Section: General Medicine

Original Research Article

UTILITY OF TREADMILL TEST IN DETECTING ASYMPTOMATIC CORONARY ARTERY DISEASE AND ITS ASSOCIATION WITH HBA1C LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder associated with both microvascular and macrovascular complications including coronary artery disease (CAD). CAD in diabetics often remains asymptomatic due to autonomic neuropathy, making its early detection challenging. Treadmill test (TMT) is a widely accessible non-invasive tool for detecting subclinical myocardial ischemia. This study aims to evaluate the utility of TMT in detecting asymptomatic CAD in T2DM patients and its correlation with HbA1c levels and diabetes duration.

Materials and Methods: A cross-sectional observational study of 80 asymptomatic T2DM patients aged 25–60 years was conducted in the department of general medicine of Adichunchungiri hospital and research centre. Clinical data including duration of diabetes, HbA1c levels and lifestyle risk factors were recorded. All patients underwent TMT using the modified Bruce protocol. A positive TMT was defined by standard ischemic ST segment depression criteria. Statistical analysis was done using SPSS v23.0 to determine the association of TMT results with HbA1c levels and diabetes duration.

Results: Among 80 participants majority were males(57.5%) and most common age group was 51–60 years (46.25%). TMT was positive in 31 (38.75%) patients. A significant association was found between longer diabetes duration and TMT positivity (p=0.0002). HbA1c levels ≥9.1% were more prevalent among TMT positive individuals (p=0.047). 80.6% of TMT positive patients had HbA1c level of more than 9% suggesting poor glycaemic control as a significant predictor of silent myocardial ischemia.

Conclusion: There was a significant correlation between elevated HbA1c levels andprolonged duration of T2DMwith TMT. Routine cardiovascular screening by TMT should be considered in asymptomatic T2DM patients particularly inthose with prolonged disease or poor glycaemic control.

Keywords: Type 2 Diabetes Mellitus, Coronary Artery Disease, HbA1c, Treadmill Test.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is characterized by chronic hyperglycemia resulting mainly from end organ resistance to insulin action. Globally, the burden of T2DM is risingand International Diabetes Federation estimated that the global prevalence of diabetes will increase from 2.8% in 2000 to 4.4% by 2030.[1] It is projected to affect over 366 million individuals worldwide by the year 2030. The implications diabetes mellitus are far reachingnot only due to the direct consequences of

hyperglycemia but more significantly due to the microvascular and macrovascular complications associated with chronic diabetes. Among these coronary artery disease (CAD) is one of the most serious and life-threatening manifestation of macrovascular involvement in T2DM.[2]

CAD in individuals with T2DM is not only more prevalent but also more likely to be asymptomatic or atypical in presentation due presence of diabetic autonomic neuropathy. This autonomic dysfunction attenuates the typical ischemic pain seen in non-diabetic individuals. This is one of the important causes of under-recognition of myocardial ischemia.[3] This is the cause of many patients with T2DM presenting with sudden cardiac death, acute myocardial infarction or advanced heart failure without prior symptoms. Numerous studies have demonstrated that the risk of cardiovascular events is substantially higher in diabetic individuals. Some studies suggest that diabetes alone confers a CAD risk equivalent to that of a prior myocardial infarction.[4]

Although routine clinical examination and resting electrocardiography (ECG) remain important in cardiovascular assessment their sensitivity in detecting occult CAD in asymptomatic diabetic patients is limited. Therefor there is growing interest in the application of non-invasive cardiovascular stress testing modalities to unmask subclinical ischemia. The Treadmill Test (TMT) or exercise electrocardiography is widely accessible and cost-effective.[5] It provides dynamic information on exercise tolerance, inducible ischemia and overall cardiovascular functional capacity. Advanced imaging techniques like myocardial perfusion imaging (MPI), coronary computed tomography angiography (CCTA) and stress echocardiographycan also be used for this purpose however their utility is limited by the cost as well as availability.TMT retains an important role in primary screening especially in resource-constrained settings.[6]

