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STUDY OF TREADMILL TEST IN DETECTING ASYMPTOMATIC MYOCARDIAL ISCHEMIA AMONG TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

INTRODUCTION: Diabetes Mellitus(DM) is a major risk factor for cardiovascular diseases, including ischemic heart disease (IHD), and significantly increases the risk of cardiovascular mortality and morbidity,compared to non-diabetics. Early detection of Asymtomatic (Silent) myocardial ischemia in diabetics,may prevent cardiovascular morbidity and mortality with timely intervention.Non-invasive tests like the Treadmill Test are cost-effective, widely available, and useful for early detection of coronary artery disease in high-risk patients.

AIM: To assess the prevalence and clinical predictors of silent myocardial ischemia in patients with Type 2 Diabetes Mellitus using Treadmill test. **METHODOLOGY:**This was a cross-sectional study conducted in the Department of Medicine, SMS Hospital, Jaipur. The study took place from April 2023 for a duration of one year, or until the required sample size was achieved, with an additional two months allocated for data compilation and analysis.**RESULT:**In this study, factors like older age, longer duration of diabetes, higher BMI, elevated HbA1c, cholesterol, and triglycerides were significantly associated with positive TMT results, indicating increased cardiovascular risk. Additionally, microalbuminuria and macroalbuminuria were strongly linked to inducible ischemia, highlighting their role in CAD risk.**CONCLUSION:**In conclusion, TMT is an effective screening tool for early detection of silent myocardial ischemia in T2DM patients, aiding in the identification of those at risk for CAD.

Keywords: myocardial ischemia, Treadmill test, CAD.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder marked by persistent hyperglycemia, resulting from impaired insulin secretion or resistance, and is a growing global public health issue, with an estimated 415 million adults affected in 2015. Chronic hyperglycemia, along with other metabolic abnormalities, leads to severe complications, including microvascular (retinopathy, nephropathy, neuropathy) and macrovascular issues, significantly increasing the risk of cardiovascular diseases[1]. Diabetes mellitus is a major risk factor for cardiovascular diseases, including ischemic heart disease (IHD), and significantly increases the risk of mortality and morbidity, with diabetic patients having a higher risk of heart-related complications compared

to non-diabetics. Both Type 1 and Type 2 diabetes contribute to an elevated risk of IHD, with Type 2 diabetes often accompanied by additional risk factors like hypertension and dyslipidemia, exacerbating cardiovascular risks[2]. Diabetes determines a pathophysiological continuum, characterized by a state of longstanding insulin resistance with a compensatory hyperinsulinemia. Initially, the hyperglycaemia remains under the threshold for the diagnosis of Diabetes Mellitus and it describes impaired glucose tolerance. Glucose metabolism impairment and endothelial dysfunction, mediated by oxidative stress and inflammation, are the main substrates of coronary atherosclerosis in diabetes mellitus[3]. A complex network of signaling pathways is involved in the multistage pathological condition leading to atherosclerosis. Imbalanced lipid metabolism and immune response lead to chronic inflammation of the arterial wall, with growth of atherosclerotic plaque[4-5]. In patients with type 2 diabetes mellitus (T2DM), coronary artery disease (CAD) is often diagnosed at an advanced stage with extensive atherosclerosis, and asymptomatic CAD carries a higher cardiac mortality risk. While routine screening for asymptomatic CAD in all T2DM patients is debated, targeted screening for high-risk individuals can guide treatment decisions, including lifestyle modifications, glycemic control, and the use of medications like β-blockers or ACE inhibitors. Identifying severe CAD through screening may also help determine the need for revascularization or anti-ischemia therapy[6]. It is generally accepted that the incidence of both asymptomatic and symptomatic coronary artery disease is high in diabetic patients. Coronary artery disease in diabetics is often symptomless due to occurrence of silent myocardial ischemia[7]. Non-invasive tests like the Treadmill Test are cost-effective, widely available, and useful for early detection of coronary artery disease in high-risk patients, complementing other diagnostic tools and enabling timely intervention[8].

AIM

To assess the prevalence and clinical predictors of silent myocardial ischemia in patients with Type 2 Diabetes Mellitus using Treadmill test.

