"SCREENING OF ASYMPTOMATIC DIABETES MELLITUS PATIENTS WITH LESS THAN 5 YEAR OLD DURATION FOR ISCHEMIC HEART DISEASE USING TREADMILL TEST"

By

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Dissertation submitted to BLDE (Deemed to be University) Vijaypura
In partial fulfillment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

.

Under the guidance of

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SHRI B.M PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE VIJAYAPURA, KARNATAKA

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Date: 25-09-2020

Place : **Vijayapura**

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LIST OF ABBREVATIONS USED

DM	:	Diabetes Mellitus
CABG	:	Coronary artery bypass grafting
CAD	:	Coronary artery disease
TMT	:	Treadmill Test
SMI	:	Silent Myocardial Ischemia.
DNP	:	Diabetic Nephropathy
ECG	:	Electrocardiography
ESRD	:	End stage renal disease
FPG	:	Fasting plasma glucose
GDM	:	Gestational diabetes mellitus
HbA1c	:	Glycosylated hemoglobin
HDL	:	High density lipoprotein
AN	:	Autonomic Neuropathy
IDL	:	Intermediate density lipoprotein
VLDL	:	Very low density lipoprotein
TG	:	Triglyceride
IRMA	:	Intra-retinal microaneurysm
LBBB	:	Left bundle branch block
LDL	:	Low density lipoprotein
LVH	:	Left ventricle hypertrophy
LP(a)	:	Lipoprotein a
AMI	:	Acute Myocardial infarction

ABSTRACT

OBJECTIVE OF THE STUDY:

`To study the prevalence of ischemic heart disease in type 2 diabetes mellitus patients with less than 5 years of duration with no coronary artery disease symptoms.

NEED FOR THE STUDY-

Coronary artery disease is the leading cause of death in patients with diabetes. Even in an asymptomatic state these patients are at high risk for cardiovascular disease and significantly higher morbidity and mortality. The challenge is to identify which of these have significant coronary artery disease and detect it as early as possible One of the diagnostic tools for the diagnostic and risk stratification of coronary heart disease is exercise tread mill testing. Treadmill test is a reliable and widely used method for evaluating patients who have or are at risk of developing cardiovascular disease.

METHODS-

This study is cross sectional study. Patients attending BLDE (Deemed to be University)SHRI B M PATIL MEDICAL COLLEGE HOSPITAL with asymptomatic diabetes mellitus with duration of diabetes < 5 years were subjected to investigations and obtained data analysed statistically.

The entire TMT procedure is clearly explained to each patient before starting the test. Treadmill test was conducted by applying the Bruce protocol. Mason-Liker modification of lead placement was used to do the TMT. Potential risks of the test were also explained to all patients.

RESULTS-

In this study out of 60 asymptomatic diabetic patients with duration of diabetes mellitus less than 5 years, 11 patients -18.3% were TMT positive and 49 were TMT negative.

CONCLUSION-

This study shows prevalence of ischemic heart disease in diabetic patients with less than 5 years duration without any cardiac history is 18.3%.

LIST OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Diabetes Mellitus (DM) is a group of common metabolic disorders with hyperglycemia either due to defect in insulin secretion or insulin resistance. It may cause progressive tissue damage and both micro and macrovascular complications. They always had insidious, latent, along with asymptomatic phase. Therefore management of DM has changed not only controlling symptoms but also preventing complications.

BMI (Body Mass Index) of any Indian of more than 23 must be investigated for diabetes[1]. The waist circumference of more than 85cm in males and 80 cm in females are the persons must be screened for DM. The yearly check up for glyacated hemoglobin and TOD (Target organ damage) is must.

Coronary heart disease, atherosclerotic CHD is the common cause of death worldwide in type 2 DM. There is high rate of asymptomatic coronary artery disease in type 2 DM and reduced myocardial flow reserve in type 2 DM.

Hyperglycemia decreases endothelium-derived NO availability and affects vascular function mainly through the increased production of ROS. Asymptomatic DM with higher median CAC scores raising frequency of silent ST segment depression and coronary perfusion changes during exercise testing.

Stress treadmill test is a readily available, cost effective, first line test for identification of coronary heart disease in DM of longer duration without any symptoms of angina.

This study was outlined to determine SMI (Silent Myocardial Ischemia) in selected asymptomatic DM by exercise tread mill test.[2]

AMIS AND OBJECTIVES

AIMS:

1. To study the prevalence of silent myocardial ischemia in asymptomatic type 2 DM patients with less than 5 year duration of DM

OBJECTIVES:

1. To study the prevalence of silent myocardial ischemia in asymptomatic type 2 DM patients by using tread mill test.

2. To analyse the clinical predictions of silent myocardial ischemia in asymptomatic type 2 DM patients.

REVIEW OF LITERATURE

DIABETES MELLITUS

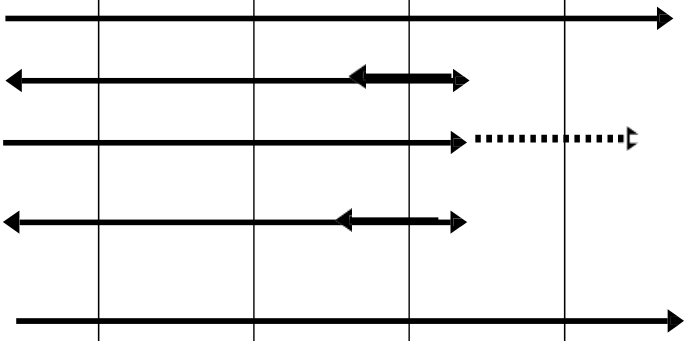
DM attributes to a collection of metabolic anarchy that contributes a phenotype of hyperglycemia. Various types of DM are brought about by interactions between genetics and environmental factors. DM is due to insulin deficiency and its action, or either of them.. DM is the predominant cause of nephropathy with ESRD, retinopathy with adult blindness, non traumatic lower extremity amputation and autonomic dysfunction.[1]

CATEGORIZATION:

DM is categorized on the ground of the pathogenic process that leads to hyperglycemia as opposed to previous criteria which based on age of onset or type of therapy.[2] The two types of DM are type 1 and type 2.

Type 1 DM is the outcome of complete or total lack of insulin. Type 2 DM is a result of insulin resistance,impaired insulin secretion and increased glucose production. Type 2 DM is anteceded by a duration of glucose homeostasis categorized as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

RANGE OF GLUCOSE HOMEOSTASIS AND DIABETES MELLITUS.

Type of Diabetes	Normal glucose tolerance	Hyperglycemia			
		Impaired fasting glucose or impaired glucose tolerance	Diabetes mellitus		
			Not insulin required	Insulin required For control	Insulin required for survival
Type1					
Type2					
Other specific types					
Gestational diabetes					
FPG (mg/dl)	<100	100-125	≥126		
2-h PG (mg/dl)	<140	140-199	≥200		
HbA1C	<5.6%	5.7-6.4%	>6.5%		

This table shows range and spectrum of glucose homeostasis and diabetes mellitus.

Table 1—Measures for the identification of diabetes

1. HbA1C ≥ 6.5%.

OR

2. FPG ≥ 126 mg/dl. Fasting is ascertained as no food intake for at least 8h

OR

3. 2-h PG ≥ 200 mg/dl during an OGTT. The procedure must be done after intake of a 75 g anhydrous glucose dissolved in water.

OR

4. Symptoms of Diabetes plus Random blood Glucose ≥ 200mg/dl

These are the criteria used for the identification of Diabetes Mellitus.

GESTATIONAL DM:

Glucose Intolerance that develops during 2nd or 3rd trimester of pregnancy known as gestational diabetes mellitus. As DM preponderance is higher among Indian pregnant women , so all pregnant women should be screened for DM whatever their age of presentation. As screening 50g OGTT was advisable in all pregnant women at their first visit. If the test was negative repeat the test with 75g OGTT during 26-28 weeks of gestation. The detection of GDM was made when the plasma glucose values are above the following values.

- Fasting :92mg/dl
- 1h: 180mg/dl
- 2h: 153 mg/dl.

HISTORICAL EVENTS:

The word diabetes was coined by Aretaeus of Cappadocia in the 2nd century AD. It originates from greek meaning siphon. He gave the clinical manifestations as polyuria, polydipsia, weight loss. Its history categorized into four cycles based on natural history and management of disease.

These are

1. Ancient period.
2. Diagnostic period
3. Experimental period
4. Scientific period.

The clinical descriptions and complications of diabetes were first witnessed in the ANCIENT period. The duration of 16th to 18th century was described as DIAGNOSTIC period as DM was designated as discrete disease entity. The 19th

century may be considered as first EXPERIMENTAL period during which the glucoregulatory role of pancreas was defined and the disturbances of biochemical reactions in diabetes were initially described. Finally the 20th century has come across there is sudden increase in knowledge about diabetes. The invention of INSULIN in 1921-22 has had social, clinical and scientific knowledge.

ETIOLOGICAL CATEGORISATION OF DIABETES MELLITUS

- TYPE 1 Diabetes

1. Immune mediated-absolute insulin deficiency
2. Idiopathic

- TYPE 2 Diabetes

Specific Types-

A. Genetic defect of beta cell development or function-

1. Mutation in HNF 4 alpha-MODY1
2. Glucokinase – MODY 2
3. .HNF 1 alpha –MODY 3
4. .Insulin promoter factor 1,HNF1 beta
5. Mitochondral DNA
6. other pancreatic islet regulators

B. Transient Neonatal diabetes

C. Diseases of Exocrine pancreas disorders - pancreatitis, cystic fibrosis, hyperthyroidism,hemochromatosis

D. Genetic defect in Insulin action- Rabsonmendenhall syndrome, Lipodystrophy Syndromes

E. Endocrinopathies- Acromegaly, Cushings Syndrome, hyperthyroidism,

pheochromocytoma

F. Drug Induced

G. Infections -Cytomegalovirus, congenital rubella

H. Other genetic syndromes-Wolframs syndrome, Downs syndrome,Klinfelters.

AFFLICTION OF DIABETIC COMPLICATIONS

The preponderance of DM will be coordinated by a parallel increase in the epidemic of its complications. The small vessel complications are

A. Diabetic retinopathy.

B. Diabetic Nephropathy

C. Diabetic Neuropathy.

The large vessel complications are

A. Cardiovascular disease.

B. Cerebrovascular disease.

C. Peripheral vascular disease.

OTHERS

- Periodontal disease
- Glaucoma
- Dermatologic
- Infections
- Gastrointestinal(gastroparesis,diarrhea)
- Genitourinary(uropathy/sexual dysfunction)
- Cataract.

DIABETIC RETINOPATHY:

Diabetic retinopathy is the commonest cause of blindness among 20-74 years old middle aged persons .In the beginning era of first two decades of disease > 60% of patients with type 2 DM and nearly 90% of patients in type 1 DM have retinopathy. In 21% of patients with type 2 DM have retinopathy in their first visit.

CLASSIFICATION (MODIFIED FROM AMERICAN ACADEMY OF OPTHALMOLOGY)

1. **Non Proliferative Diabetic Retinopathy (NPDR**)

- **Mild NPDR:** Presence of one microaneurysm in the retina and one or more of the following-soft exudates, retinal hemorrhage, hard exudate.
- **Moderate NPDR**: Micoaneurysms or hemorrhages or both in at least in one quadrant and one or more of following: IRMA, soft exudates and venous bleeding.
- **Severe NPDR*:*** Hemorrhages or microaneurysms or both in all quadrants, venous beeding in two or more quadrant, IRMA in at least one quadrant.

2. **PDR: (Proliferative Diabetic Nephropathy)**

- **Early PDR**

One or more of the following:

- NVE
- NVD
- Vitreous or preretinal hemorrhage
- NVE <½ disc area.
- High risk PDR
- NVD>1/4-1/3 disc area
- NVD with vitreous or preretinal hemorrhage

- NVE >½ disc area. Preretinal or vitreous hemorrhage.
- Advanced PDR

High risk PDR, traction retinal detachment involving macula or vitreous hemorrhage obscuring ability to grade NVD or NVE.

- IRMA–lntraretinal microvascular abnormalities.
- NVD–Neovascularisation disc.

DIABETIC NEPHROPATHY:

DM is the dominant cause of ESRD and CKD requiring renal replacement therapy. Albuminuria in DM patients is associated with increased risk of cardiovascular diseases. Individuals with diabetic nephropathy commonly have diabetic retinopathy. Only 20-40% of diabetic patients develop diabetic nephropathy.[2]

The nephropathy that develops in type 2 DM differes from that type 1 DM in following aspects-

1. Micro or macroalbuminurea can be present at the time of diagnosis of type 2 DM.
2. hypertension more commonly accompanies micro or macroalbumin urea in type 2 DM.

SCREENING OF MICROALBUMINURIA

To detect the presence of urinary microalbumin should be done at diagnosis in patients with type 2 DM and after 5 years of disease duration in those with type 1 DM, and then repeated annually. Screening for microalbuminuria may be done by three methods.

1. Analysis of the albumin to creatinine ratio in a random spot urine collection:>30mg/g → Albuminuria

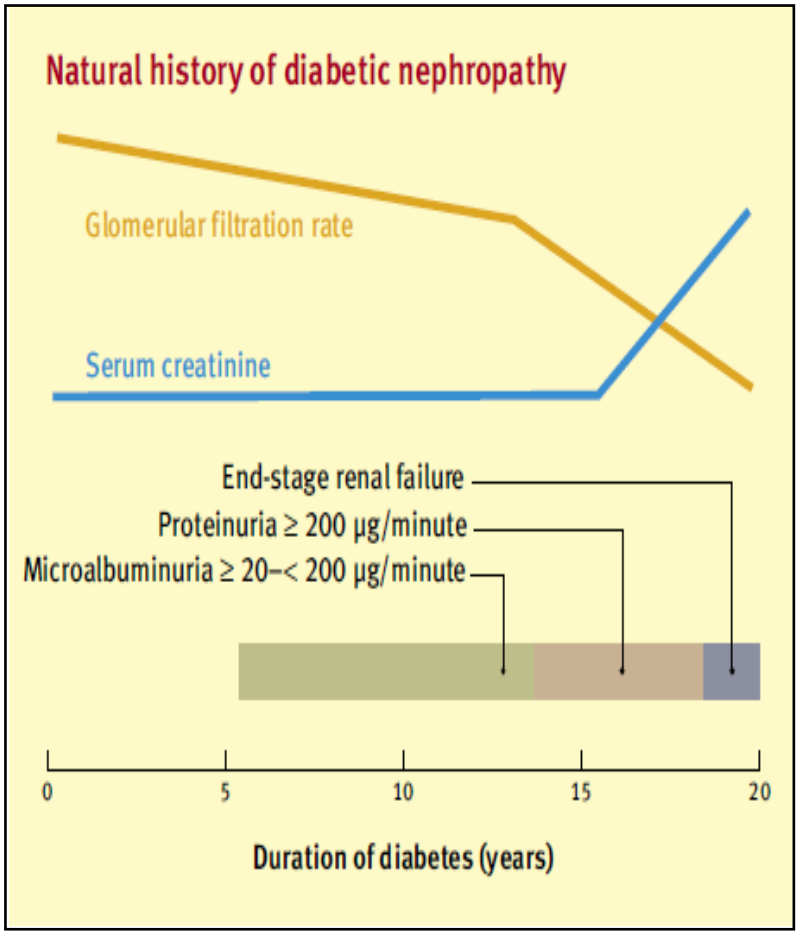
2. 24hr Urine collection and detection of albumin excretion.
3. Timed (e.g. 4 hr or overnight) collection.

Table–2: Definitions of abnormalities in albumin excretion

Category	Spot collection (µg/mg creatinine)	24 hr collection (mg/24hrs)	Timed collection (µg/min)
Normal	< 30	< 30	< 20
Micro albuminuria	30-299	30-299	20-199
Clinical albuminuria	≥ 300	≥ 300	≥ 200

Albuminuria is the first manifestation of diabetic nephropathy. In both forms of diabetes, albuminuria acts as the marker for cardiovascular mortality and morbidity [6].

NATURAL HISTORY OF DIABETIC NEPHROPATHY



CORONARY HEART DISEASE

Coronary heart disease is a state of insufficient supply of blood and oxygen to a section of myocardium. CAD results from disproportion between oxygen supply and demand. Genetic factors, smoking, sedentary life style are attributed to the occurrence of CAD. Type 2 DM, obesity ,insulin resistance are significant risk factors for IHD.