In recent years, glycated hemoglobin (HbA1c) has emerged not only as a diagnostic and monitoring tool for glycaemic control but also as a surrogate marker for cardiovascular risk. Elevated HbA1c levels reflect chronic glycaemic exposure. Chronic hyperglycemia (HbA1c above 7) contributes to endothelial dysfunction, inflammation, oxidative stress, and accelerated atherosclerosis. All these changes are responsible for pathogenesis of CAD. Several observational and cohort studies have shown a positive correlation between higher HbA1c levels and the incidence and severity of CAD.[7]

The interrelationship between increased HbA1c and silent ischemia has been analysed in various studies.[8] However controversies remain regarding the predictive power of HbA1c for occurrence of asymptomatic CAD. While some studies suggest a linear association between increasing HbA1c levels and positive TMT results others have found no such correlation. Furthermore the prevalence of positive TMT findings among asymptomatic T2DM patients varies significantly across populations. This variability may be secondary to factors such as age, duration of diabetes, lipid profiles and co-existing risk factors such as hypertension, obesity and smoking.[9]

In light of these considerations the current study aims to explore the clinical utility of the treadmill test in identifying asymptomatic coronary artery disease in patients with type 2 diabetes mellitus and to determine its association with duration of diabetes and glycaemic control.

MATERIALS AND METHODS

This observational cross-sectional study was conducted in the Department of General Medicine of Adichunchungiri hospital and research centre. The study included adult T2DM patients between the age group of 25 and 60 years. The diagnosis of Type 2 Diabetes Mellitus (T2DM) was done on the basis of American Diabetes Association (ADA) criteria (HbA1c ≥6.5%, fasting blood sugar >125 mg/dL, or postprandial blood sugar >200 mg/dL). 10

Patients were included only if they had a normal 12-lead electrocardiogram (ECG) and normal 2D echocardiography at baseline, and had no symptoms suggestive of coronary artery disease (CAD), thus meeting the definition of asymptomatic.Each patient underwent a detailed clinical assessment including history of diabetes duration, current anti-diabetic therapy and lifestyle risk factors such as tobacco or alcohol use. A general physical examination was done in all cases. It was followed by laboratory investigations including complete blood count (CBC), fasting blood sugar (FBS), postprandial blood sugar (PPBS) and glycosylated hemoglobin (HbA1c). Particular attention was given to precise estimation of HbA1c levels as this parameter was central to the study objective of assessing its association with coronary artery diseases in cases of T2DM.

All participants underwentbaseline 12-lead ECG and 2D echocardiography to rule out pre-existing significant ECG changes or presence of significant echocardiographic abnormalities. Subsequently, a treadmill stress test (TMT) was done using the Modified Bruce protocol. The test was terminated upon achieving the target heart rate (220 minus age in years), onset of significant symptoms (e.g., angina, dyspnea, fatigue) or the appearance of an ischemic response. A positive TMT result was defined 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 millisecond after the J pointin three successive beats with a stable baseline. The primary outcome was the correlation between TMT positivity (as a surrogate for asymptomatic CAD) and HbA1c levels. Secondary outcomes included

associations with duration of diabetes and TMT positivity.

Data was compiled using Microsoft Excel and analyzed using SSPS 23.0 software. The statistics includedmean and standard deviation for continuous variables and frequencies (percentage) for categorical variables. Student's t-test for independent samples was used to determine statistical significance of difference in the mean values of continuous variable between TMT positive and negative groups. Chi-square test was used to determine if the frequency distribution across the levels of categorical variables has any statistical association with TMT findings

Inclusion Criteria

1. Patients aged between 25 and 60 years.
2. Ready to give consent to be part of study.
3. Diagnosed with Type 2 Diabetes Mellitus (T2DM) as per ADA criteria (HbA1c ≥6.5%, Fasting Blood Sugar >125 mg/dL, Postprandial Blood Sugar >200 mg/dL).
4. Asymptomatic for coronary artery disease (CAD).
5. Normal 12-lead ECG findings.
6. Normal 2D Echocardiography findings.

Exclusion Criteria

1. Known congenital heart disease.
2. Established CAD, valvular heart disease, or unstable angina.
3. Uncontrolled hypertension.
4. Severe anemia (Hemoglobin <8 gm%).
5. Physical disability preventing performance of TMT (e.g., severe osteoarthritis).
6. Patients who refused written informed consent.