METHODOLOGY

This was a cross-sectional study conducted in the Department of Medicine, SMS Hospital, Jaipur. The study took place from April 2023 for a duration of one year, or until the required sample size was achieved, with an additional two months allocated for data compilation and analysis. Informed and written consent was obtained from all patients before the commencement of the study.The inclusion criteria for the study included subjects diagnosed with Type 2 Diabetes Mellitus according to the American Diabetes Association (ADA) criteria, aged ≥30 years, and with no signs or symptoms of coronary artery disease (CAD). Exclusion criteria included patients who were pregnant, hemodynamically unstable, or had a history of angina pectoris, acute coronary syndrome, congenital heart disease, abnormal baseline ECG, severe valvular heart disease, any form of cardiomyopathy, heart failure, or severe hypertension (>200/110 mmHg). Additionally, individuals with a history of myocardial infarction, cardiovascular disease (CVD), or coronary revascularization, as well as those unwilling to provide consent, were also excluded from the study.

RESULT

Table 1:Baseline characteristics of study subjects (n=105)

Variables	Mean	SD
Age (years)	58.01	9.67
Duration of Diabetes Mellitus (years)	9.17	5.38
BMI (kg/m^2)	26.75	3.68
Total Cholesterol (mg/dl)	188.7	35.77
Triglycerides (mg/dl)	153.90	37.60
HDL (mg/dl)	49.12	9.64
LDL (mg/dl)	106.46	26.70
HbA1c (%)	8.50	1.22
FBS (mg/dl)	159.1	23.65
BUN (mg/dl)	12.69	3.81
Creatinine (mg/dl)	1.00	.22

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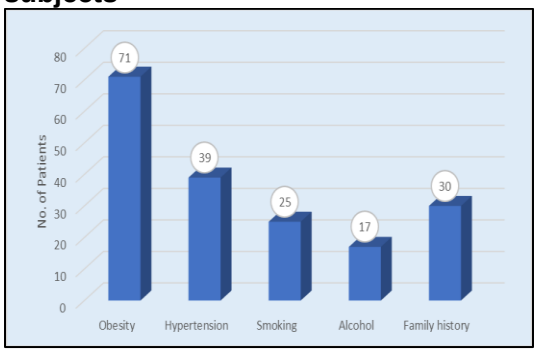
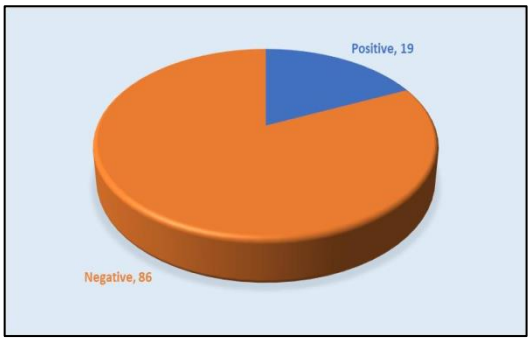
The 105 study participants are middle-aged (average age 58) with poor glucose control (mean HbA1c 8.50%) and signs of dyslipidemia (elevated triglycerides and LDL). While overweight (mean BMI 26.75 kg/m²), kidney function is stable, and overall cholesterol levels are within acceptable ranges.

Graph:Risk factors for coronary artery disease and Treadmill test-positive and negative subjects





Obesity (67.61%) is the most prevalent risk factor for CAD in the study population, followed by hypertension (37.14%) and a family history of CAD (28.57%). Smoking (23.80%) and alcohol use (16.19%) also contribute to the overall risk profile.Among the 105 study subjects, 19 individuals (18.1%) tested positive on the treadmill test (TMT), while 86 individuals (81.9%) tested negative.

Table 2:Comparison of age between treadmill test-positive and negative subjects

	TMT Positive (n=19) Mean ± SD	**TMT Negative (n=86) Mean ± SD**	**P value**
Age (Years)	62.26± 8.0	57.08 ± 9.80	<0.05
Duration of Diabetes yr	12.6± 4.53	8.40± 5.2	
BMI kg/m2	29.57 ±3.90	26.1 ± 3.34	
HBA1C	9.7 ± 1.01	8.22 ± 1.08	

TMT-positive subjects had a longer diabetes duration, older age, higher BMI, and poorer blood glucose control compared to TMT-negative subjects, indicating a potential link between these factors and increased cardiac risk. Specifically, a longer diabetes duration, higher BMI, and poorer HbA1c levels were associated with a higher likelihood of positive treadmill test results, suggesting greater cardiovascular risk.

Table 3:Association between TMT and Duration of DM (n=105)

Duration of DM	**TMT Positive(n=19)**	**TMT Negative (n=86)**	**Total (n=105)**
Less than 5 years	1(4.54%)	21 (95.45%)	22
5-9 Years	4(9.75%)	37(90.25%)	41
10-15 Years	9(29.03%)	22(70.97%)	31
More than 15	5(45.45%)	6(54.55%)	11
P value	<0.05		

A significant association was found between longer diabetes duration and positive treadmill test (TMT) results, with the likelihood of a positive TMT increasing as the duration of diabetes extended. The chi-square test ($p<0.05$) confirmed this relationship, suggesting that prolonged diabetes may elevate cardiovascular risk.

