

Role of Treadmill Test in Detection of Asymptomatic Coronary Artery Disease in Patients with Type 2 Diabetes Mellitus

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Abstract

Original Research Article

Background: Coronary artery disease (CAD) remains asymptomatic in many patients with Type 2 Diabetes Mellitus (T₂DM) making its diagnosis challenging. There is high incidence of silent myocardial ischemia in diabetic patients. This study was carried out with the aim of determining the prevalence of asymptomatic CAD in diabetic patients using treadmill test and study the relationship between duration of T₂DM, glycemic control and dyslipidemia with Treadmill Test (TMT) changes. **Method:** This observational study which included 75 patients was conducted at SAMC & PGI, Indore. All the patients above the age of 18 years who had been diagnosed with T₂DM and were found to have no clinical, electrocardiographic or echocardiographic evidence of CAD were included in the study. **Results:** Fifty-seven (76%) of the patients were men and 18 (24%) were women with mean age of study population being 53.27 ± 9.22 years. Twenty patients were found to have positive TMT, most of them belonging to the age group of 48-57 years. The prevalence of asymptomatic CAD in diabetic patients was found to be 26.66% in our study. Asymptomatic CAD was significantly associated with the duration of diabetes, glycemic control and deranged lipid profile. **Conclusion:** T₂DM is an important independent and modifiable risk factor for development of the CAD. TMT is a safe, reliable and non-invasive tool for the timely diagnosis of asymptomatic CAD in diabetic patients. A routine TMT screening for inducible ischemia should be performed in diabetic patients with longer duration of disease, deranged lipid profile and poor glycemic control. Early and aggressive screening of diabetic patients for the evidence of silent myocardial ischemia may prevent catastrophic cardiac events and decrease mortality.

Keywords: Coronary Artery Disease; Type 2 Diabetes Mellitus; Complications; Silent Myocardial Ischemia; Treadmill Test.

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INTRODUCTION

Diabetes mellitus is a metabolic entity characterised by raised blood sugar levels resulting from defect in insulin release, action of insulin or both. It may be accompanied by other biochemical derangements and the presence of progressive diabetic tissue damage with micro and macrovascular complications [1]. Diabetes mellitus is accepted as a worldwide epidemic with an estimated increasing prevalence from 2.8% in 2000 to 4.4% by 2030 [2]. It is the most common endocrine disease affecting mankind. The incidence of this disease continues to be on the rise all over the world specially in our country. India is known as “the diabetic capital of the world”. It is assessed to have 77 million people influenced by it, with every 6th diabetic person in the world being an Indian. As per International Diabetes Federation’s

estimation 134 million Indians will have diabetes by the end of the 2045. Cardiovascular diseases are more prevalent in diabetics and is the foremost cause of deaths in patients with type 2 diabetes and is often asymptomatic because of silent myocardial ischemia. The prevalence of CAD in our country earlier varied from 15-65/1000 population, but now it has increased to about 80-120/1000, making it substantial cause of mortality and morbidity [3].

Coronary artery disease (CAD) is multifactorial in etiology and has several important risk factors, out of which diabetes is considered an important modifiable risk factor. CAD manifests itself silently and prematurely in diabetic patients. It has been observed in the Framingham heart study that there is a poor prognosis of cardiac disease in diabetics. Mortality

related to cardiovascular disease is doubled in diabetic men and quadrupled in diabetic women over that in their non-diabetic counter parts [4]. The association between diabetes and asymptomatic coronary artery disease has been accredited to Autonomic Neuropathy [5]. CAD can be asymptomatic in diabetes and may present itself with sudden cardiac arrest, myocardial infarction, silent myocardial ischemia, arrhythmia, or heart failure. Prompt and early recognition of asymptomatic CAD in diabetes mellitus type 2 patients can prevent catastrophic cardiac events. However, resting ECG and thorough clinical examination may fail to diagnose coronary artery disease. Hence sophisticated cardiovascular non-invasive tests should be proposed for recognition of CAD in these high-risk patients at an early stage.

Exercise electrocardiograph can identify most of the patients likely to have ischaemia during their daily activities and remain the most important screening test for CAD [5]. The aim of this study was to determine the prevalence of asymptomatic coronary artery disease in patients of type 2 diabetes mellitus using Treadmill Test (TMT) and study the relationship between duration of T2DM, HbA_{1c} levels and dyslipidemia with TMT changes.