RESULTS

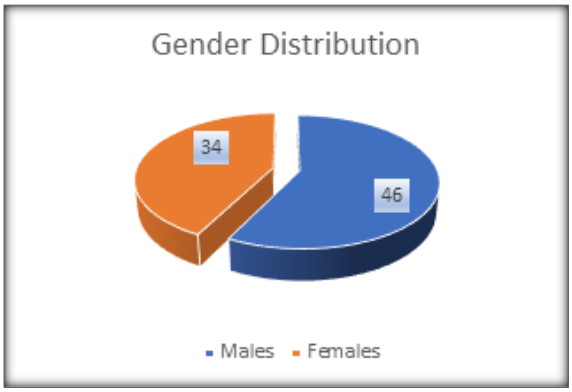

Figure 1: Gender Distribution of studied cases.

The analysis of the age distribution of the studied cases showed that the majority of patients belonged to the 51–60 years age group (46.25%) followed by the 41–50 years (38.75%). A smaller proportion of patients were in the 31–40 years (10.00%), while the least number of patients were in the 25–30 years group (5.00%). The mean age of the patients was 55.01±7.952 years (Table 1).

Table 1: Mean age of the studied cases

Age Group (Years)	Number of Patients	Percentage (%)
25–30	4	5.00%
31–40	8	10.00%
41–50	31	38.75%
51–60	37	46.25%
Total	80	100.00%
Mean Age = 55.01 +/-7.952.		

The analysis of the duration of disease among the studied cases showed that the highest proportion of patients had a disease duration of less than 5 years (45.00%) followed closely by those with a duration between 5 to 10 years (42.50%). A smaller group of patients had been living with the disease for more than 10 years (12.50%) (Table 2).

Table 2: Duration of T2DM in studied cases

Duration of disease (in years)	No of patients	Percentage%
<5	36	45.00%
5- 10	34	42.50%
>10	10	12.50%
Total	80	100.00%

The analysis of HbA1c levels among the studied cases showed that the highest proportion of patients had HbA1c values in the range of 9.1–10.0% (35.00%), followed by those in the 8.1–9.0% range (27.50%) and more than 10.0% (20.00%). A smaller proportion of patients had HbA1c levels between 7.0–8.0% (12.50%), while the least number of patients had values below 7.0% (5.00%) (Table 3).

Table 3: HbA1c Levels in Studied cases

HbA1c Range (%)	Number of Patients (n = 80)	Percentage (%)
< 7.0	4	5.00%
7.0 – 8.0	10	12.50%
8.1 – 9.0	22	27.50%
9.1 – 10.0	28	35.00%

> 10.0	16	20.00%
Total	80	100.00%

The analysis of disease duration in relation to TMT outcomes showed that among TMT positive patients, the majority had a disease duration of 5–10 years (21.25%), followed by those with duration more than 10 years (10.00%), and less than 5 years (7.50%). In contrast, among TMT negative patients, the highest proportion had a disease duration of less than 5 years (37.50%), followed by 5–10 years (21.25%), while the least had disease duration of more than 10 years (2.50%). A higher occurrence of TMT positivity was seen in patients with longer disease duration as compared to those with lesser duration of diabetes and the difference was found to be statistically significant (P=0.0002) (Table 4).

Table 4: Duration of T2DM and its correlation with TMT results

Duration of Disease (in years)	TMT Positive (n = 31)	Percentage (%)	TMT Negative (n = 49)	Percentage (%)
< 5 years	6	7.50%	30	37.50%
5 – 10 years	17	21.25%	17	21.25%
> 10 years	8	10.00%	2	2.50%
Total	31	38.75%	49	61.25%
P= 0. 000278 (Significant)				

The analysis of HbA1c levels in relation to TMT outcomes showed that among TMT positive patients, the majority had HbA1c levels between 9.1–10.0% (20.00%), followed by >10.0% (11.25%) and 8.1–9.0% (5.00%), while lower proportions were observed in the 7.0–8.0% (1.25%) and <7.0% (1.25%) groups. In contrast, TMT negative patients most commonly had HbA1c values in the 8.1–9.0% range (22.50%), followed by 9.1–10.0% (15.00%), 7.0–8.0% (11.25%), >10.0% (7.50%), and <7.0% (5.00%). The difference between the groups was statistically significant (P = 0.047) (Table 5).

