	90	130	90	168	130	124	134	124	132	124	132	124	8	122	0.92			

ANNEXURE III - MASTER CHART

Serial Number	In / out patient number	Age (Years)	Sex	Diabetic history					History		Family history of diabetes	Personal history		General physical examination						Investigation													
																BP (mm Hg)				BSL	IASBP difference (mm Hg) (Readings)												
																Supine		Standing			1		2		3		Mean					
				Age of onset (Years)	Duration (Years)	Medication	Polyuria	Unexplained weight loss	Coronary artery disease	Cerebrovascular diseae		Smoking	Alcohol consumption	Pulse rate (/Minute)	Respiratory rate (/Minute)	Systolic	Diastolic	Systolic	Diastolic	Fasting (mg/dL)	Right Arm	Left Arm	Right Arm	Left Arm	Right Arm	Left Arm	Right Arm	Left Arm	Difference (mm Hg)	Lower limb SBP (mm Hg)	Ankle brachial index			
31	464668	76	M	53	23	INS	-	-	-	-	+	+	+	70	17	146	94	140	90	201	146	132	146	132	146	132	146	132	14	100	0.68			
32	493641	72	F	41	31	INS	-	-	-	-	-	-	-	80	18	128	80	120	80	110	128	124	128	124	128	124	128	124	4	120	0.94			
33	511416	76	F	60	16	OHA	-	-	-	-	-	-	-	84	18	150	90	146	90	186	148	134	152	134	150	134	150	134	16	78	0.52			
34	503269	70	M	57	13	OHA	-	-	+	-	-	+	-	86	17	140	86	136	80	141	140	126	140	126	140	126	140	126	14	90	0.64			
35	486507	56	F	42	14	OHA	-	-	-	-	-	-	-	70	17	130	90	130	90	157	130	126	130	126	130	123	130	126	4	118	0.90			
36	511024	64	M	40	24	BTH	-	-	-	-	-	+	+	74	17	144	84	140	80	168	142	140	146	140	144	140	144	140	4	130	0.90			
37	468469	55	M	41	14	OHA	-	-	+	-	+	-	-	70	16	132	90	130	90	140	132	128	130	128	134	128	132	128	4	118	0.90			
38	503632	60	F	40	20	BTH	-	-	-	-	-	+	-	80	17	130	70	130	70	180	130	118	130	118	130	118	130	118	12	80	0.62			
39	468494	71	M	46	25	OHA	-	-	-	-	+	-	-	76	18	126	74	120	70	112	126	120	126	120	126	120	126	120	6	116	0.90			
40	468461	55	F	39	16	INS	-	-	+	-	-	-	-	84	18	128	80	120	80	139	168	124	130	124	126	124	128	124	4	112	0.87			
41	503162	64	M	39	25	INS	-	-	+	-	+	+	+	76	17	136	76	130	70	147	136	122	136	122	136	122	136	122	14	88	0.64			
42	490092	50	F	40	10	OHA	-	-	-	-	-	-	-	78	18	140	78	140	70	168	140	134	140	134	140	134	140	134	6	126	0.90			
43	511017	78	M	51	27	INS	-	-	-	-	-	+	-	70	18	134	90	130	90	110	132	120	136	120	134	120	134	120	14	94	0.70			
44	490126	65	F	41	24	BTH	-	-	-	-	-	-	-	80	17	140	80	140	76	140	140	134	140	134	140	134	140	134	6	126	0.90			
45	468361	73	M	43	30	OHA	-	-	-	-	-	+	-	84	18	110	90	110	80	160	108	104	112	104	110	104	110	104	6	96	0.90			