MATERIAL AND METHODS

This observational study was carried out in the Dept. of Medicine between October 2018 to May 2020. Patients ranging from age of 18 to 70 years seeking medical attention, who had been diagnosed with Type-2 Diabetes Mellitus using ADA criteria (HbA_{1c} >6.5%, FBS > 125 mg/dl, PPBS > 200 mg/dl) undergoing Treadmill Test were included in this study after obtaining a written-informed consent. The exclusion criteria of the study were as follows:

1. Individuals with pre-existing congenital heart diseases, Coronary Artery Disease, Valvular Heart disease, Uncontrolled Hypertension, and unstable angina.
2. Patients with physical disabilities including severe osteoarthritis and others who could not carry out the Treadmill test.
3. Anemic patients (Hb < 8 gm%)
4. Patients who refused to give written-informed consent for the study.

All the patients included in the study were interviewed about relevant medical history which included duration of diabetes, treatment history and addictions. A general physical examination was carried out, and blood samples were sent for laboratory investigations which included Complete Blood Count, Fasting Blood Sugar, Post Prandial Blood Sugar, Glycosylated Hemoglobin (HbA_{1c}), and Fasting Lipid Profile. A baseline 12-lead ECG was done and 2D Echocardiography was done using Phillips™ iE33 machine. All the patients were then subjected to a Treadmill Test (TMT) performed on the GE™ MAC

5500 Machine using Bruce protocol. Exercise test was terminated in all patients following the achievement of target pulse rate (220 - Age in years) or an unusual ischemic response which was characterized as development of 0.1 mV (1 mm) of J point depression with a comparatively flat ST segment slope (<1 mV/sec), depressed ≥ 0.10 mV 60 to 80 msec after the J point in three successive beats with a stable baseline. Exercise test was also stopped if patient developed shortness of breath, fatigue, or angina.

Statistical Analysis

The categorical or dichotomous variables were expressed as absolute values and percentages and were compared with Pearson χ^2 test. The continuous variables with a normal distribution were described as the mean (SD). Variables that did not present a Gaussian distribution were compared with the Mann-Whitney U test. The correlation between two quantitative variables was carried out by using Karl Pearson's/ Spearman's coefficient of correlation. A p value less than 0.05 was considered statistically significant.

RESULTS:

In the present study, 75 patients of Type 2 Diabetes Mellitus without any clinical, electrocardiographic and echocardiographic evidence of coronary artery disease were studied. Fifty-seven (76%) of the 75 subjects were men and 18 (24%) were women (Figure-1).

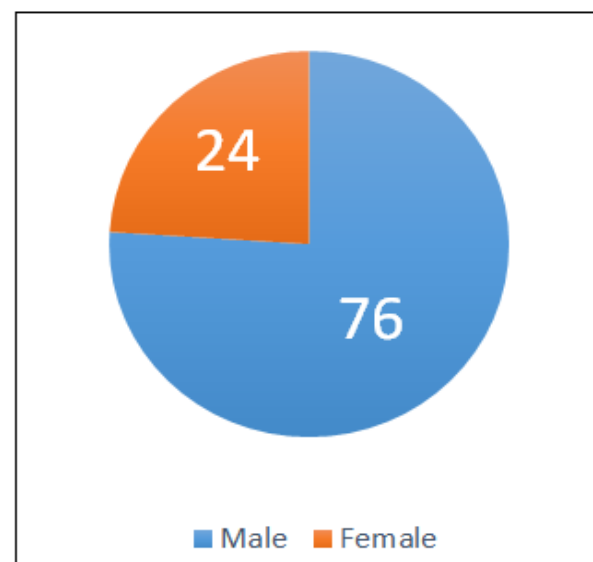


Fig-1: Gender distribution of study population

The mean age was 53.27 ± 9.22 years; with a range of 28 to 70 years. Most of the study subjects belonged to the age group of 48-57 years (Table-1).

Table-1: Age wise distribution of study population

Age	Frequency	Percentage (%)
28-37	4	5.3
38-47	13	17.3
48-57	31	41.3
Equal and above 58	27	36.0
Total	75	100

Duration of diabetes less than 5 years was found in 33 subjects (44%) (Table-2).