Table 5: HbA1c levels and its correlation with TMT results

HbA1c Range (%)	TMT Positive (n = 31)	Percentage (%)	TMT Negative (n = 49)	Percentage (%)
< 7.0	1	1.25%	4	5.00%
7.0 – 8.0	1	1.25%	9	11.25%
8.1 – 9.0	4	5.00%	18	22.50%
9.1 – 10.0	16	20.00%	12	15.00%
> 10.0	9	11.25%	6	7.50%
Total	31	38.75%	49	61.25%
P = 0.047 (Significant)				

DISCUSSION

This study explored the correlation between treadmill test (TMT) positivity and duration of diabetes as well as glycaemic control in asymptomatic patients with type 2 diabetes mellitus (T2DM). Many similar studiessupport the utility of non-invasive stress testing in identifying subclinical coronary artery disease (CAD) in diabetic patients. The first important observation from our results was the demographic distribution of the study population where the majority of participants were in the 51–60 years age group and males comprised 57.5% of the cohort. This aligns with observations made by Janand-Delenne et al who reported a similar age and gender distribution in their study of silent myocardial ischemia among asymptomatic diabetic patients.[11] In this study the authors reported thatsilent myocardial ischemia with significant lesions occurred in 20.9% of type 2 diabetic male patients who were totally asymptomatic for CAD. Based on these findings the authors recommended routine screening for patients in whom the duration of type 2 diabetes is >10 years or even less when more than one cardiovascular risk factor was present. Similar demographics in cases of silent ischemia in diabetics has also been reported by Hernandez et al,[12] and Dale AC et al.[13]

The second notable result from our study was the analysis of diabetes duration where patients with a disease duration of more than 10 years had a significantly higher rate of TMT positivity (8 out of 10) compared to those with a shorter duration. Similar positive correlation between diabetes duration and TMT positivity had also been reported by Valensi et al who showed that the risk of asymptomatic ischemia significantly increased with longer diabetes duration.[14] The authors proposed that in long standing T2DM cases cumulative glycaemic damage, endothelial dysfunction and autonomic neuropathy is responsible for development of asymptomatic ischemia. In this study the main predictive factors of silent myocardial infarction were reported to be hypertension, history of cardiovascular diseases and diabetes duration. Similar findings were reported by Wackers FJ et al who reported that the strongest predictors for silent ischemia in cases of diabetes were male sex and duration of diabetes.[15] These observations underline the progressive nature of atherosclerosis in chronic diabetes and support the hypothesis that prolonged exposure to hyperglycemia accelerates coronary artery disease

even in asymptomatic individuals. Similar positive correlation between duration of diabetes and myocardial ischemia has also been reported by the authors such as Baviera M et al,[16] and Nagrani S et al.[17]

In our study there was a significant positive correlation between poor glycaemic control and TMT positivity suggestive of silent myocardial ischemia. In this study out of 31 patients with TMT positivity 25 had a HbA1c level above 9.This distribution reflects a direct and significant correlation between glycaemic control and myocardial ischemia. In a study by Stratton et al a linear relationship between HbA1c and cardiovascular events was established.[18] The study found that the incidence of clinical complications was significantly associated with severity of hyperglycaemia. Each 1% reduction in updated mean HbA(1c) was associated with reductions in risk of 21% for any end point related to diabetes including death related to diabetes, myocardial infarction and microvascular complications. Similarly, Selvin et al conducted a meta-analysis in which it was found that elevated HbA1c levels were significantly associated with increased incidence of coronary heart disease.[19] These results substantiate the importance of strict glycaemic control in decreasing cardiovascular risk even in the absence of overt symptoms. Similar correlation between glycaemic control and myocardial ischemia has also been reported by authors such as Ghaffari S et al.[20]

CONCLUSION

There is a significant correlation between elevated HbA1c levels and positive treadmill test results. This suggests that there is an increased risk of asymptomatic coronary artery disease in poorly controlled Type 2 diabetes mellitus patients. Moreover, a longer duration of diabetes was also significantly associated with TMT positivity. These findings underscore the importance of stringent glycaemic control and routine cardiovascular screening even in asymptomatic diabetic individuals particularly in long standing cases as well as those having suboptimal glycaemic control.

Conflict of Interest: None.

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