Coronary atherosclerosis is a localized process that results in non- uniform pattern of ischemia. Atherosclerosis is the event of plaque formation in blood vessels.

The atherosclerotic event is characterized by many coronary risk factors such as hypercholesterolemia, smoking, DM and HT.[7-9] .Recently few researchers have found that inflammation had a role in formation and rupture of plaque.[10-15] during the episodes of ischemia ventricular contractility was disturbed which causes ventricular akinesia, dyskinesia and hypokinesia.

PREVALENCE OF CARDIOVASCULAR DISEASE IN DIABETES.

In diabetic patients prevalence , incidence and mortality of all groups of CVD (cardiovascular disease) such as cerebrovascular disease, peripheral vascular disease, and congestive heart failure are increased in diabetes than non diabetics.[16-19] In patients with (IFG) and (IGI) and insulin resistance are also under the excess risk of either cardiovascular disease (CVD) or subclinical atherosclerosis.[19-23]

The obesity and the diabetes were first identified and remains as an upcoming epidemic in the united states in 1990s.

During the period of 1999-2000 implied that the age at diagnosis of T2DM was, on average ,47 yrs. Until1992, 2% to 4% of all juvenile diabetes was accounted by Type2 DM. In 1994 16% of pediatric cases was accounted by Type 2 DM.[24]

In the United Kingdom Prospective Diabetes Study (UKPDS) evaluated the risk factors in T2DM patients which revealed five modifiable risk factors for CAD and for myocardial infarction.[38]The risk markers are-

1. Reduced levels of HDL cholesterol.
2. Raised Blood pressure
3. Smoking
4. Elevated levels of LDL cholesterol
5. Hyperglycemia.

Prevention of life threatening coronary events assumes form of a first priority. In one study, 1 year case fatality rate due to first MI was 45% in men with DM and 39% in women with diabetes, compared to 38% and 25% for men and women without diabetes, respectively.[38]Those persons who died with DM 50% of men and 25% women died before hospitalization. To prevent onset of CVD among diabetics primary prevention is essential.

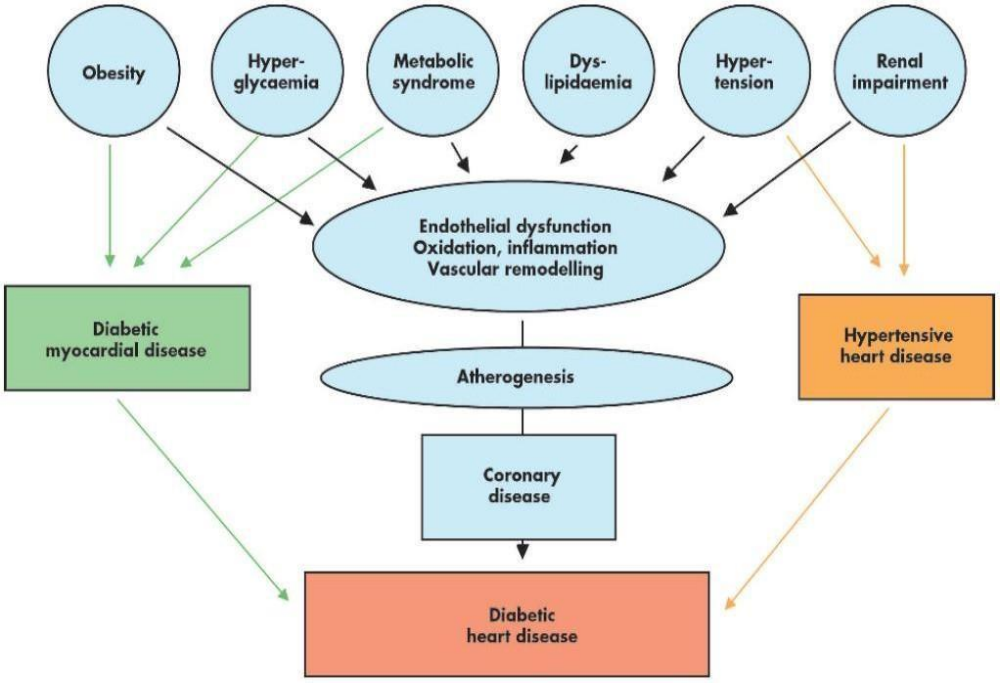
HIGH SENSITIVITY C-REACTIVE PROTEIN.

The acute-phase reactant, CRP, a simple downstream marker of inflammation, has now arisen as a major CVD risk factor. HsCRP → Predicts ↑risk of MI, Stroke, PAD & Sudden cardiac death as shown by large series of prospective studies. It indicates an increased propensity for plaque disruption and /or thrombosis.

INFLAMMATION –THE UNDERLYING LINK BETWEEN DIABETES AND CVD.

Data suggest that plasma CRP, arise as an important predictive value in predicting the risk of future CAD.

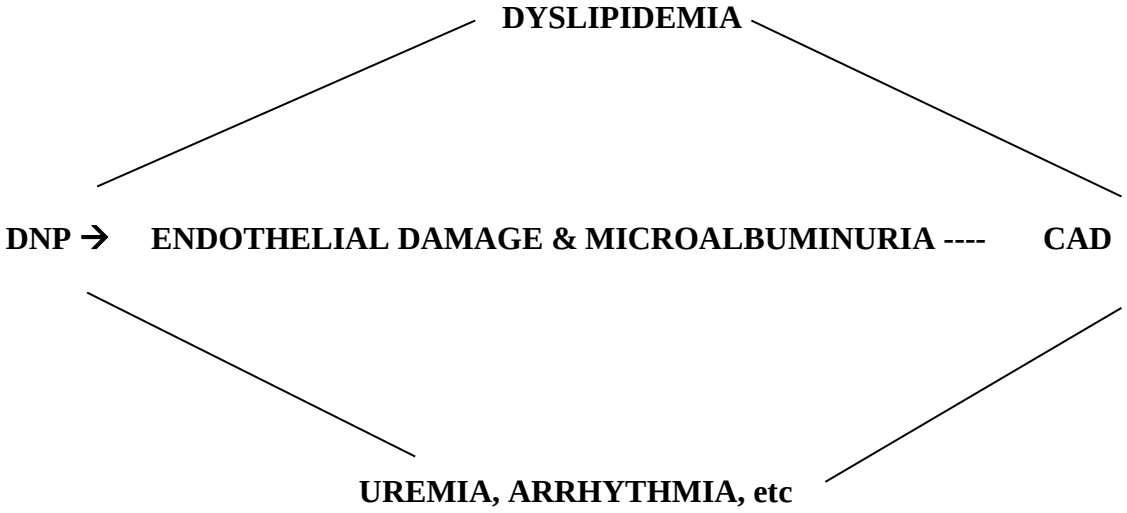
PATHOPHYSIOLOGY OF DIABETIC HEART DISEASE.



DM vs Non-DM CAD- differences

- Extent of the disease in the coronary arteries is greater.
- Higher incidence of multivessel disease and a greater number of diseased vessels.
- Occurs at a younger age and women are affected as often as men.
- Silent ischemia-autonomic denervation of the heart.
- Higher occurrence of left main stem disease.
- Decreased coronary artery collateral recruitment.
- Increased rates of both restenosis and progression of coronary disease.
- More perioperative no cardiac morbidity, such as renal failure and sternal wound infection.

DIABETIC NEPHROPATHY& HEART – CONNECTING BRIDGES.



DIABETES MELLITUS AND SILENT ISCHEMIA:

Prevalence of silent myocardial infarction and SMI is more in diabetics. In DM, there is greater prevalence of painless sudden death particularly during sleep. Silent myocardial ischemia is evidenced during treadmill and thallium stress tests. Incidence of painless ST depression is twice in diabetics (75%) versus non diabetics (35%).[25]

In a study by Hume LG et al [26] of 30 asymptomatic diabetics, all patients underwent exercise ECG and they found that 23.33% patients had abnormal responses. Another study by Joshi AS et al[27]of 120 asymptomatic stable type2 diabetes were assessed for presence of silent ischemia by a standard treadmill test using Bruce protocol. It was found that 51 (42.5%) had evidence of ischemia.

In another study by PK Garg et al [28], in group I (40 patients) of type2 diabetes mellitus and in group II (30 healthy person) control were taken. All subjects underwent exercise test (bicycle ergometry). It was found occurrence of SMI was higher in type 2 DM.

Another study[29] of 136 asymptomatic diabetics and 80 asymptomatic controls with exercise ECG, 24 hour holter, Thallium Scintigraphy and coronary

angiography.29% diabetics and 5% controls were positive in one or more non invasive test. 12/34 diabetic who underwent angiography had significant stenosis, where only one control had unimportant stenosis.

Another study by Marín EH et al[30] evaluated the prevalence and characteristics of silent myocardial ischemia in 50 asymptomatic, non insulin dependent diabetes mellitus patients with normal resting electrocardiogram on 48 hours holter monitoring. They found that occurrence of SMI during daily activities in asymptomatic DM patients was very high (58%). Further, SMI was related to the presence of other risk factors for coronary artery disease and to diabetic complication like retinopathy, neuropathy and nephropathy.

In another study by Murray D P et al[31] 30 diabetics with established or doubtful CAD with exercise electrocardiogram and autonomic function test, they found that 60% had painless ST segment changes: Of those with severe autonomic neuropathy, 92% had no pain, where as those with mild autonomic dysfunction or normal autonomic function had 39% prevalence of silent myocardial ischemia.

2,223 patients were studied[32] and were categorized according to oral glucose tolerance test into normal, diabetic or the impaired glucose tolerance (IGT). They used the Rosa questionnaire and resting ECG to determine prevalence of IHD. They found that IHD by all criteria was significantly more common in men and women with NIDDM and women without.

The prevalence of MI was higher in NIDDM especially women. Angina pectoris was not related to NIDDM or IGT .

Table - The Prevalence of CAD in India.

Risk Factors	Indians (%)	West (%)
Smoking	3	27
Hypertension	14	19
Elevated cholesterol	17	23
Obesity	3	31
Diabetes	8	1

This table shows prevalence of CAD in Indians is higher inspite of lower prevalence of traditional risk factors.

- **EVALUATION OF CORONARY ARTERY DISEASE :**

1. Resting ECG
2. Ambulatory ECG monitoring
3. Exercise test:
   A. Exercise electrocardiography
   B. Exercise Echocardiography
   C. Pharmacological Exercise echocardiography
   D. Stress thallium.
1. Coronary angiography
2. Intra coronary vascular ultrasound.

RESTING ECG

The resting electrocardiogram in diabetics in about one half of patients with chronic stable angina is normal. The most common ECG changes in diabetes are abnormal ST-T wave changes with or without evidence of previous MI. In diabetic patients with angina the sensitivity and specificity of resting ECG is low, so it may not be accurate to identify DM and chest pain with or without symptoms.

Ambulatory 24 hrs electrocardiography:

It is used to identify SMI or ventricular arrhythmias in DM patients with doubtful or known CAD.

The continuous ambulatory 24 to 48 hour ecg :

The continuous ambulatory (24 to 48 hours) ECG monitoring is recorded technologically by;

1. A conventional tape (Holter) recording and appropriate playback instrumentation systems.
2. Solid state technology using real time analysis microcomputer and memory storage.
3. Solid state storage with data review methods of completion of the examination.

STRESS TESTING METHODS AND PROTOCOLS: TREADMILL

It is the most widely used dynamic testing modality in the United States and India since most patients are more familiar with walking, than they are with bicycling.

DIPYRIDAMOLE TEST:

In outpatients who cannot walk on treadmill because of osteoarthritis, neurological deficits, etc, stress can be induced by Dipyridamole infusion at rate of 0.75 mg/kg/min, over 4 min. ECG is to be recorded during post infusion period for about 6-10 minutes and to be compared with pre-infusion ECG.

TREADMILL PROTOCOLS :

The various protocols are available for clinical use include an initial low load (warm up), and progressive increase in workload in stages. Though there are many protocols available for clinical use name will be ideal for every clinical situation. The suitability varies according to the objectives of the exercise test. For example, a vigorous exercise protocol may be suitable for screening a relatively healthy individual. On the other hand, a milder exercise protocol may be adequate for functional evaluation of a known cardiac patient and lighter workloads are needed for

pre-discharge post infarction evaluation. Thus an ideal exercise protocol should have an initial workload well within a given individuals anticipated physical working capacity and the workloads, should be increased gradually and maintained for a sufficient length of time to achieve a near physiologic steady state.

BRUCE PROTOCOL:

This is the most commonly used protocol. It consists of 7 stages in which speed and grade are increased every 3 minutes. Bruce protocol has the advantage of being relatively short in duration. It also has many disadvantages. It's high workloads may not be suitable for most cardiac patients or elderly sedentary individuals. The large increments in work make the estimation of maximal oxygen consumption less accurate. The 4^{th} stage may either be run or worked, which results in differing oxygen costs.

MODIFIED BRUCE PROTOCOL:

This protocol to an extent overcomes the disadvantages of the Bruce protocol. Here the first two stages are run at 1.7 mph at 0% and 5% grades. The third stage of modified Bruce corresponds to 1st stage of Bruce. The remaining stages correspond to that of Bruce protocol.

NAUGHTON'S PROTOCOL:

In this protocol the workloads are increased every two minutes. The increments being small and gradual, this protocol is quite useful in post myocardial infarction stress evaluation.

McHENRY'S PROTOCOL:

It also provides a small initial workload and gradual increase every 3 minutes.

MODIFIED BALKE-WARE PROTOCOL:

This consists of constant brisk walking speed (3.4 mph) with 1% increase in grade every minute.

In summary, it is important to individualize the protocol selection for the patient being tested the optimal protocol is 6 to 10 minutes in length if longer, endurance is tested rather than aerobic capacity. Stress capacity should be reported in METS, not minutes.

Table–3: Bruce Protocol

Stage	Speed (km/hr)	Grade (%)	Duration (Min)	METS
1.	2.7	10	3	4-5
2.	4.0	12	3	6-7
3.	5.4	14	3	8-10
4.	6.7	16	3	13-16
5.	8.0	18	3	21
6.	8.8	20	3	-
7.	9.6	22	3	-

This table depicts bruce protocol and its 7 stages.

Table–4: Modified Bruce Protocol

Stage	Speed (km/Hr)	Grade (%)	Duration (Min)	METS
1.	2.7	0	3	1.6-2
2.	2.7	5	3	2-4
3.	2.7	10	3	4-5
4.	4.0	12	3	6-7
5.	5.4	14	3	8-10
6.	6.7	16	3	13-16
7.	8.0	18	3	21
8.	8.8	20	3	-
9.	9.6	22	3	-

This table depicts Modified Bruce Protocol and its stages

Table – 5: Naughton's Protocol

Stage	Speed (km/Hr)	Grade (%)	Duration (Min)	METS
1.	1.6	0.0	2	1
2.	3.2	0.0	2	2
3.	3.2	3.5	2	3
4.	3.2	7.0	2	4
5.	3.2	10.5	2	5
6.	3.2	14.0	2	6
7.	3.2	17.5	2	7

This table shows Naughton s Protocol and its stages.

INDICATIONS AND CONTRAINDICATIONS

GENERAL INDICATIONS FOR EXERCISE TESTING[33,34]:

CLASS – I:

Conditions where there is general opinion that stress testing is needed.

1. In patients with symptoms or other findings that are suggestive of CAD, to detect CAD, but not diagnostic of coronary disease.
2. To assess the prognosis of patients with established CAD and functional capacity.
3. After an uncomplicated myocardial infarction to assess the prognosis or functional capacity of the out patients with CAD (before discharge or early after discharge).
4. In congenital heart disease patients to assess functional capacity of patients.
5. To determine coronary artery revascularization after CABG and coronary angioplasty.

CLASS-II:

Conditions where the exercise testing is frequently performed but in which there is a divergence of opinion with respect to its value and appropriateness.

1. Screening for latent silent CAD in asymptomatic outpatients over the age of 40 with two or more risk factors forced.
2. To assess outpatients with variant angina.
3. To determine response and functional capacity to drug therapy in CAD or heart failure patients.
4. Functional capacity of cardiac patients with valvular heart disease.
5. To assess on a routine, yearly basis patients who remain silent after a revascularization procedure.
6. To determine patients with resting ECG changes.