Table 4:Association between TMT and BMI (n=105)

BMI	TMT Positive(n=19)	TMT Negative (n=86)	Total
Underweight (<18.5 kg/m2)	0	1(100%)	1
Normal Weight (18.5–22.9 kg/m2)	0	12 (100%)	12
Over weight (>23 kg/m2)	2 (9.5)	19(90.5)	21
Obese (>25kg/m2)	17(23.9)	54 (76.1)	71
P-value	<0.05		

A significant association was found between higher BMI and positive treadmill test (TMT) results, with 23.9% of obese subjects showing positive TMT results, as confirmed by a chi-square test ($p<0.05$).

Table 5:Association between TMT and HbA1c (n=105)

HbA1c	TMT Positive(n=19)	TMT Negative (n=86)	Total	P-value
6.5-8 %	0	38(100%)	38	<0.05
8-10 %	12(23%)	40(77%)	52	
>10%	7(46.7%)	8(53.3%)	15	

A significant association was found between higher HbA1c levels and positive treadmill test (TMT) results, with 46.7% of subjects with HbA1c >10% testing positive, indicating a link between poor glucose control and increased cardiovascular risk ($p<0.05$).

Table 6:FBS between treadmill test-positive and negative subjects

	TMT Positive (n=19) Mean ± SD	TMT Negative (n=86) Mean ± SD	P-
FBS, mg/dl	176.52± 13.4	155.34 ± 23.75	<0.05
Total Cholesterol, mg/dl	214.8± 33.91	183 ± 33.71	<0.05
LDL, mg/dl	123.07± 26.7	102.7 ± 25.4	<0.05
Triglycerides, mg/dl	181.15 ± 47.02	147.88 ± 32.54	<0.05
Creatinine, mg/dl	1.11 ±.28	.98± .20	<0.05
HDL, mg/dl	48.43 ± 8.08	49.27± 9.99	0.73

TMT-positive subjects had significantly higher mean levels of fasting blood sugar, total cholesterol, LDL cholesterol, and creatinine, suggesting a link between these factors and increased cardiovascular risk. However, no significant difference was observed in HDL cholesterol levels between TMT-positive and TMT-negative subjects.

Table 7: Association between TMT and Microalbuminuria (n=105)

Microalbuminuria	TMT Positive(n=19)	TMT Negative (n=86)	Total	P-value
Yes	15(31.9%)	32(68.1%)	47	<0.05
No	4(6.9%)	54(93.1%)	58	

The presence of microalbuminuria was significantly associated with positive treadmill test (TMT) results, with 31.9% of those with microalbuminuria testing positive, suggesting a link between kidney function and cardiovascular risk ($p<0.05$).

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Table 8: Positive predictive value (PPV) of TMT positive patients

TMT	CAG	
Positive (n=19)	16	3
Negative (n=86)	N/A	N/A
Total (n=105)		
Sensitivity	N/A	
Specificity	N/A	
PPV	84.21%	
NPV	N/A	

The positive predictive value (PPV) of the treadmill test (TMT) was 84.21%, indicating an 84.21% chance that a positive TMT result reflects the actual condition, as no coronary angiography was performed for negative TMT results.

DISCUSSION

Coronary artery disease (CAD) has a multifactorial origin with several significant risk factors, one of which is diabetes—a modifiable factor. Early detection of asymptomatic CAD in patients with type 2 diabetes (T2DM) can help prevent severe cardiac events.To achieve this, advanced non-invasive cardiovascular tests are essential for the early identification of CAD in diabetic patients[2] Risk factors for CAD such as obesity, hypertension, history of smoking, alcohol and family history showed a significant correlation with TMT positivity. Among the clinical predictors a significant correlation with TMT positivity was seen with increased age, longer duration of T2DM, higher BMI, higher levels of HbA1C, triglycerides, LDL, creatinine and presence of microalbuminuria.

Among the 105 diabetic patients without any prior indication of coronary artery disease (CAD), 19 individuals (18.1%) tested positive on the treadmill test (TMT), indicating potential ischemia. These results align with findings from other studies Handargal NH et al.[9] 2021 reported that 38.9% of their patients had positive TMT results, while 61.1% tested negative.