Table-2: Distribution of study population as per duration of diabetes mellitus

Duration of Diabetes	Male	Female	Total
< 5 years	26	7	33 (44%)
5-10 years	24	8	32 (42.6%)
>10 years	7	3	10 (13.3%)
Total	57	18	75 (100%)

The prevalence of TMT positivity in our study was 26.66% (20 patients, Figure-2) of which majority of subjects (65%) belonged to the age group of 58 years and above (Table-3).

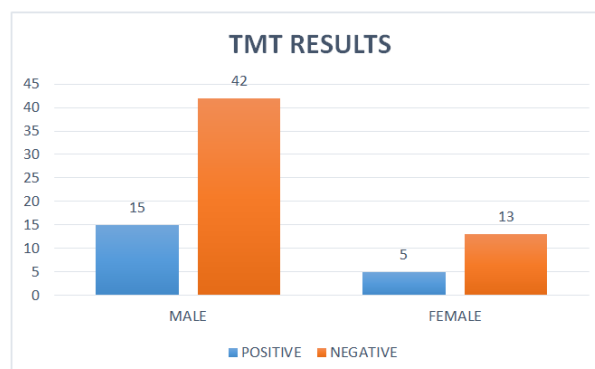


Fig-2: Gender distribution of TMT results in the study population

Table-3: Correlation between age and TMT results

Age	Treadmill Test (TMT)				Fisher's exact test p-value
	Negative		Positive		
	Frequency	Percentage	Frequency	Percentage	
28-37	4	7.3	0	0	0.004
38-47	13	23.6	0	0	
48-57	24	43.6	7	35.0	
≥ 58	14	25.5	13	65.0	
Total	55	100	20	100	

Correlation between duration of diabetes and TMT positivity showed that 65% study subjects had diabetes duration of 5 to 10 years (Table-4).

Table-4: Correlation between duration of diabetes and TMT results

Duration of Diabetes (years)	Treadmill Test (TMT)				Fisher's exact test p-value
	Negative		Positive		
	Frequency	Percentage	Frequency	Percentage	
<5	33	60.0	0	0	<0.0001
5-10	19	34.5	13	65.0	
>10	3	5.5	7	35.0	
Total	55	100	20	100	

The mean HbA1c of the cases with TMT positive result was 9.82% ± 1.35% as compared to 8.07% ± 1.34% in cases with TMT negative result which was statistically significant (p value <0.0001). The mean age of cases with positive TMT result was 60.05 years as compared to 50.80 years with negative

result which was statistically significant (p value <0.0001). The correlation between Fasting blood sugar (FBS), Post-prandial blood sugar (PPBS) levels, lipid profile (Total cholesterol, High density lipoprotein, Low density lipoprotein and Triglyceride levels) is described in Table-5.

Table-5: Correlation between age, glycemic control and lipid profile amongst diabetic patients with and without silent myocardial ischemia

Parameter	Group	Mean	SD	p-value
Age	Positive	60.05	5.02	<0.0001
	Negative	50.80	9.27	
FBS	Positive	191.75	53.53	0.001
	Negative	148.40	46.08	
PPBS	Positive	317.00	63.93	<0.0001
	Negative	222.73	81.33	
HbA1c	Positive	9.82	1.35	<0.0001
	Negative	8.07	1.34	

Parameter	Group	Mean	SD	p-value
	Negative	8.07	1.34	
Total Cholesterol	Positive	203.15	24.64	<0.0001
	Negative	170.35	44.04	
HDL	Positive	31.65	5.10	<0.0001
	Negative	41.36	10.16	
LDL	Positive	122.20	18.69	0.004
	Negative	103.20	35.10	
Triglycerides	Positive	247.85	74.09	<0.0001
	Negative	167.64	93.17	