USES OF EXERCISE TESTING IN DIAGNOSIS AND EVALUATION OF CORONARY ARTERY DISEASE:

Evaluating patients with chest pain may be one of the most challenging events faced by physician. If the chest pain pattern is suspicious, but not classical for angina, the presence or absence of disease can be often by established by a maximal stress test. Though coronary arteriography remains the GOLD STANDARD for diagnosing CAD, exercise electrocardiography remains a valuable non-invasive diagnostic tool for initial work up. The reliability is dependent on the magnitude and time of onset of the ST changes, on the HR and BP response and very importantly, in the study population, the disease prevalence.

The severity and prognosis of CAD can be determined with considerable accuracy with exercise testing. In the past few years, pre discharge exercise test after myocardial infarction has become an accepted approach to assess the residual ischemic and for stratification of risk for further events. This naturally has lot of therapeutic implications regarding the line of management (Drugs, CABG, and Angioplasty). Evaluation of functional capacity of individuals who have angina or have had a myocardial infarction is very essential. It is very much essential to decide how much exercise the patient can tolerate. This is very essential for planning further treatment and for proper rehabilitation of a cardiac patient. Demonstrating how much exercise that a person can do goes a long way in reassuring the anxious patients of myocardial infarction and their family.

The functional evaluation is also helpful in patients who have undergone coronary revascularization by CABG or PTCA

The exercise testing is also useful in evaluating the efficacy of medical therapy of CAD and also in evaluating coronary patients before and after CABG or angioplasty.

CONTRAINDICATIONS [35,36]:

Absolute Contraindications:

1. Recent acute MI (generally < 6days).
2. Unstable progressive chest pain. (Including angina at rest).
3. Severe symptomatic LVD.
4. Potentially serious cardiac dysarrhythmias like ventricular and atrial tachyarrhythmias and advanced second or third degree heart block
5. Acute pericarditis, myocarditis and endocarditis.
6. Severe aortic stenosis.
7. Acute pulmonary embolus or infarction.
8. Acute or serious general illness like acute infections, hyperthyroidism or severe anemia.
9. Patients with locomotive problems (amputation severe arthritis or deformity, etc).
10. Acute thrombophlebitis or deep vein thrombosis.
11. Known severe left main disease (>70%).
12. Severe resting hypertension (> 240/130).

RELATIVE CONTRAINDICATIONS:

1. Any less serious non cardiac disorder (uncontrolled metabolic disease such as DM, myxoedema or thyrotoxicosis, asthma, hepatitis, pneumonia etc.)
2. Arterial hypertension (generally greater than 200 mmHg of systolic or 120 mmHg diastolic).
3. Moderate valvular or myocardial heart disease.
4. Known or suspected left main obstruction.
5. Hypertrophic cardiomyopathy with significant outflow obstruction.
6. Drug effect or electrolyte abnormalities (Digitalis intoxication, hypokalemia, tranquilizers, alcohol, disopyramide, quinidine etc.)
7. Psychiatric disease.
8. Inability or lack of desire or motivation to perform the test.

SAFETY PRECAUTIONS:

Even though stress testing is a safe procedure, but there are many studies showed of acute infarctions and deaths occurring secondary to this procedure. So certain safety precautions have to be taken. They may be summarized as follows:

1. Indications and contraindications must be carefully considered.
2. Informed consent must be obtained before the exercise test for medicolegal purposes
3. ECG (preferably 12 lead ECG) should be monitored continuously during and after exercise until completion of the test (usually 8-10 minutes during recovery period)
4. It is essential to take 2 sets of complete 12-lcad electrocardiograms. Pre exercise ECG and post exercises.
5. Proper skin preparations and good quality electrodes are important to avoid

artifacts and problems of interpretations.

6. Blood pressure should be recorded before, during and after test (ideally Every minute).

COMPLICATIONS:

CARDIAC COMPLICATIONS:

1. Hypertension
2. Myocardial infarction
3. Severe cardiac dysarrhythmias
    a. Tachyarrhythmias: Atrial, Junctional, and Ventricular.
    b. Bradyarrhythmias: Sinus, Junctional, Ventricular, A-V block, Asystole.
    c. Brady-tachyarrhythmia syndrome.

1. Hypotension and shock
2. Sudden death
3. Congestive heart failure

NON CARDIACCOMPLICATIONS:

1. Musculoskeletal pain
2. Cerebrovascular accidents
3. Phlebitis.

CONDUCT OF EXERCISE TEST

PATIENT PREPARATION

Preparations for exercise testing include the following:

1. The patient should be instructed not to eat or smoke for 2 to 3 hours prior to the test and to come lightly dressed for exercise.
2. A complete history and physical examination should be accomplished to rule

out any contraindications for exercise testing.

3. The use of certain medications like digitalis, beta blockers, calcium channel blockers, nitrates, which interfere with the result of the exercise test should be curtailed wherever possible.
4. In most of the exercise laboratories, drug therapy is withdrawn 24 to 48 hours before performing the test.

- A resting 12 lead ECG should be obtained. This is important because detection of changes of acute MI may prohibit testing and detection of LBBB, LVH and WPW syndrome etc may make the interpretation more difficult.
- Another ECG should be recorded during 20-30 seconds of hyperventilation as this procedure can produce ECG changes similar to ischemic patients. Appearance of such changes suggests the increased possibility of false positive test results. Informed consent should be obtained after explaining the possible risks involved in exercise testing.

1. The testing procedure should be carefully explained to the patient and treadmill walking should be demonstrated.
2. Skin preparation and electrodes placement: The proper skin preparation is essential for obtaining high quality ECG recordings. The removal of superficial keratinized layer is the most important factor. The areas for electrode applications are first rubbed with an alcohol or acetone saturated gauze (after shaving in moles with hairy chest) to remove the superficial only layer. Then these area re rubbed with fine sand paper or rough material to obtain good electrode contact. This reduces the contact impedance from 10-50 k. ohms to 1-5 k ohms. The most reliable electrodes are light weight liquid contact silver chloride electrodes. They have a plastic housing and a light

flexible cable. The liquid conductor system minimizes the loss of contact and artifacts that tend to occur at peak exercise levels. Both reusable and disposable types of electrodes are available. Since a standard 12 leads ECG with electrodes placed on the limbs could not be obtained during exercise, other electrode placements have been used.

3. The arm electrodes and lower limb electrodes are brought on to the trunk and placed at sites nearest to the respective limbs. This modified placement (Mason-Likar modification) lessening the motion artifact without producing much difference from the standard 12 lead ECG.

LEAD SYSTEM AND RECORDING DEVICES

Selection of a proper lead system is very essential for a good exercise ECG test various types of unipolar and bipolar precordial systems have been in use for a number of years and have produced satisfactory results.

Bipolar leads

They were the first to be used to detect ECG changes during exercise.

They are easy to apply and free from motion artifacts. The usual positive electrode is placed in position V_5. The position of negative electrode determines the type of bipolar lead system.

CM_5 : Over manubrium

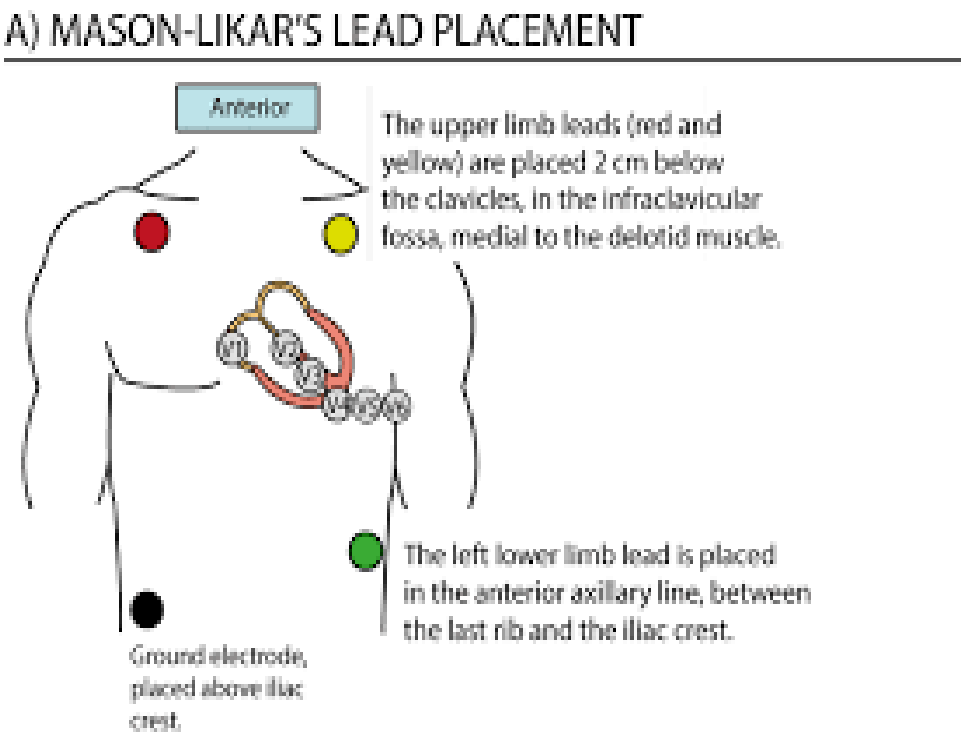
CC_5 : Over right V_5

CS_5 : Just below right clavicle

CA lead : On the right medial scapular ridge.

CB lead : On right inferior scapular angle.

The CM_5 system was the most popular for many years and has been demonstrated to have the highest incidence of positive changes in patients with known ischemia.



INDICATIONS FOR TERMINATION OF EXERCISE TEST[36]:

In a patient with known or suspected heart disease, the physician administering the test must continuously observe the patient and the monitor. The electrocardiographic printout is often more informative than the image on the oscilloscope and must be available for immediate infarction whenever needed.

The forewarning for ending of stress tests has been summarized below:

1. Anginal pain is progressive.
2. Drop in systemic blood pressure below the resting value or non raising SBP with continued exercise. A fall of more than 20 mmHg in systolic pressure occurring after the normal initial rise.
3. Frequent premature ventricular contractions developing in pairs or with

increasing frequency as exercise increases or ventricular tachycardia and ventricular fibrillation development.

4. Atrial tachycardia, atrial fibrillation or atrial flutter supervenes.
5. Hypertensive response of SBP>280 mmHg and diastolic BP > 140 mmHg.
6. Onset of second or third degree heart block.
7. ST segment depression has become marked. Most could end the exercise at 3mm or more ST depression.
8. ST segment elevation of 2 mm or more.
9 Patient is unable to continue because of dyspnoea fatigue or feeling of faintness or dizziness.
10 Signs of poor perfusion like pallor, cyanosis and cold extremities and sweating.
11 Marked apprehension, mental confusion or lack of coordination.
12 Technical problems with monitoring the ECG or systolic blood pressure.
13 Patient's request.

Technique of treadmill test:

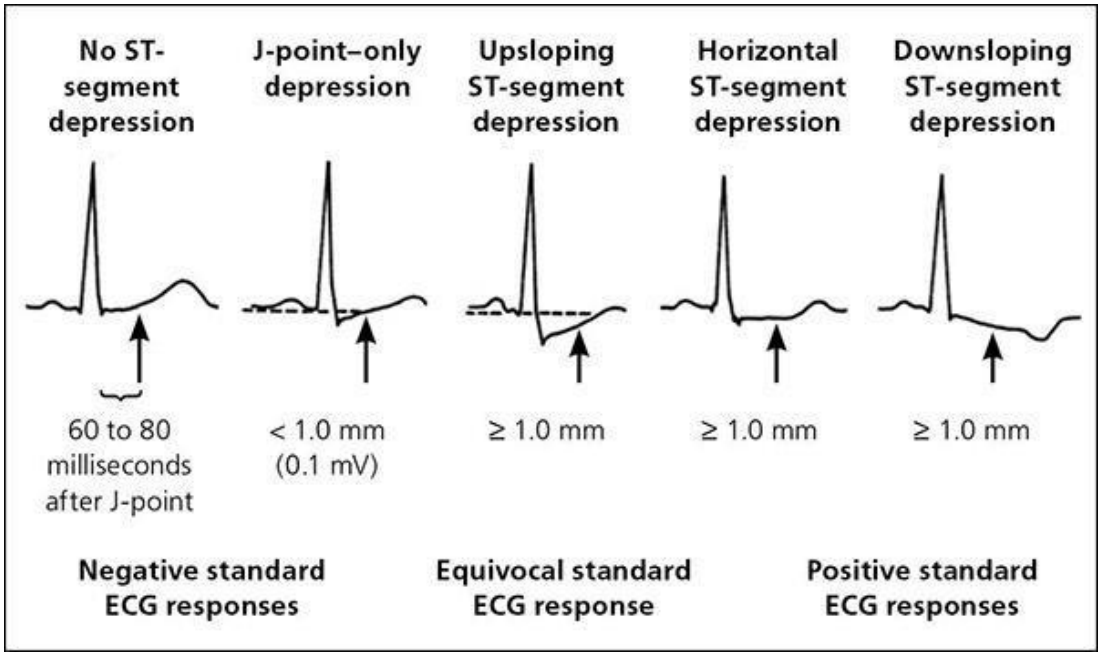
The patient was instructed not to eat or drink caffeinated beverages three hours prior to testing and to wear comfortable shoes and loose fitting clothes. A brief physical examination was performed prior to the test and a written informed consent was taken.

A standard 12 lead electrocardiogram was taken following which a torso ECG was obtained in the supine position and in the sitting or standing position the sitting or standing position.Blood pressure was recorded in both positions.

The heart rate, blood pressure and electrocardiograms were recorded at the end of each stage of exercise, immediately before and after stopping the exercise and for each minute for at least 5 to 10 minutes in the recovery phase.

Exercise test was terminated in all patients following the achievement of target heart rate or an abnormal ischemic response

This was defined as development of 0. 10 mV (1 mm) of J point depression measured from the PQ junction, with a relatively flat ST segment slope (< lmV/sec), depressed ≥ 0.10 mV 60 to 80 msec after the J point in three consecutive beats with a stable baseline. Exercise test was also terminated if patient developed dyspnoca, fatigue or chest pain



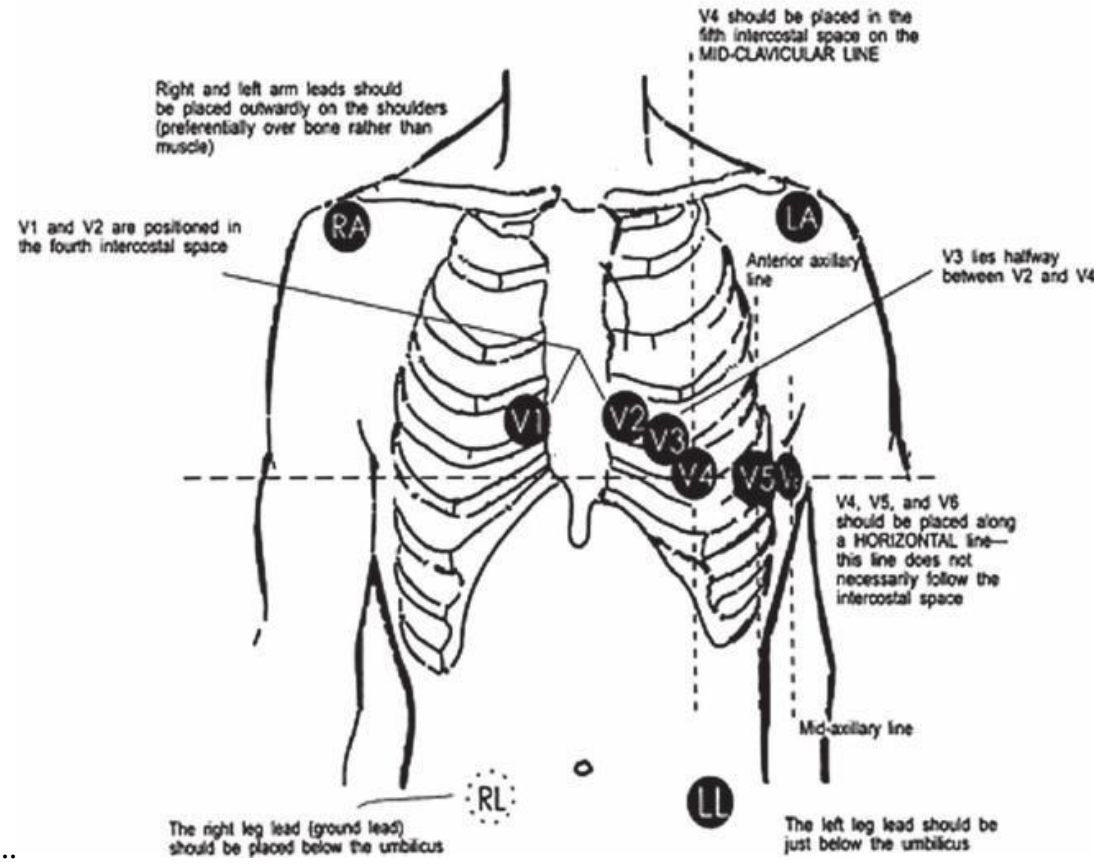
ST-segment depression during exercise. Downsloping of more than 2 mm is a relative indication for termination. (ECG=electrocardiography.)