In our study, the mean age of participants was 58.01 years, TMT-positive subjects had a significantly higher mean age (62.26 ± 8.0 years) compared to TMT-negative subjects (57.08 ± 9.80 years), with a p-value less than 0.05, indicating that older individuals were more likely to have positive TMT results. In comparison, Sharma CS et al[10] 2020 reported a mean age of 47.89 years, while Kim MK et al.[7] 2011 found a mean age of 57.2 years in their study. Overall, the age distribution in our study aligns with previous research, though the mean age in our study was slightly higher than in some others.

We also found that TMT-positive subjects had a significantly longer mean duration of diabetes (more than 12 years) compared to TMT-negative cases. Our results were in concordance with the study conducted by Handargal NH et al.[9] (2021) found a significant difference in mean diabetes duration between TMT-documented silent myocardial infarction (SMI) cases and non-cases ($P < 0.001$).

We also found that obesity was the most prevalent risk factor, affecting 67.61% of participants among them TMT-positive subjects had a significantly higher mean BMI of 29.57 ± 3.90 kg/m² compared to 26.1 ± 3.34 kg/m² in TMT-negative subjects ($p < 0.05$). This suggests that a higher BMI is associated with an increased likelihood of positive TMT results, indicating a potential link between elevated BMI and cardiac stress during the treadmill test. Supporting this, studies have shown that increased BMI is a significant risk factor for cardiovascular conditions. For instance, research by Aneni EC et al.[11] 2014 2015) indicated that higher BMI is linked to adverse outcomes on exercise stress tests, reinforcing the association between elevated BMI and cardiac stress.

In our study analysis revealed a significant difference in HbA1c levels between TMTpositive and TMT-negative subjects. TMT-positive individuals had a higher mean HbA1c of 9.7 ± 1.01%, compared to 8.22 ± 1.08% in TMT-negative individuals ($p < 0.05$). This indicates that higher HbA1c levels, which reflect poorer long-term blood glucose control, are associated with a greater

likelihood of positive TMT results and increased cardiovascular risk. Similarly, the research by Chen J et al.[12] 2023 demonstrated that higher HbA1c levels are associated with a higher incidence of cardiovascular disease in diabetic patients. These findings suggest that poor blood glucose control, as indicated by elevated HbA1c levels, is a significant risk factor for cardiovascular issues, as evidenced by the increased likelihood of positive results on the treadmill test.

In our study, we found that higher TC, LDL, and TG levels were significantly associated with silent ischemia. Specifically, TMTpositive subjects had elevated total cholesterol (214.8 ± 33.91 mg/dl vs. 183 ± 33.71 mg/dl), LDL cholesterol (123.07 ± 26.7 mg/dl vs. 102.7 ± 25.4 mg/dl), and triglycerides (181.15 ± 47.02 mg/dl vs. 147.88 ± 32.54 mg/dl) compared to TMT-negative subjects, all with p-values < 0.05. However, no significant difference in HDL cholesterol levels was observed (48.43 ± 8.08 mg/dl vs. 49.27 ± 9.99 mg/dl, p = 0.73), suggesting that while total cholesterol, LDL, and triglycerides are linked to increased cardiovascular risk, HDL may not be a strong indicator in this setting.

Microalbuminuria and macroalbuminuria are well-recognized risk factors for coronary artery disease (CAD), particularly in individuals with Albuminuria signifies endothelial dysfunction and vascular damage, which are critical contributors to the development of atherosclerosis. Our study confirms the same and resulted into sensationally high association of macroalbuminuria with increased risk of inducible ischemia. Lavekar AS et al. [13] 2013 also found association of macroalbuminuria with CAD. Several studies have confirmed the strong association between macroalbuminuria and inducible ischemia, indicating that patients with significant albumin leakage are at a much greater risk of developing serious cardiovascular complications[14].

CONCLUSION

Our findings demonstrate that TMT is a valuable tool in identifying asymptomatic CAD in T2DM patients. The study revealed a significant association between positive TMT results and several clinical indicators, including older age, longer duration of diabetes, higher body mass index (BMI), elevated HbA1c, fasting blood sugar (FBS), total cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and creatinine levels. These factors were more pronounced in TMT-positive subjects compared to those with negative results. Significantly, 84.21% of TMT-positive patients had confirmed significant blockages on CAG, emphasizing TMT's utility in identifying patients at higher risk for CAD. In conclusion, TMT serves as an effective screening tool for early detection of silent myocardial ischemia in T2DM patients, helping to identify those at risk for CAD and potentially prevent serious cardiac events. This highlights the importance of incorporating TMT in routine cardiovascular risk assessment for patients with Type 2 Diabetes Mellitus.

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