DISCUSSION

Coronary Artery Disease (CAD) detection in asymptomatic Type 2 DM is often delayed. Silent CAD is an important cause of premature death of diabetic patients. The present study was aimed to detect the prevalence of asymptomatic CAD in the form of silent myocardial infarction in patients of Type 2 Diabetes Mellitus using Treadmill test (TMT). We included 57 men and 18 women as per the inclusion criteria. Out of the total 75 patients TMT positive result was found in 20 patients (26.66%) out of which 15 were males and 5 were females and 55 had TMT negative result. The prevalence of silent myocardial ischemia was found to be 26.66% in patients of Type 2 Diabetes Mellitus. Our findings correlate with other similar studies. Sharda M *et al.*, reported that prevalence of silent myocardial ischemia was 37.3% in patients of Type 2 DM [6]. In a similar study by Lavekar AS *et al.*, prevalence of silent myocardial ischemia in patients of type 2 DM was found to be 21.1% [7]. Similarly, Joshi *et al.*, [8] found out that 24% of patients with type 2 DM without previous history of CAD had positive TMT test. In the present study the mean age was 53.27 ± 9.22 years. The patient with a positive TMT test had a mean age of 60.05 ± 5.02 years as compared to 50.08 ± 9.27 years for negative TMT test, which was statistically significant (p value <0.0001). Similar results were reported by Sharda M. *et al.*, in which mean age of TMT Positive and TMT negative were 56.14 ± 7.71 years and 51.14 ± 9.59 respectively which was statistically significant [6]. In the study by Lavekar *et al.*, the mean age of TMT positive group (53.56 ± 7.41 years) was greater than that of TMT negative group (48.71 ± 8.72 years) with a statistically significant [7]. Thus, increasing age is an important risk factor for silent myocardial ischemia in diabetic patients. In our study of 75 patients of type 2 DM, 20 were TMT positive for inducible ischemia. 33 patients had diabetes for duration less than 5 years, none had a TMT positive test. 32 patients had duration of diabetes for 5 to 10 years out of which 13 were TMT positive 10 patients had duration of diabetes of more than 10 years out of which 7 were TMT positive. Our findings are similar to other studies in which duration of diabetes in TMT positive cases was significantly higher to those of a negative test (4.91 ± 2.51 years vs. 3.59 ± 2.13 year) [6]. Lavekar AS *et al.*, described that the duration of diabetes for TMT positive cases in their study was 6.23

± 4.01 years as compared to 3.95 ± 2.63 years for TMT negative cases [7]. Joshi *et al.*, reported in their study of 50 diabetic patients that the mean duration of diabetes for TMT positive cases was 13 ± 4 years as compared to 9 ± 5 years of TMT negative cases [8]. Higher level of HbA_{1c} indicates poor glycaemic control which has a significant influence on CAD. In this present study mean HbA_{1c} levels of TMT positive and negative cases were 9.82% and 8.07% respectively. Statistically significant p value <0.0001 was found in HbA_{1c} levels of both groups. In the study by Khanapure *et al.*, HbA_{1c} greater than 10% was found in 44% TMT positive cases and 45.5% TMT positive cases had HbA_{1c} of 8.9 to 9.9% [9]. We found 15 of 20 (75%) patients with TMT positive result and 30 of 55 patients (54.44%) with TMT negative result had dyslipidaemia. Among the asymptomatic T₂DM patients, total serum cholesterol > 200mg/dl, triglycerides > 150mg/dl, LDL levels > 100mg/dl, and HDL levels <40, had higher prevalence of positive TMT results. Similar results were observed in other studies which found dyslipidaemia was very common in type 2 diabetes and the most common abnormality noted is hypertriglyceridemia (serum TG levels more than 150 mg/dl), followed by Low HDL cholesterol levels (<40 mg/dl).

CONCLUSION

Type 2 Diabetes Mellitus is an important ailment and along with CAD it represents a serious threat to the modern society. CAD has a high prevalence in Asians. T₂DM is also an important independent and modifiable risk factor for development of the CAD. In our study with diabetic patients having no clinical, electrographic, and echocardiographic evidence of CAD, the prevalence of asymptomatic CAD was 26.66%. TMT is a safe, reliable and non-invasive tool for the timely diagnosis of asymptomatic CAD in diabetic patients. A routine TMT screening for inducible ischemia should be performed in diabetic patients with longer duration of disease, deranged lipid profile and poor glycemic control. Early and aggressive screening of diabetic patients for evidence of silent myocardial ischemia may prevent catastrophic cardiac events and decrease mortality.

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