A negative TMT or Stress Test is declared when the patient can reach a certain heart rate without showing any ECG changes. This rate is known as target heart rate and it is also calculated by a formula **(Target Heart Rate = 220 – age of patient**).

If this rate is reached by the patient without producing any ECG changes, though the TMT can be called negative, but it would not mean that the blockage is zero.

It means the person performing the test probably has blockage of less than 70%.

12-lead ECG Electrode Placement



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MATERIALS AND METHODS

OBJECTIVE OF THE STUDY:

To study the prevalence of ischemic heart disease in type 2 diabetes mellitus patients with less than 5 years old of duration with no coronary artery disease symptoms.

STUDY DESIGN:

This study is cross sectional study.

SOURCE OF DATA:

The study will include outpatients and inpatients of BLDE (DU) Shri B.M.Patil Medical College hospital and research centre, Vijayapura.

- The patients will be informed about study in all respects and informed consent will be obtained.
- Period of study is from December 2018 to June 2020.

METHODS:

Patients attending BLDE(DU)'S SHRI BM PATIL MEDICAL COLLEGE HOSPITAL with asymptomatic diabetes mellitus with duration of diabetes < 5 years will be subjected to investigations and obtained data will be analyzed statistically.

The entire TMT procedure is clearly explained to each patient before starting the test. Treadmill test will be conducted by applying the Bruce protocol. Mason-Liker modification of lead placement will be used to do the TMT. Potential risks of the test were also explained to all patients.

At the end of the TMT, the following responses were considered a positive response:

I. Horizontal or downsloping or slowly upsloping ST segment depression of 1mm or more occurring at 0.08 seconds after j point in two or more leads during exercise

II. Hypotensive response (fall of systolic blood pressure >20mmHg or diastolic blood pressure >10 mmHg) during the TMT

III. ST segment depression (horizontal or down sloping or slowly up sloping), which appeared shortly after exercise during the recovery period

All necessary cardiopulmonary resuscitative facilities along with a trained TMT technician and defibrillator will be made available in the exercise room.

METHOD OF COLLECTION OF DATA

Study patients:

A detailed history, general physical examination, systemic examination, investigation will be performed on all patient who will fulfil inclusion criteria,both male and female who will be attending opd and admitted in Shri B M Patil medical college, hospital and research centre vijayapur,who have been diagnosed as diabetes with less than 5 year duration.

SAMPLE SIZE:

A sample size of 60 subjects will allow the study to determine the clinical profile of patients with asymptomatic diabetes mellitus with less than 5 year duration with 95% confidance level and margin of error + 6 % with finite population correction (N=200).

Formula Used:

$$n = \frac{Z^2P(1-P)}{d^2}$$

Z = Z statistic at 5% level of significance

P =anticipated Incidance rate of ischemic heart disease in asymptomatic diabetes mellitus less than 5 year duration (p-36.3%)

d = margin of error

STATISTICAL ANALYSIS: Data will be analysed using

1)Mean SD

2) T test

3)Chi-square test

INCLUSION CRITERIA:

1. All type 2 diabetic patients with duration of diabetes less than 5 years and no symptoms suggestive of coronary artery disease like chest pain,shortness of breath,palpitations.
2. Patients with type 2 diabetic mellitus with duration of diabetes less than 5 years and resting normal ECG.

EXCLUSION CRITERIA:

1. Previous history of myocardial infarction, Heart failure.
2. History of angina pectoris
3. Anaemia
4. Hypertension
5. Renal disease

6. ECG evidence of Q wave MI, Ischemic ST segment or T wave changes or completed LBBB.
7. Patients with Retinal changes of diabetes mellitus.
8. Limited life expectancy due to cancer and end stage renal or liver disease

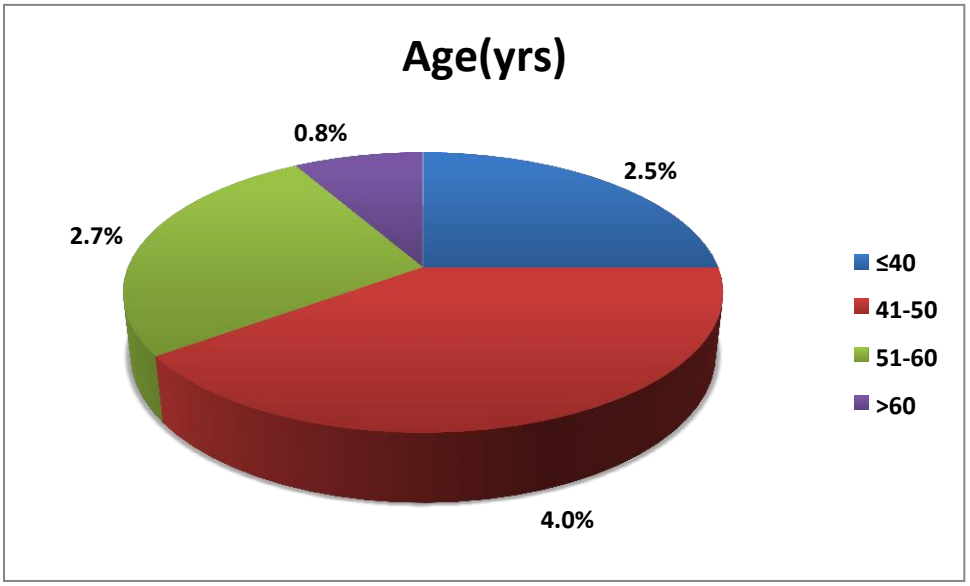
RESULTS AND OBSERVATION

We studied around 60 patients of asymptomatic type 2 DM beyond clinical and electrocardiographic documentation of CAD in BLDE Hospital, Shri B M Patil Medical College Vijayapura and following results were noted.

Table: Distribution of Cases according to Age

Age(yrs)	N	Percent
≤40	15	25
41-50	24	40
51-60	16	26.7
>60	5	8.3
Total	60	100

Figure: Distribution of Cases according to Age



In the age group of 31-40 yrs of age 15 patients were present. 13 were males, 2 were females. In the age group of 41-50 yrs of age 24 were present, 22 were males, and 2 were females. In the 51-60 yrs of age group 11 were males, 5 were females. Most patients were in the age group of 41-50 yrs.

Table: Distribution of Cases according to Sex

Sex	N	Percent
Male	49	81.7
Female	11	18.3
Total	60	100

Out of 60 patients 49 were males and 11 were females.

Figure: Distribution of Cases according to Sex

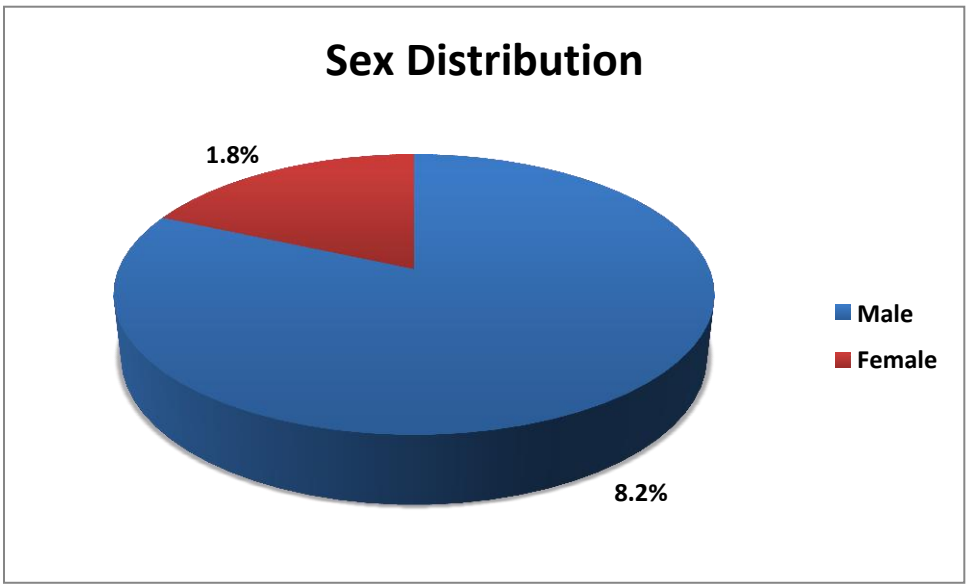


Table: Association of Age and Sex

Age(yrs)	Male		Female		p value
	N	%	N	%	
≤40	13	26.5%	2	18.2%	0.157
41-50	22	44.9%	2	18.2%	
51-60	11	22.4%	5	45.5%	
>60	3	6.1%	2	18.2%	
Total	49	100.0%	11	100.0%	

Table: Association of Age and Sex

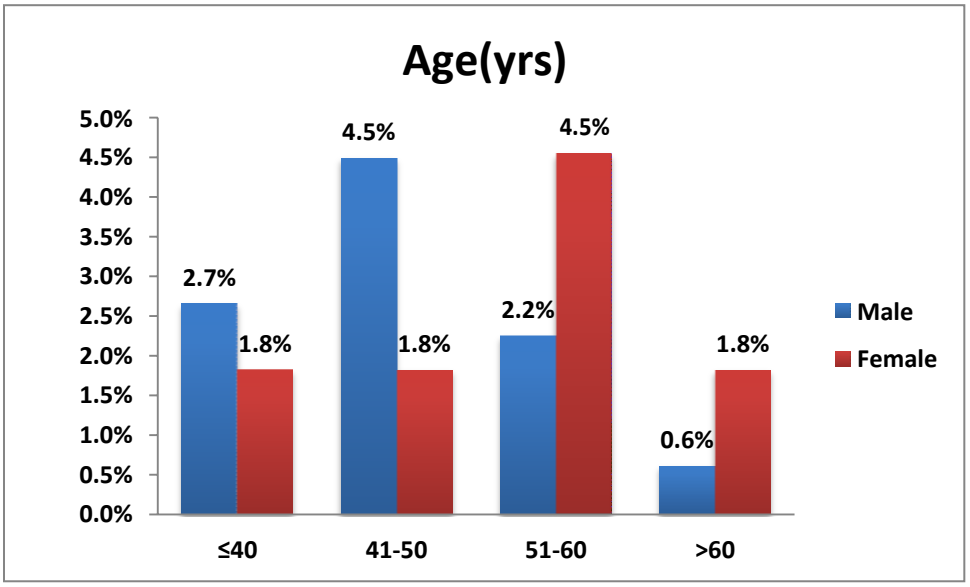


Table: Distribution of Cases according to Duration of DM

Duration of DM (yrs)	N	Percent
<1	5	8.3
1-3	26	43.3
3-5	29	48.3
Total	60	100

This table shows, more number of patients (29 i.e., 48.3%) were having diabetes with 3-5 years of duration, followed by 26 patients (43.3%) with the duration of 1-3 years, next 5 patients (8.3%) less than 1 year of duration.

Figure: Distribution of Cases according to Duration of DM

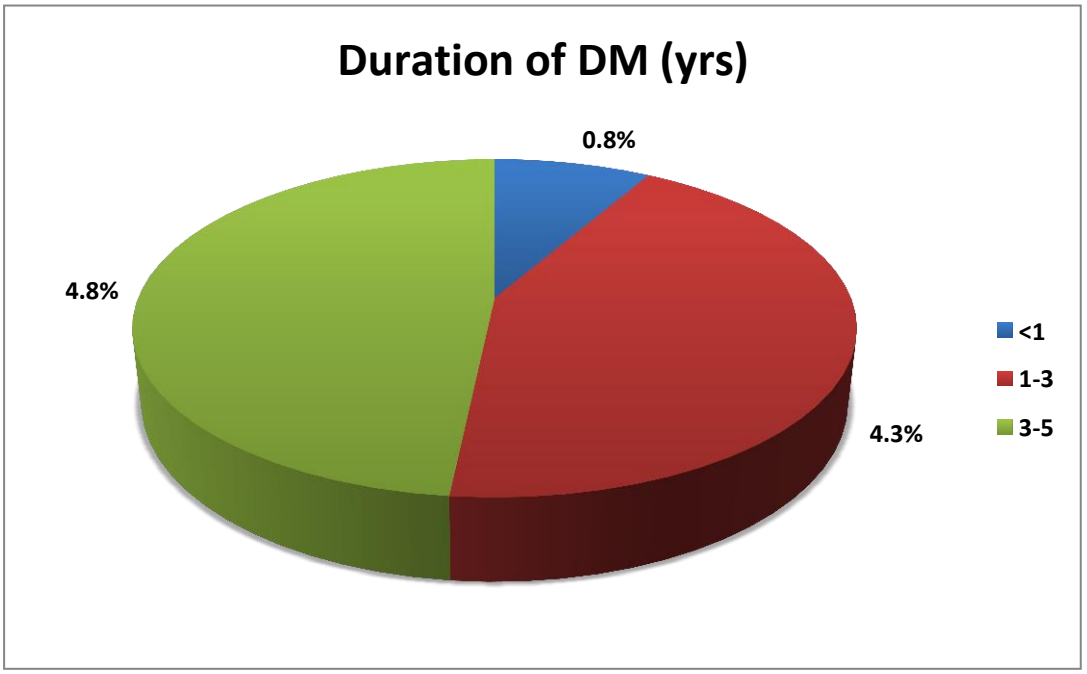
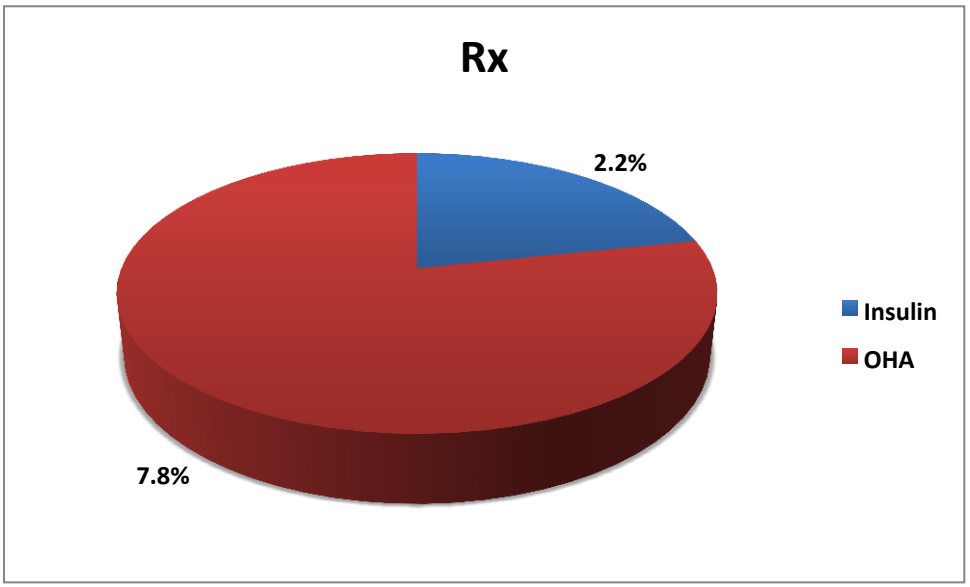


Table: Distribution of Cases according to Rx

Rx	N	Percent
Insulin	13	21.7
OHA	47	78.3
Total	60	100

Figure: Distribution of Cases according to Rx



In our 60 patients, 47 (78.3%) were on one or other OHA's, 13 (21.7%) were on one or other form of insulin. There is a significant difference between duration of diabetes and treatment regimen.

Table: Distribution of Cases according to HbA1c

HbA1c (gm %)	N	Percent
<6.5	7	11.7
6.51-8.50	34	56.7
>8.5	19	31.7
Total	60	100

In this study more number of patients i.e. 34 (56.7%) were with HbA1c 6.51 to 8.50 gm% followed by 19 patients with HbA1c more than 8.5gm% and 7 patients with less than 6.5 gm%.

Figure: Distribution of Cases according to HbA1c

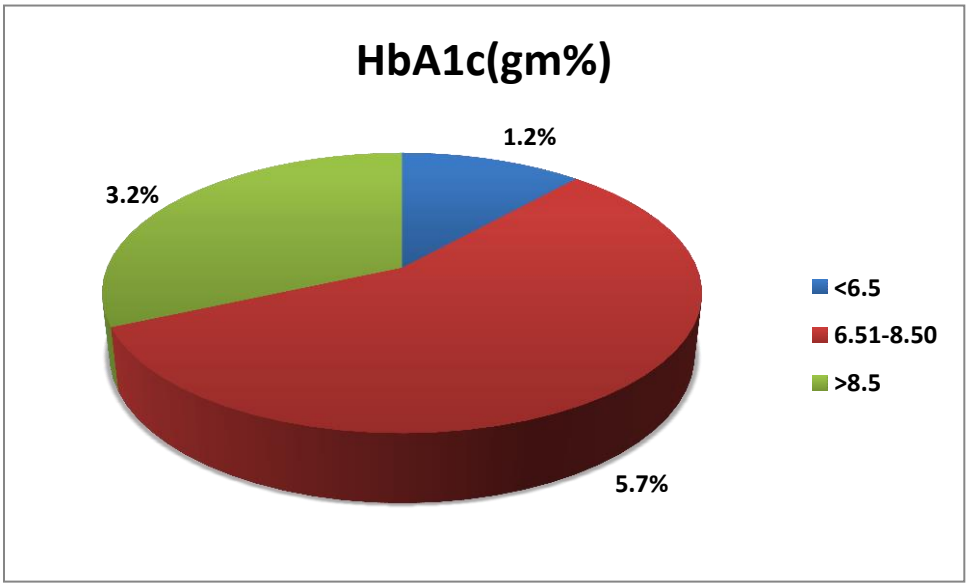


Table: Distribution of Cases according to TMT

TMT	N	Percent
Positive	11	18.3
Negative	49	81.7
Total	60	100

Out of 60 patients 11 i.e 18.3% were TMT positive and 49 were TMT negative.

Figure: Distribution of Cases according to TMT

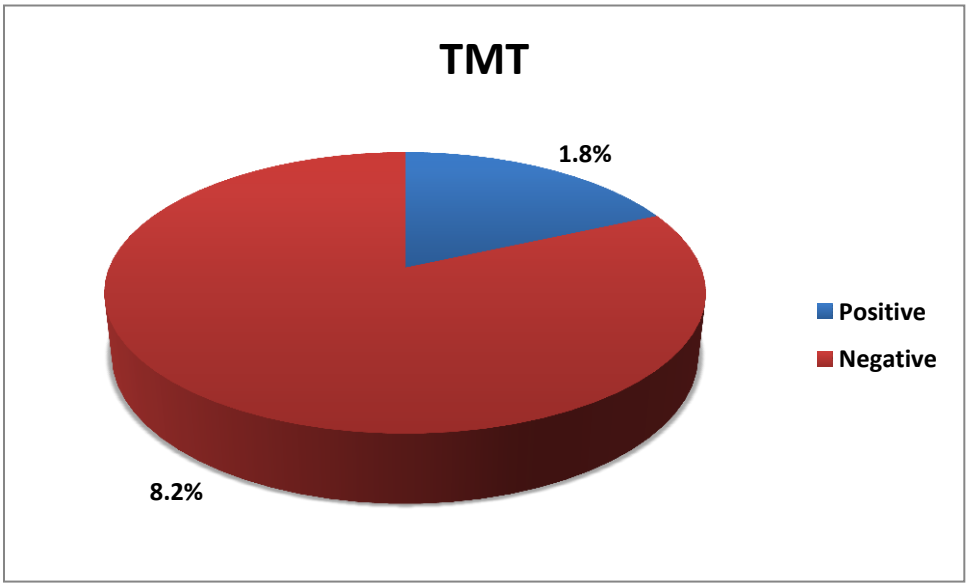


Table: Distribution of HbA1c according to Duration of DM

HbA1c (gm %)	Duration of DM (yrs)		p value
	Mean	SD	
<6.5	1.4	0.9	0.001*
6.51-8.50	3.1	1.6	
>8.5	3.9	1.2	
Total	3.1	1.6	

Note: * significant at 5% level of significance (p<0.05)

This table shows as there is increase in duration of DM, there is an increase in HbA1C level and there is a statistically significant difference between duration of diabetes and HbA1C level.

Figure: Distribution of HbA1c according to Duration of DM

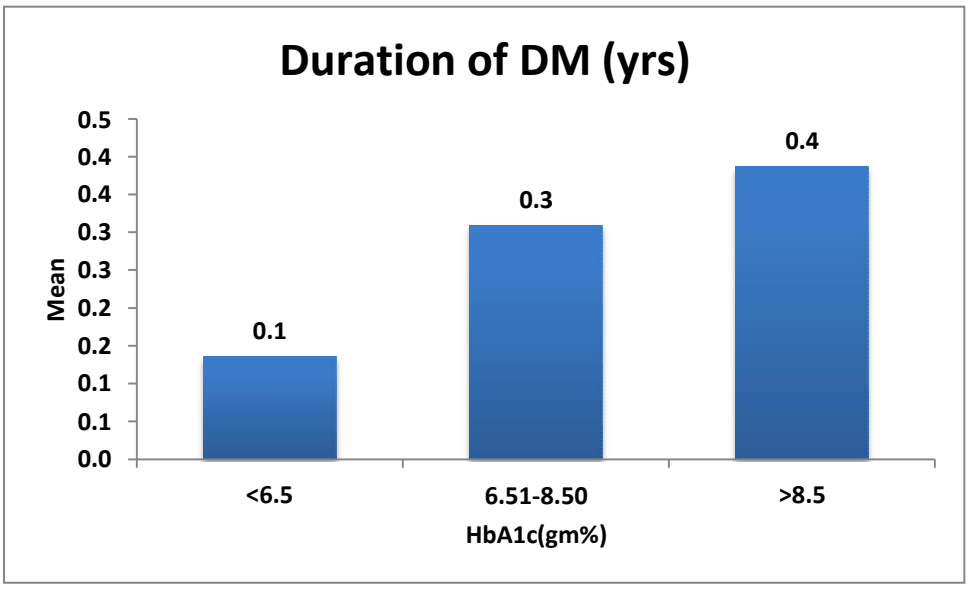


Table: Distribution of Age according to TMT

Age(yrs)	TMT+ve		TMT-ve		p value
	N	Percent	N	Percent	
≤40	3	27.3%	12	24.5%	0.994
41-50	4	36.4%	20	40.8%	
51-60	3	27.3%	13	26.5%	
>60	1	9.1%	4	8.2%	
Total	11	100.0%	49	100.0%	

Maximum patients with TMT positive were in the age group of 41-50 years i.e. 36.4% while only one patient with TMT positive was above 60 years age. In this study the distribution of age according to TMT was not significant statistically.

Figure: Distribution of Age according to TMT

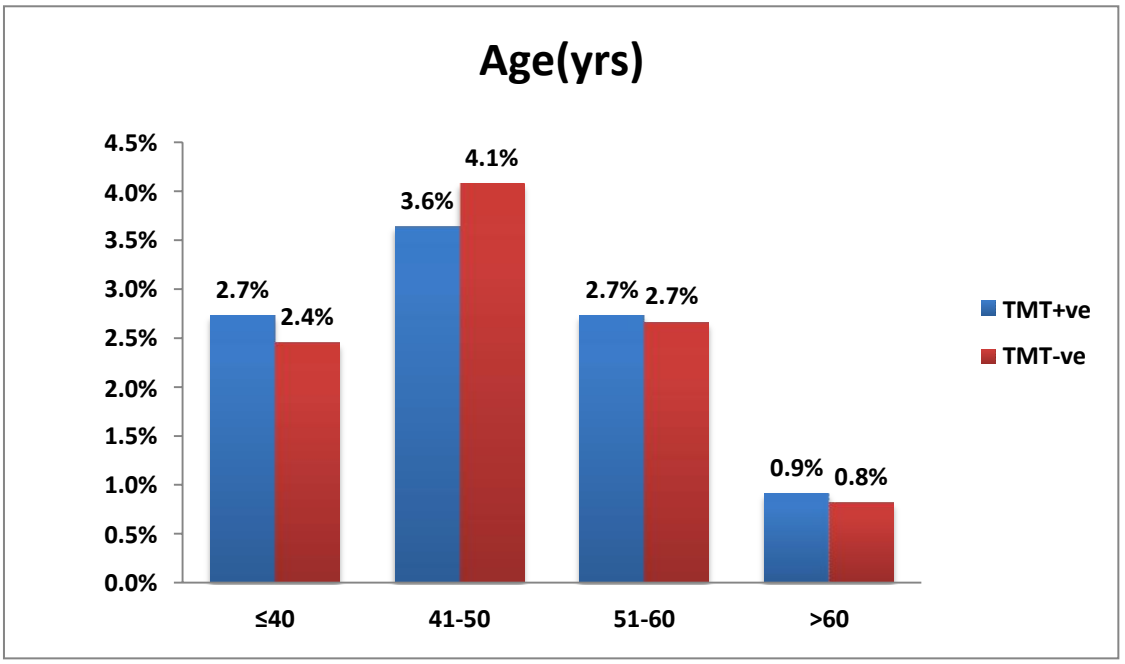
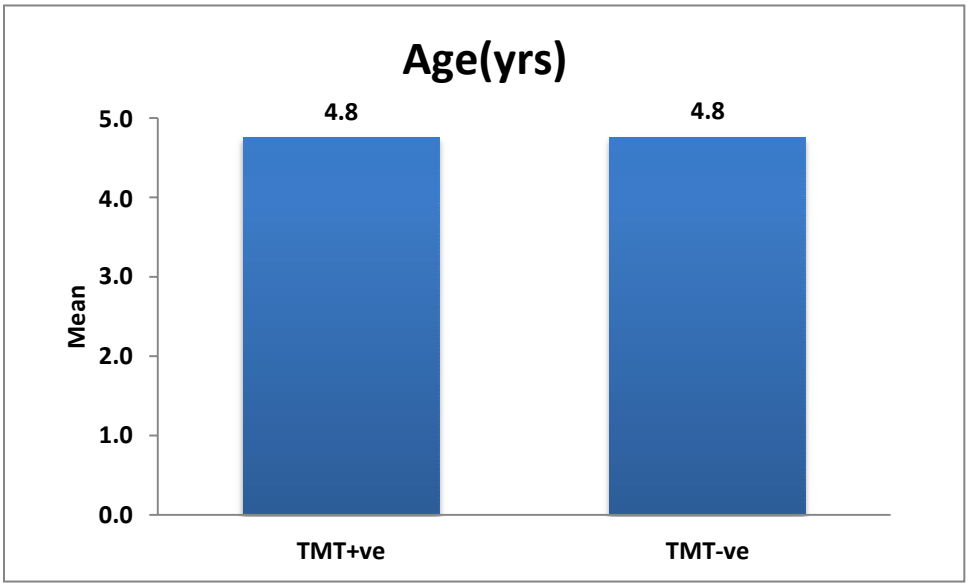


Table: Mean Age between TMT +ve and TMT –ve cases

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
Age(yrs)	47.5	11.5	47.6	10.4	0.999

Figure: Mean Age between TMT +ve and TMT –ve cases



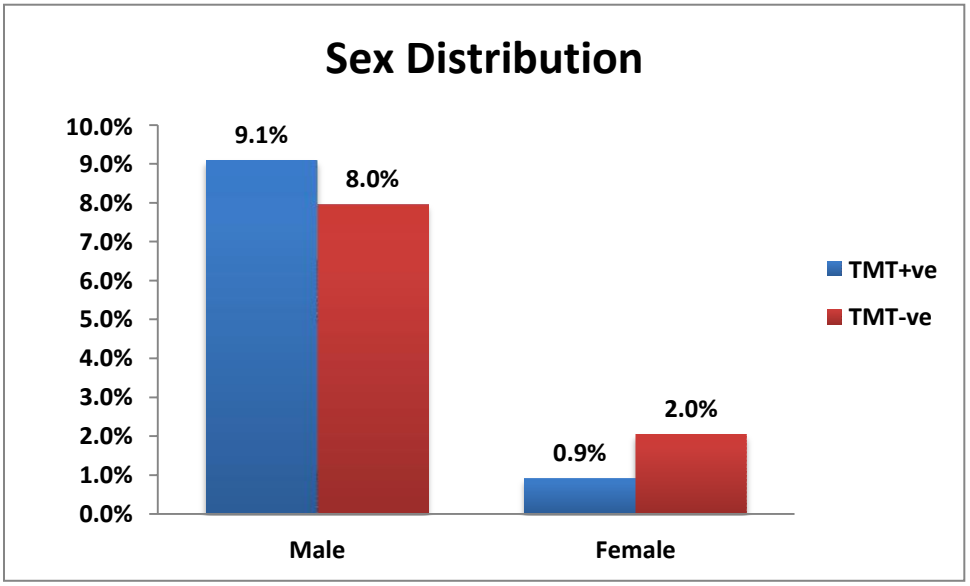
In this study, Mean age for TMT positive and TMT negative cases were 47.5 years and

47.6 years respectively.

Table: Distribution of Sex according to TMT

Sex	TMT+ve		TMT-ve		p value
	N	Percent	N	Percent	
Male	10	90.9%	39	79.6%	0.381
Female	1	9.1%	10	20.4%	
Total	11	100.0%	49	100.0%	

Figure: Distribution of Sex according to TMT



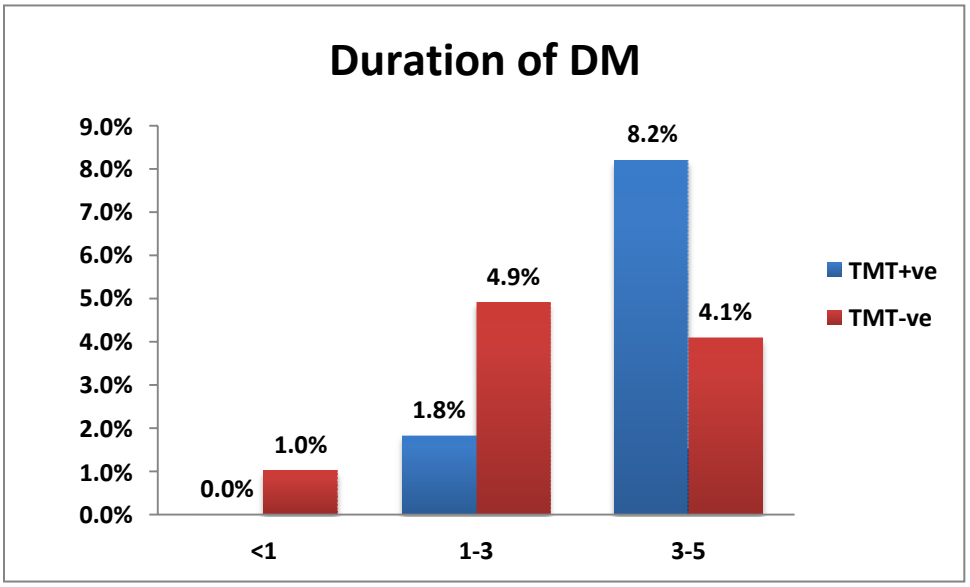
Out of 11 positive cases 90.9% were men and 9.1% were women. Statistically there was no significant difference in silent MI in male and female patients (p>0.05).

Table: Distribution of Duration of DM according to TMT

Duration of DM	TMT+ve		TMT-ve		p value
	N	Percent	N	Percent	
<1	0	0.0%	5	10.2%	0.045*
1-3	2	18.2%	24	49.0%	
3-5	9	81.8%	20	40.8%	
Total	11	100.0%	49	100.0%	

Note: * significant at 5% level of significance ($p<0.05$)

Figure: Distribution of Duration of DM according to TMT



Out of 11 TMT positive patients 81.8% patients were having duration of DM more than 3 years .Duration of diabetes mellitus and TMT positive prevalence was statistically significant.

Table: Mean Duration of DM between TMT +ve and TMT –ve cases

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
Duration of DM (yrs)	3.9	1.3	3.0	1.6	0.095

Figure: Mean Duration of DM between TMT +ve and TMT –ve cases

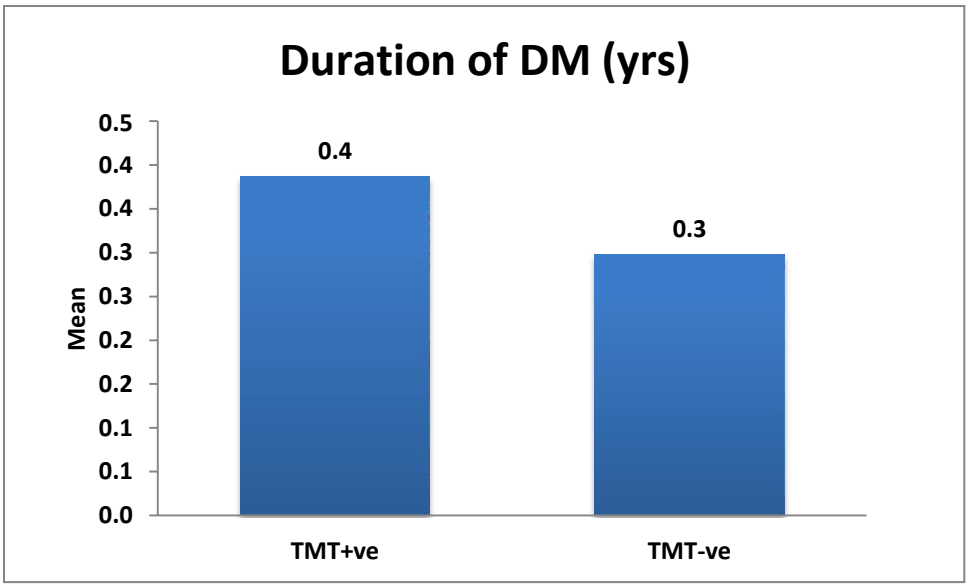


Table: Distribution of Rx according to TMT

Rx	TMT+ve		TMT-ve		p value
	N	Percent	N	Percent	
Insulin	3	27.3%	10	20.4%	0.617
OHA	8	72.7%	39	79.6%	
Total	11	100.0%	49	100.0%	

Figure: Distribution of Rx according to TMT

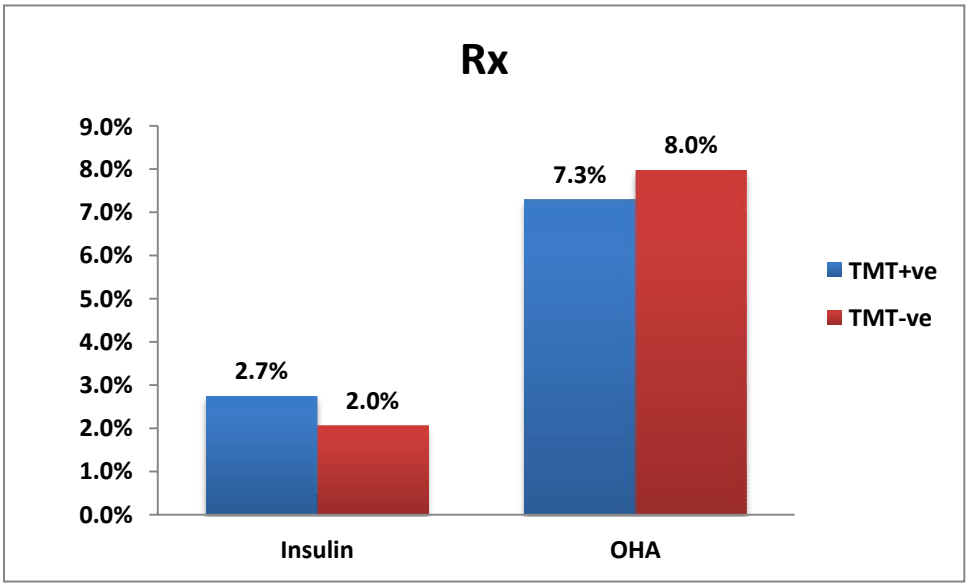


Table: Distribution of HbA1c according to TMT

HbA1c (gm %)	TMT+ve		TMT-ve		p value
	N	Percent	N	Percent	
<6.5	1	9.1%	6	12.2%	0.194
6.51-8.50	4	36.4%	30	61.2%	
>8.5	6	54.5%	13	26.5%	
Total	11	100.0%	49	100.0%	

Figure: Distribution of HbA1c according to TMT

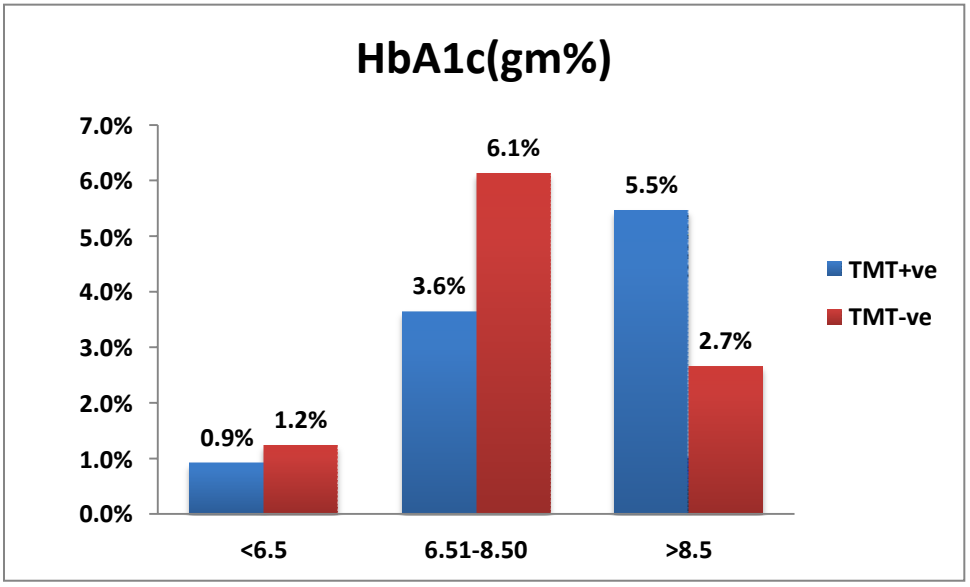


Table: Mean HbA1c according to TMT

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
HbA1c (gm %)	8.6	1.5	7.7	1.7	0.121

As the p value >0.05 mean HbA1c according to TMT is not significant according to this study.

Figure: Mean HbA1c according to TMT

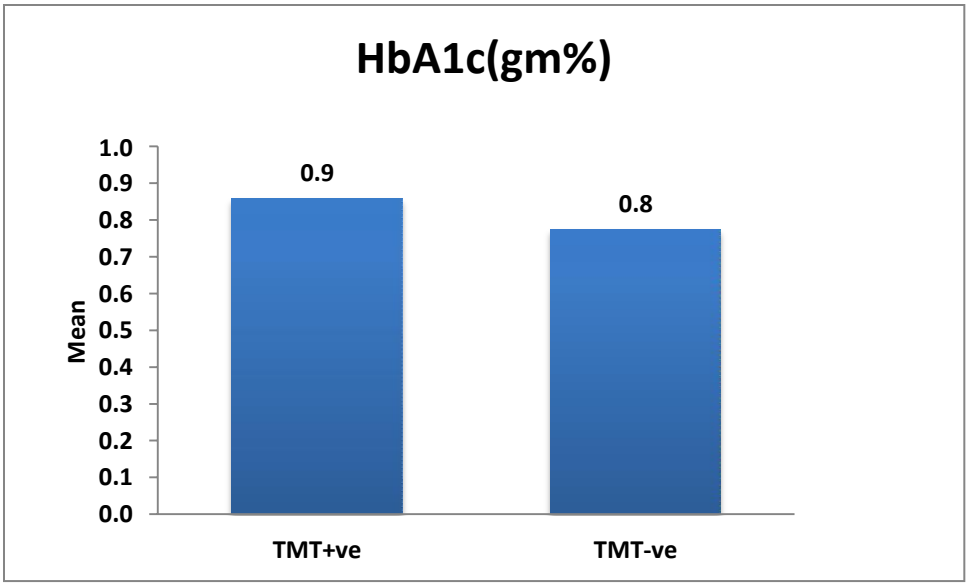


Table: Mean FBS and PPBS according to TMT

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
FBS (mg/dl)	152.4	41.8	125.0	36.9	0.034*
PPBS(mg/dl)	193.1	33.6	173.3	45.0	0.175

Note: * significant at 5% level of significance ($p<0.05$)

Mean FBS for TMT positive patients is 152.4mg/dl and for TMT negative patients is 125 mg/dl and the difference is statistically significant.

Figure: Mean FBS and PPBS according to TMT

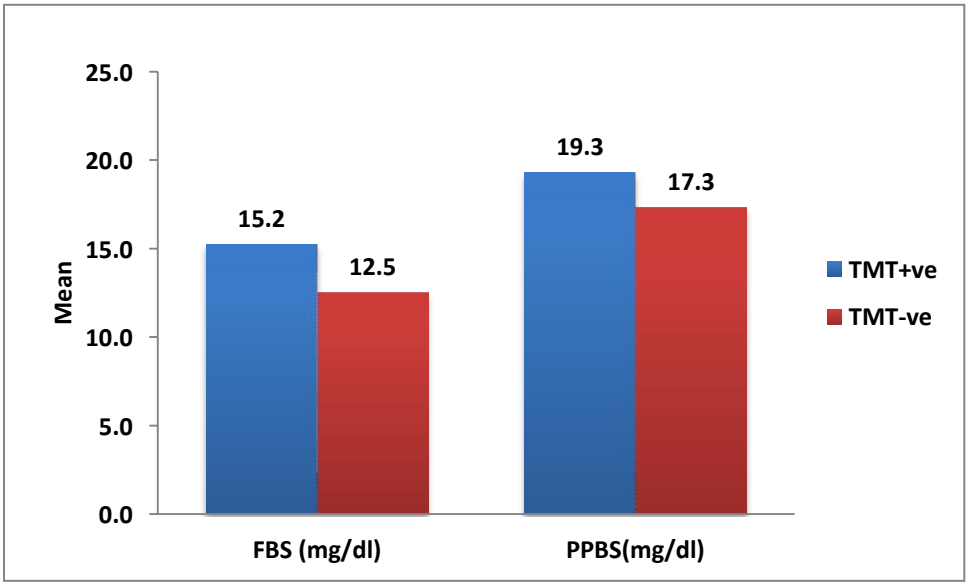
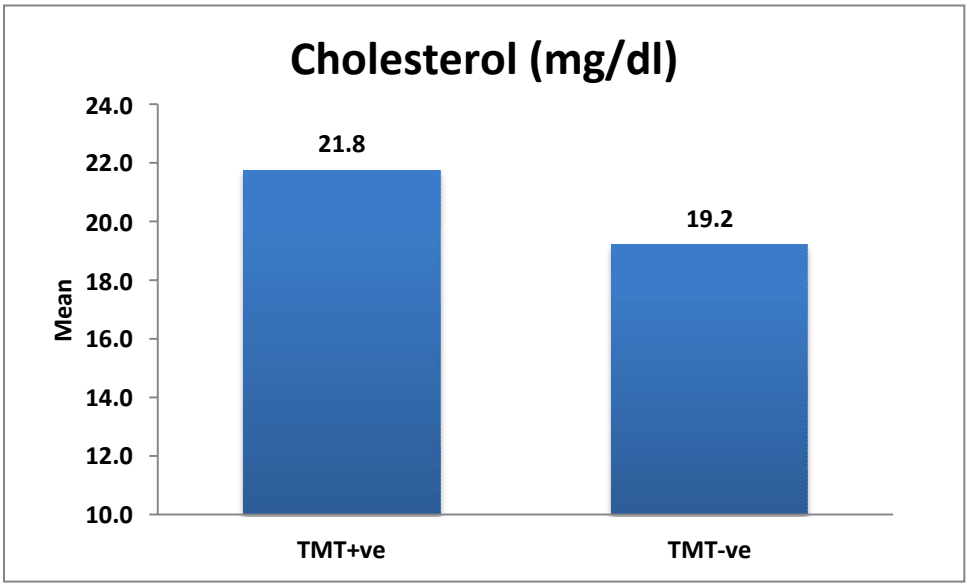


Table: Mean Cholesterol according to TMT

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
Cholesterol (mg/dl)	217.5	27.3	192.2	36.6	0.035*

Note: * significant at 5% level of significance ($p<0.05$)

Figure: Mean Cholesterol according to TMT



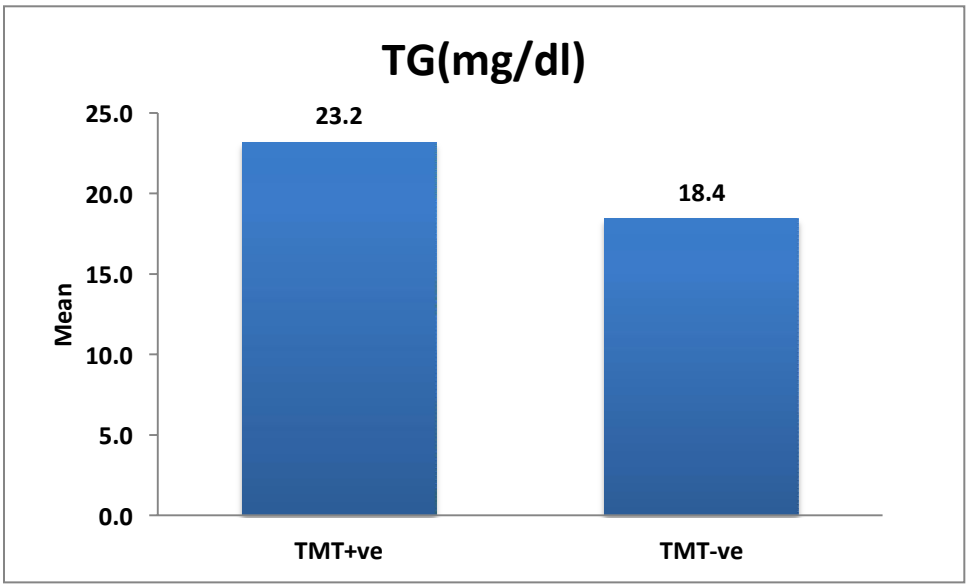
Mean cholesterol for TMT positive and negative patients were 217.5 mg/dl and 192.2 mg/dl respectively, and the difference was statistically significant.

Table: Mean TG according to TMT

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
TG(mg/dl)	231.9	109.1	184.4	62.4	0.048*

Note: * significant at 5% level of significance ($p<0.05$)

Figure: Mean TG according to TMT

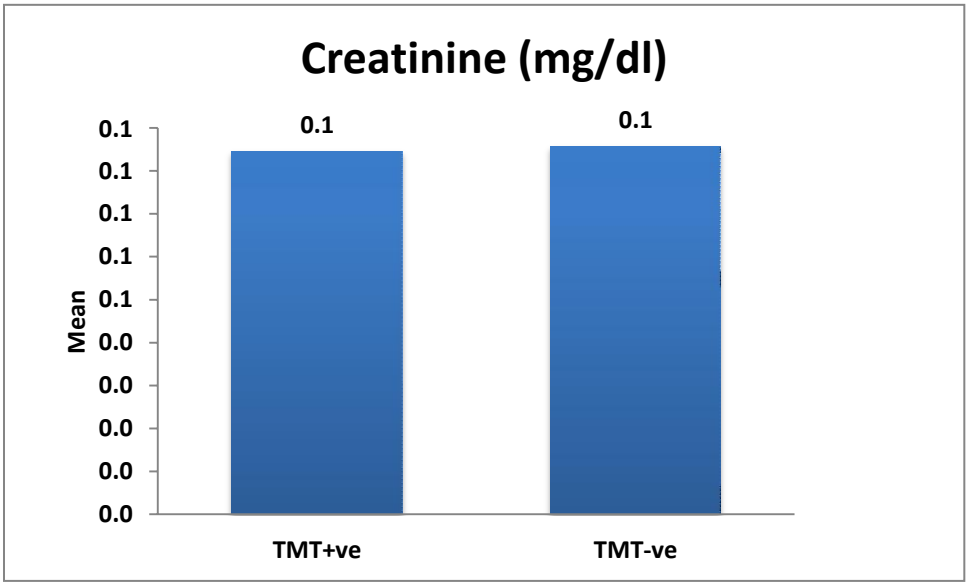


From this study there was statistically significant difference between mean triglycerides and silent MI, as mean triglycerides for TMT positive cases was 231.9mg/dl i.e. more than that for TMT negative cases 184.4mg/dl.

Table: Mean Creatinine according to TMT

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
Creatinine (mg/dl)	0.8	0.1	0.9	0.2	0.824

Figure: Mean Creatinine according to TMT



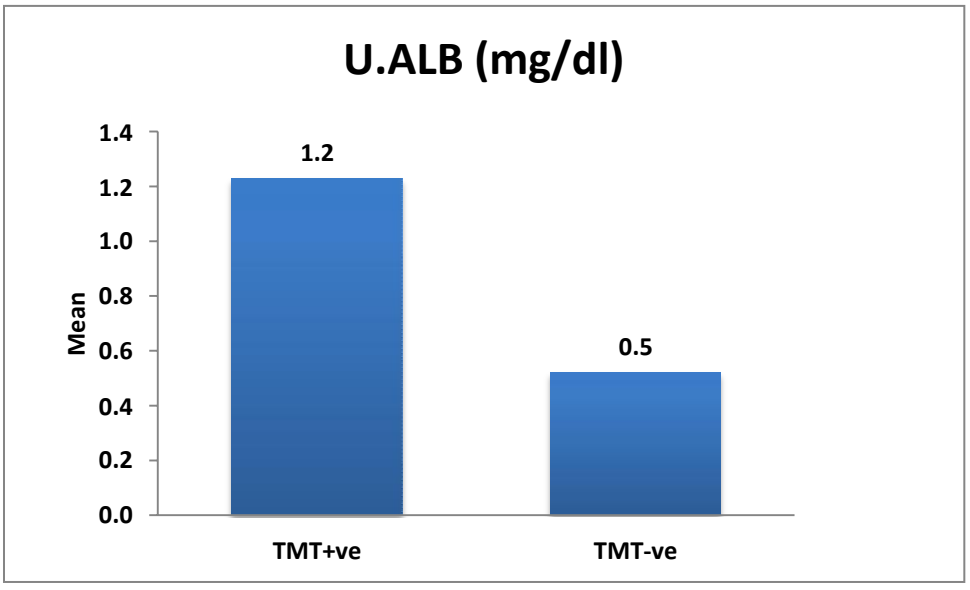
Mean creatinine for TMT positive and negative patients was 0.8 mg/dl and 0.9 mg/dl respectively and the difference was statistically insignificant.

Table: Mean U.ALB according to TMT

Parameters	TMT+ve		TMT-ve		p value
	Mean	SD	Mean	SD	
U.ALB (mg/dl)	12.3	4.7	5.2	11.3	0.031*

Note: * significant at 5% level of significance ($p<0.05$)

Figure: Mean U.ALB according to TMT



Mean urine albumin for TMT positive patients was 12.3 mg/dl and for TMT negative patients was 5.2 mg/dl, and the difference was statistically significant.

TABLE: COMPARISION OF DIABETIC SUBJECTS WITH AND WITHOUT ASYMPTOMATIC CORONARY ARTERY DISEASE

Parameters	TMT	Mean	Std. Deviation	P value	Inference
Avg Age [yrs]	Positive	47.5	11.5	0.999	NotSignificant
	Negative	47.6	10.4		
Avg Duration of DM[years]	Positive	3.9	1.3	0.095	NotSignificant
	Negative	3.0	1.6		
Avg HbA1C[%]	Positive	8.6	1.5	0.121	NotSignificant
	Negative	7.7	1.7		
Avg FBS [mg/dl]	Positive	152.4	41.8	0.034	Significant
	Negative	125.0	36.9		
Avg PPBS[mg/dl]	Positive	193.1	33.6	0.175	Not Significant
	Negative	173.3	45.0		
Avg Total Cholestrol [mg%]	Positive	217.5	27.3	0.035	Significant
	Negative	192.2	36.6		
Urine Albumin[mg/dl]	Positive	12.3	4.7	0.031	Significant
	Negative	5.2	11.3		
On OHAs	Positive	8	72.7%	0.617	Not significant
	Negative	39	79.6%		
On Inj Insulin	Positive	3	27.3%		
	Negative	10	20.4%		
Avg Triglycerides[mg/dl]	Positive	231.9	109.1	0.048	Significant
	Negative	184.4	62.4		
Avg Creatinine[mg/dl]	Positive	0.8	0.1	0.824	Not significant
	Negative	0.9	0.2		

DISCUSSION

Coronary Artery Disease detection in asymptomatic type 2 DM is often delayed. The preponderance of SMI in type 2 DM is variable and ranges from 9 to 75%.[41,42,43] My study was anticipated at the asymptomatic presentation of CAD in the form of SMI in asymptomatic DM patients. It consisted of two aspects; First the prevalence of SMI in asymptomatic patients with type 2 DM. Secondly to assess clinical predictors of SMI in these patients.

This study consists of 60 known asymptomatic type 2 diabetics without clinical and electrocardiograpic evidence of CAD and were evaluated for the preponderance of SMI by using exercise treadmill testing.

In my study out of 60 cases 49 were males and 11 were females. In the age group of 31-40 yrs of age 15 patients are present-13 were males, 2 were females.In the age group of 41-50 yrs of age 24 were present ,22 were males,2 were females. In the 51-60 yrs of age group 11 were males, 5 were females. Most patients in the age group of 41-50 yrs of age.

In the study population, more number of patients (29 i.e., 48.3%) were having diabetes with the duration of 3-5 years, followed by 26 patients (43.3%)with the duration of 1-3 years, next 5 patients(8.3%) less than 1 year of duration of diabetes.

As the duration of diabetes increased there is an increase in HbA1C level in cases of >3 yrs duration of diabetecs. This shows poor glycemic control. There is a statistically significant difference between duration of DM and HbA1C level.

In our 60 patients, 47 (78.3%) were on one or other OHA's, 13 (21.7%) were on one or other form of insulin. There is a significant difference between duration of diabetes and treatment regimen.

In my study out of 60 cases TMT positive cases are 11 (18.3%) and negative cases are 49 (81.7%) .

In my study, the percentage of SMI in type 2 asymptomatic DM was turned out to be 18.3% (11/60).

Our findings were similar to previous studies. Study done by Langer A et al [48] found 12.1% of diabetics free of CAD to have SMI on exercise electrocardiogram testing.

Study done by 'Milan Study on Atherosclerosis and Diabetes (MiSAD)' Group [43] found that 29% diabetes who were asymptomatic for CAD had SMI on 24 hour ambulatory monitoring exercise electrocardiogram.

Another similar study done by Sukhija R et al[44] had shown higher predominance of SMI in DM as compared to non diabetics.

Another study by Emilia Be et al [46] identified that 38.3% of DM beyond prior CAD had SMI on treadmill test.

One more study by Mathura KC et al [47]found that 62/500 patients (12.4%) had SMI in outpatients with type DM by using exercise electrocardiogram.

Another study by Quek DK et al[49], found that SMI was positive in 14(46.7%) out of 30 DM patients by treadmill test.

One more study population by Gupta SB et al[50]identified that a total of 113/522 patients (22%) had SMI using stress testing in asymptomatic patients with type 2 diabetes mellitus.

Another study by Mathura KC et al [51] from India, reported 50% incidence of silent myocardial ischemia in diabetics on exercise electrocardiogram and 35% on ambulatory monitoring.

In our study As duration of diabetes for patients was less than 5 years, the prevalence for silent MI with the help of TMT was lesser i.e 18.3% compared to other studies.

So in my study it shows that DM patients had a higher prevalence of silent myocardial ischemia.

Patients had normal resting echo, but when subjected to TMT, a significant proportion of cases were positive for silent ischemia, which otherwise would have been unnoticed. We believe that TMT remains the cornerstone for screening the population at risk where angiography is not readily available.

DURATION OF TYPE 2 DIABETES MELLITUS AND SILENT MYOCARDIAL ISCHEMIA.

In 60 of patients, Treadmill test positive cases are 11 patients (18.3%) and negative cases are 49 patients(81.7%).

- 29 patients with diabetes duration 3 to 5 years,Tread mill test was positive in 9 (81.8%).
- 26 patients with diabetes duration between 1 to 3 years.Treadmill test was positive in 2 (18.2%).
- TMT was negative for 5 patients who were with duration less than 1 year. Our results are similar to one study by Murray DP et al[52] that found that 70% subjects (7/10) with DM of <5 years duration had associated silent myocardial ischemia while only 30% subjects (3/10) with DM of >5years duration had associated SMI. Another study by Mathura KC et al[51] including 500 patients with type 2 diabetes mellitus with normal resting ECG found that, 62(12.4%) patients had asymptomatic coronary artery disease on exercise treadmill testing. The abnormalities of exercise test were associated with longer duration of diabetes ($p<0.005$).

DYSLIPIDEMIA AND SILENT MYOCARDIAL ISCHEMIA

In the present study, we found average total cholesterol in TMT positive and negative cases were 217.5% and 192.2mg % respectively. Average triglyceride in Treadmill test positive and negative cases 231.9mg% and 184.4 mg% respectively. Statistically significant value of $p<0.05$ was found in triglycerides levels between both the groups.

The same results were observed in previous study[57]which found that

dyslipidemia was common in type 2 DM and most common aberrancy was elevated serum triglyceride levels (73.3%).The next aberrancy was decreased serum HDL levels (66.7%).

Another study from India by Tandon R et al[56], found that CAD had strong complementation with elevated levels of triglycerides (0.82) and low HDL (- 0.81).

Yet another study by Bhatia LC et al[57] found that triglyceride levels were elevated in 28 treadmill positive cases compared to 15 treadmill negative cases ($p<0.01$).

GLYCOSYLATED HEMOGLOBIN AND SILENT MYOCARDIAL ISCHEMIA.

The increased levels of glycated hemoglobin indicates poor glycemic control and it has great influence on CAD.

In my study we found average HbA1C (%) in Treadmill test positive and negative cases were 8.6 and 7.7 respectively. Statistically significant value of $p<0.05$ was not found in HbA1C (%) levels between both the groups.

One study[60] found that among those who had diabetes mellitus, silent myocardial ischemia was present 27 of 54 patients (50%) who had HbA1c level >or=7.6% and in 39 of 137 (28%) with hemoglobin A1c level ($p<0.005$).

One more study by Shahim B et al[58] shows eloquent increasing trend of HbA1c levels over the augmenting number of coronary vessels involvement with CAD ($p<0.0001$).

CONCLUSION

1. In my study population, the preponderance of SMI in type 2 DM, without previous clinical and electrocardiographic signs of ischemic heart disease or hypertension is 18.3%.
2. Duration of diabetes mellitus is directly proportional to increased risk of silent ischemia in type 2DM.
3. Triglyceride was found to be in higher levels in persons who had silent ischemia.
4. Glycated hemoglobin levels was found to be more in diabetics, who had greater prevalence of silent myocardial ischemia on TMT.
5. Age, duration of diabetes, serum triglyceride levels and glycated hemoglobin are strong clinical predictors of silent myocardial ischemia.
6. Early detection of patients with type 2 DM for SMI may prevent catastrophic cardiac events.
7. Based on our study, a routine screening for Silent Myocardial Ischemia in asymptomatic type 2 DM patients who had longer duration of diabetes, high triglycerides and HbA1C levels can be done using TMT Test.

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ANNEXURES -I

B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103 IEC-NO-286/18
17/11/2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Screening of asymptomatic diabetes mellitus patients with less than 5 year old duration for ischemic heart disease using treadmill test.

Name of P.G. Student : Dr Tejashree Dubal
Department of General Medicine.

Name of Guide/Co-investigator: Dr. S.S.Devarmani, Professor of General Medicine.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

ANNEXURES -II

INFORMED CONSENT FORM:

TITLE OF RESEARCH: "**SCREENING OF ASYMPTOMATIC DIABETES MELLITUS PATIENTS WITH LESS THAN 5 YEAR OLD DURATION FOR ISCHEMIC HEART DISEASE USING TREADMILL TEST**

GUIDE : **DR S S DEVARMANI**

M.D GENERAL MEDICINE

P.G.STUDENT : **DR TEJASHREE DUBAL**

All aspects of this consent form are explained to the patient in the language understood by him or her.

PURPOSE OF STUDY:

I have been informed that the purpose of this study is to study for presence of ischemic heart disease or silent myocardial infarction in patients diagnosed of diabetes mellitus less than 5 year duration, using treadmill test.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations

BENEFITS:

I understand that my participation in this study will have no direct benefit to me other than the potential benefit of treatment which is planned to prevent further morbidity and mortality .

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulation of hospital. If the data is used for publication the identity will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

(Signature of Guardian) (Signature of patient)

STUDY SUBJECT CONSENT FORM:

I confirm that Dr.Tejashree Dubal has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all above in detail in my own language and I understand the same. I agree to give my consent to participate as a subject in this research project.

DATE SIGNATURE OF PARTICIPANT

ANNEXURES -III

PROFORMA

SCREENING OF ASYMPTOMATIC DIABETES MELLITUS PATIENTS WITH LESS THAN 5 YEAR OLD DURATION FOR ISCHEMIC HEART DISEASE USING TREADMILL TEST'

IDENTIFICATION DETAILS:

Name	
Age/Sex	
OP/IP NO.	
Occupation	
Address	

DURATION OF DIABETES MELLITUS:

PRESENTING COMPLAINTS:

PAST HISTORY:

TREATMENT HISTORY:

FAMILY HISTORY:

PERSONAL HISTORY: DIET

SLEEP

APPETITE

BOWEL AND BLADDER HABBITS

ADDICTIONS

GENERAL PHYSICAL EXAMINATION:

PULSE RATE: **SUPINE BP**

STANDING BP

SYSTEMIC EXAMINATION :

I. CARDIOVASCULAR SYSTEM:

II. RESPIRATORY SYSTEM:

III. ABDOMINAL AND GENITO URINARY SYSTEM.

IV.CENTRAL NERVOUS SYSTEM:

INVESTIGATIONS :

A.HEMATOLOGICAL-

1) Hemoglobin	gm. %
2) Total WBC counts	Cells/mm^3
3) Platelet count	

B.BIOCHEMICAL

FASTING BLOOD SUGAR	
POSTPRANDIAL BLOOD SUGAR	
FASTING LIPID PROFILE	
CHOLESTEROL	
TRIGLYCERIDE	
GLYCOSYLATED HEMOGLOBIN-HBA1c	
S.CREATININE	

URINE EXAMINATION-

FUNDOSCOPY-

ECG-

2D ECHO-

TREAD MILL TEST

CONCLUSION-

BLDEU Shri B.M.Patil Medical College, Hospital

Ashram road, Vijayapura

PATIENT ID : 34559
PATIENT NAME : HYANAMANTRAYA 34/M

Summary Report

Report time : 10:08 am
October 10, 2018 10:08 am

PROTOCOL : BRUCE
PATIENT HEIGHT : 0 Cm PATIENT WEIGHT : 0.00 Kg
PATIENT ADD. :

Ref. By : Not Applicable
(Not Applicable)

OBJECT OF TEST	: Chest pain diagnosis
RISK FACTOR	: Male, Diabetes
ACTIVITY	: Moderate active
MEDICATION	:
BRIEF HISTORY	:
OTHER INVESTIGATION	:
REASON FOR TERMINATION	: Dysponea
EXERCISE TOLERANCE	: Good
EXERCISE INDUCED ARRHYTHMIA	: No
HAEMO RESPONSE	: Normal
CHRONO RESPONSE	: Normal
FINAL IMPRESSION	: TERMINATED IN VIEW OF DYSPNEA

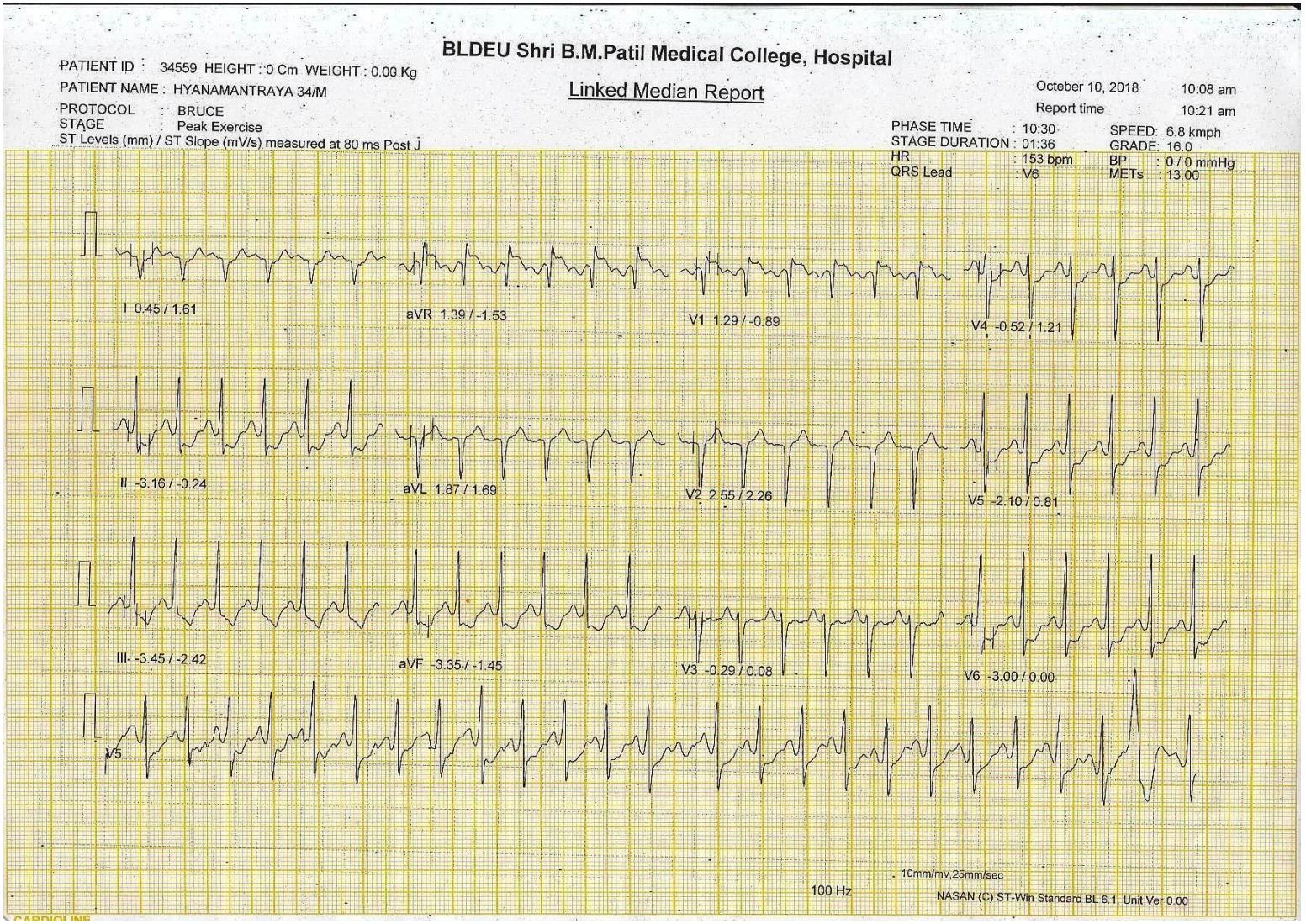
THR ACHIEVED

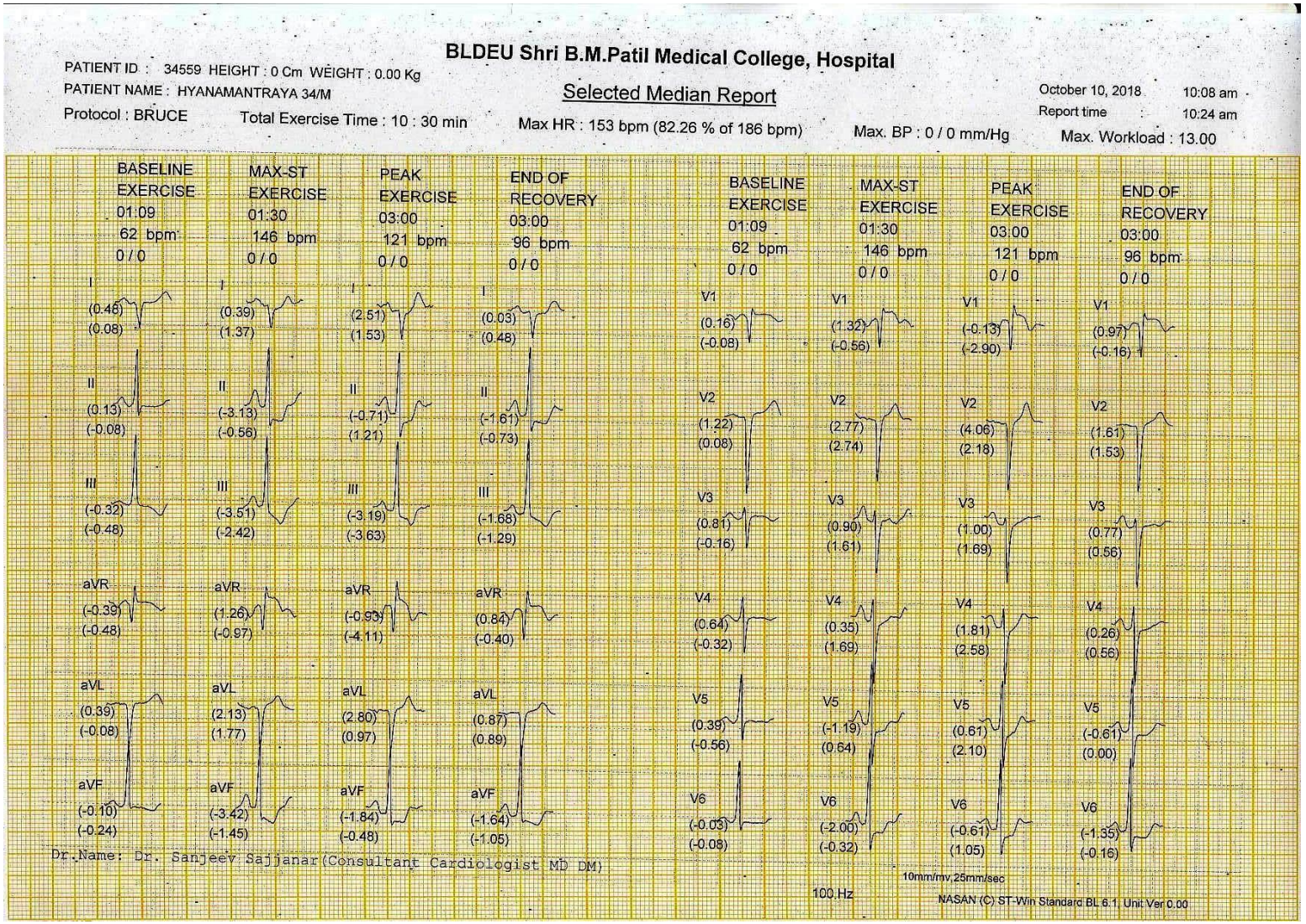
SIGNIFICANT ST DEPRESSION IN INFERIOR AND LATERAL LEADS

POSITIVE FOR INDUCIBLE ISCHEMIA ATGIVEN WORKLOAD

Dr. Sanjeev Sajjanar
Consultant Cardiologist MD DM

NASAN (C) ST-Win Standard BL 6.1, Unit Ver 0.00





MASTER CHART

SR NO.	NAME	IP NO.	AGE (yrs)	SEX	DURATION DM (yrs)	Rx	PULSE (bpm)	SBP(mmhg)	DBP (mmhg)	RS	CVS	PA	AN SIGNS	FBS (mg/dl)	PPBS(mg/dl)	HBA1C (%)	CHOL (mg/dl)	TG (mg/dl)	CREAT (mg/dl)	U.ALB (mg/dl)	TMT RESULT
1	Hynamatraya	34559	34	M	2yrs	OHA	80	130	80	N	N	N	-	86	216	10.6	268	205	0.7	-	+
2	Jakappa	34779	33	M	2yrs	OHA	78	126	80	N	N	N	-	169	200	7.8	212	176	0.6	-	-
3	Chandrashekhar	391480	45	M	3 and half	OHA	98	138	90	N	N	N	-	159	201	7.9	212	176	0.9	-	+
4	Shivanand	396971	48	M	3	OHA	86	130	80	N	N	N	-	98	136	7.2	196	156	0.8	-	-
5	Laxmibai	400437	60	F	5	OHA	80	126	70	N	N	N	-	99	109	8.6	176	150	0.6	-	-
6	Devesh Patil	31141	42	M	4	OHA	98	140	88	N	N	N	-	114	200	7.9	240	186	0.9	30	-
7	Jose Valentin	90265	47	M	2	OHA	78	150	90	N	N	N	-	91	155	8.2	211	120	1.1	30	-
8	Shridhar Jalihal	110543	41	M	5	OHA	66	136	90	N	N	N	-	101	151	6.9	265	221	1.1	30	-
9	Yallappagauda	10378	27	M	2	OHA	88	126	80	N	N	N	-	104	168	7.9	200	140	0.9	-	-
10	B S Kambale	119630	45	M	5	OHA	98	136	80	N	N	N	-	85	116	7.2	156	160	0.6	-	-
11	Kallappa Kichali	136709	53	M	4	InjMixtard	86	146	80	N	N	N	-	106	225	10.8	212	160	0.6	-	-
12	Mahesh Devgiri	140639	45	M	3	OHA	88	120	80	N	N	N	-	116	169	8.6	216	155	0.9	-	-
13	Dakshinmurthy	193946	44	M	3	injActra.	68	136	76	N	N	N	-	156	186	8.5	205	168	0.9	30	-
14	Anand Nagneshwar	102328	35	M	6months	OHA	78	130	80	N	N	N	-	75	128	6.7	75	128	0.8	-	-
15	Vilasrao Kulkarni	82117	46	M	2months	OHA	88	140	76	N	N	N	-	145	158	7.5	158	104	0.8	-	-
16	Vilas Irkal	70571	45	M	2months	OHA	86	140	80	N	N	N	-	92	116	6.5	180	308	1	-	-
17	Govind Deshmukh	70619	57	M	2	OHA	88	150	80	N	N	N	-	118	200	6.4	211	277	0.9	-	-
18	Rajshekhar Kumasi	69042	75	M	1	OHA	86	148	86	N	N	N	-	94	112	5.4	169	157	0.9	-	-
19	Saubhagya B	66637	37	F	6months	OHA	90	120	80	N	N	N	-	88	150	5.7	159	162	0.9	-	-
20	Shashikant	58702	46	F	4	OHA	86	140	80	N	N	N	-	197	252	9.2	147	147	0.5	-	-
21	sanjay honagandi	108934	49	M	4	OHA	88	130	70	N	N	N		92	168	6.8	183	137	0.8	-	-
22	mallikarjun patil		50	M	2	OHA	87	126	80	N	N	N	-	85	117	6.5	186	115	0.8	-	-
23	Ramesh inamdar	133098	57	M	5	Inj Actr	90	140	86	N	N	N	-	186	202	8.4	202	164	0.8	-	+
24	Sharath Shetty	113587	41	M	2	OHA	98	112	80	N	N	N	-	109	212	6.7	168	134	1.1	-	-
25	Vilasrao Kulkarni	115316	46	M	3	OHA	96	130	80	N	N	N	-	116	204	6.8	168	115	1	-	-
26	Indumati Biradar	133708	68	F	5	Injmixtar	100	130	90	N	N	N	-	146	202	7.8	204	164	0.6	-	-
27	Somappa Andegavi	9655	60	M	5	injActra.	78	128	80	N	N	N	-	84	156	7.6	138	132	0.8	-	-
28	Darshan chinagi	108921	29	M	1	OHA	88	140	80	N	N	N	-	126	150	5.8	220	225	1	-	+

29	Rajshekhar Pawar	39887	35	M	1 AND HALF YR	OHA	88	130	88	N	N	N	-	241	289	13.5	184	380	0.9	30	-
30	Sharad More	35941	43	M	1	OHA	90	126	88	N	N	N	-	87	112	6.8	265	177	0.9	15	-
31	Rameshkumar Mehta	29174	55	M	2	OHA	76	117	80	N	N	N	-	118	202	6.5	231	235	0.9	-	-
32	Sadanand Patil	25294	49	M	5	OHA	88	130	70	N	N	N	-	99	140	7.2	187	166	0.8	-	-
33	Siddangauda Patil	1545	40	M	5	OHA	78	110	70	N	N	N	-	88	142	8.2	170	86	0.8	-	-
34	Kashinath Kadakbhavi	23556	37	M	5	OHA	88	150	80	N	N	N	-	229	252	10.4	222	525	0.6	15	+
35	Govind D.	21695	52	M	1	OHA	76	134	70	N	N	N	-	141	202	6.2	217	225	1	-	-
36	Paramangauda B	6581	49	M	2`5	OHA	88	140	80	N	N	N	-	134	150	6.9	168	150	0.8	-	-
37	Dundawwa	1913	45	F	4	InjMixtard	90	128	70	N	N	N	-	168	212	10.2	216	168	0.8	30	+
38	Kasturibai Gundalli	13791	58	M	5	InjMixtard	88	136	80	N	N	N	-	160	212	9.2	256	212	0.6	30	-.
39	Anilkumar Wali	93935	51	M	4	injActra.	78	140	70	N	N	N	-	146	168	6.6	206	143	1	30	+
40	Narayana Ghorpade	4776	48	M	5	OHA	98	128	80	N	N	N	-	178	202	8.9	222	169	1	30	+
41	Rushikumar Mehta	29174	52	M	4	0HA	88	130	70	N	N	N	-	118	168	6.5	231	235	0.9	-	-
42	Kullasuma Nadaf	24935	60	F	5	InjMixtard	88	128	70	N	N	N	-	167	178	8.6	198	204	1.1	-	-
43	Rajshekhar Pawar	39887	35	M	2	OHA	88	150	80	N	N	N	-	241	303	13.5	184	380	0.9	30	-
44	Asha Totad	42843	62	F	5	InjActra.	78	128	70	N	N	N	-	145	178	9.2	270	202	1	-	-
45	Santosh V	92077	35	M	3	OHA	78	136	70	N	N	N	-	110	135	7.2	156	168	1	-	-
46	Mallangauda Patil	109270	47	M	1	OHA	80	132	80	N	N	N	-	103	128	6.3	132	95	0.7	-	-
47	Hanmanth Putti	8907	43	M	2	OHA	80	136	80	N	N	N	-	158	189	6.9	189	196	1	-	-
48	Parubai rathod	5757	60	F	5	OHA	68	136	70	N	N	N	-	148	169	7.6	200	198	0.8	-	-
49	kaveri	94758	36	F	3	OHA	88	140	80	N	N	N	-	139	156	8.6	196	245	1	-	-
50	Ullas Gopane	8709	35	M	5	OHA	88	120	80	N	N	N	-	129	189	8.9	188	166	0.7		-
51	Ramesh karbartal	108913	47	M	3	OHA	76	140	80	N	N	N	-	100	136	5.3	234	276	1.1	-	-
52	Ravi manoddar	24090	32	M	6months	OHA	88	136	80	N	N	N	-	140	176	6.7	188	200	0.9	-	-
53	Mehboob Patel	327968	58	M	4	OHA	76	140	76	N	N	N	-	166	203	9.2	223	198	1	-	+
54	H H Bijapur	319142	69	M	5	OHA	88	128	70	N	N	N	-	144	189	7.6	245	266	0.7	-	+
55	Siddappa yallamalli	315374	53	M	4	INJActra.	80	150	80	N	N	N	-	134	168	6.7	189	149	1	-	-
56	Santosh biradar	328152	34	M	1	OHA	76	126	80	N	N	N	-	114	145	6.8	176	189	0.8	-	-
57	Kallappa Jatti	27663	50	M	4	OHA	72	140	80	N	N	N	-	88	129	8.9	157	312	0.8	30	+
58	Jayashree Patil	345961	55	F	4	InjMixtard	88	134	70	N	N	N	-	145	168	9.3	166	233	1.1	30	-
59	Drakshayani	291470	57	F	5	OHA	88	130	80	N	N	N	-	118	176	7.6	178	202	0.6	-	-
60	C B Hiremath	266567	66	M	3	InjActra.	78	136	88	N	N	N	-	167	289	9.4	232	197	0.8	-	-