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EXPLORING SILENT MYOCARDIAL INFARCTION AND ITS ASSOCIATIONS IN TYPE 2 DIABETIC PATIENTS: A CROSS-SECTIONAL STUDY IN A HOSPITAL SETTING.

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ABSTRACT.

Introduction: Insulin resistance or insufficient insulin production in the body causes diabetes mellitus type 2, which primarily affects adults. Numerous micro and macrovascular issues are linked to long-term diabetes mellitus type 2. The objective of this study was to determine the incidence of silent MI in unaffected individuals with diabetes mellitus through the utilization of exercise treadmill testing.

Materials and Methods: The Darbhanga Medical College & Hospital Department of Medicine conducted this cross-sectional observational study. The study included 120 asymptomatic type 2 Diabetes Mellitus patients with normal resting electrocardiograms and no coronary artery disease. Patients with myocardial infarction (MI), heart failure, angina pectoris, or other chronic illnesses were excluded from the study. The treadmill test (TMT) utilizing the "Bruce protocol" and CASE/T2100 sr number GE MAC revealed silent myocardial infarction.

Results: 11.8% had silent MI (positive TMT). TMT positive was substantially linked to advanced age, diabetes for more than ten years, dyslipidemia, and an HbA1c of more than 10%. In comparison to TMT-negative patients, TMT-positive patients were shown to have considerably higher levels of total cholesterol, LDL, and triglycerides. TMT-positive individuals had considerably lower HDL levels than TMT-negative patients.

Conclusion: A considerable fraction of individuals with T2DM had asymptomatic CAD or silent myocardial infarction (11.8%). Silent MI was more common in diabetics who were obese, dyslipidemic, older, and had high HbA1c. TMT may be a straightforward, non-invasive method for spotting silent MI early on.

Recommendations: Treadmill testing (TMT) should be used to screen asymptomatic type 2 diabetics for silent myocardial infarction, especially those who are older, obese, have had diabetes for more than ten years, or have dyslipidemia and high HbA1c levels. TMT can identify silent MI in this population non-invasively.

Keywords: *Asymptomatic Coronary artery disease; Silent ischaemia; Exercise stress test; Diabetes; TMT*
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INTRODUCTION.

Diabetes Mellitus (DM) is a metabolic pathology distinguished by hyperglycemia, denoting elevated levels of glucose in the bloodstream. Type 2 diabetes, the prevailing manifestation of this pathological state, primarily presents itself in the adult population and is characterized by the notable presence of insulin resistance or insufficient insulin secretion. Consequently, this metabolic disorder results in diminished utilization of glucose and heightened glucose production. According to the World Health Organization's report in 2015, the occurrence of diabetes in India was assessed to be 69.2 million individuals [1]. This figure indicates a significant rise in the incidence of diabetes, particularly in developing nations. In the Indian population, there was a notable surge in the prevalence of diabetes, with a substantial increase of 72.3% observed over 14 years, specifically from 1989 to 2004 [2].

Diabetes mellitus is intricately linked to a plethora of both acute and chronic complications. The acute complications include Diabetic ketoacidosis (DKA), Hyperosmolar hyperglycemic nonketotic coma (HHNK), and hypoglycemia. Chronic complications can be categorized into two primary classifications: microvascular complications, which are exclusive to individuals diagnosed with diabetes, and macrovascular complications, which bear resemblance to those encountered in individuals without diabetes but exhibit a higher incidence rate in individuals with diabetes. Microvascular complications encompass conditions such as Retinopathy, Neuropathy, and Nephropathy, which are directly associated with diabetes. These complications primarily affect small blood vessels and tissues in various parts of the body. On the other hand, macrovascular complications, including Peripheral Arterial Disease (PAD), Coronary Heart Disease (CHD), and Cerebrovascular Disease, are characterized by the involvement of larger blood vessels. While these

complications can also occur in non-diabetic individuals, they are more prevalent in individuals with diabetes.

Silent coronary disease, also known as asymptomatic coronary artery disease, is frequently encountered in individuals diagnosed with T2DM. The conventional risk factors linked to cardiovascular disease (CVD) in the setting of T2DM include hypertension, dyslipidemia, obesity, inadequate physical activity, suboptimal glycemic control, and tobacco use [3]. Nonconventional risk factors include hyperinsulinemia, insulin resistance, postprandial hyperglycemia, microalbuminuria, glucose variability, hematologic factors, inflammation, thrombogenic factors, vitamin deficiencies, and hyperhomocysteinemia among other factors [4].

Patients diagnosed with diabetes mellitus frequently exhibit an elevated prevalence of silent ischemia in comparison to individuals without diabetes mellitus. Hyperglycemia exerts a deleterious impact on the bioavailability of nitric oxide (NO) and exerts adverse effects on vascular function. The American Diabetes Association (ADA) recommends stress testing for diabetic patients who exhibit specific risk factors or symptoms [5]. Nevertheless, routine clinical examinations and resting ECGs may not invariably yield conclusive results in the detection of CAD, thereby necessitating the inclusion of exercise electrocardiograms as an indispensable component of screening protocols.

Physical exercise is widely recognized as a fundamental component of diabetes management, with patients frequently advised to partake in various forms of physical activity, including treadmill exercises. At present, there exists a dearth of evidence-based guidelines about the screening of asymptomatic diabetic individuals for CAD. Exercise treadmill testing, a widely investigated screening modality for CAD has demonstrated its efficacy even in individuals without apparent symptoms [6]. The primary aim of this investigation is to determine the incidence of silent MI in unaffected individuals with diabetes mellitus through the utilization of exercise treadmill testing. The effectiveness of this diagnostic approach was evaluated in individuals diagnosed with T2DM.

MATERIAL AND METHODS.

Study Design.

This investigation employed a cross-sectional observational study design to examine the phenomenon under investigation. This investigation adopts an observational study design.

Participants.

The study population consisted of individuals diagnosed with asymptomatic type 2 Diabetes Mellitus, aged between 40 and 60 years, of both genders. These individuals did not exhibit any clinical signs or symptoms of Coronary Artery Disease and were having a normal resting ECG. The participants were recruited from the Diabetology or medicine outpatient department (OPD).

Study setting.

The present study was conducted at the Department of Medicine, Darbhanga Medical College & Hospital, Darbhanga, Bihar, within a duration of one year (2021-2022).

Inclusion Criteria.

This study encompasses individuals who have received a diagnosis of Type 2 Diabetes Mellitus. The patient's age falls within the range of 40 to 60 years. The patient exhibits no symptoms indicative of Coronary Artery Disease. The ECG obtained during a state of rest exhibits normal findings.

Exclusion Criteria.

1. Individuals with a well-documented medical background of Myocardial Infarction (MI).
2. Patients exhibiting clinical manifestations consistent with heart failure.
3. Clinical evidence substantiating the existence of angina pectoris.
4. Individuals with a clinical manifestation consistent with a confirmed diagnosis of renal disease.
5. Electrocardiogram (ECG) findings consistent with a Q wave myocardial infarction (MI), ischemic ST-segment or T wave abnormalities, or a complete left bundle branch block (LBBB).
6. Any chronic medical condition that has the potential to interfere with or hinder the advancement of the study.

Data collection.

The Treadmill Test (TMT) was employed as the diagnostic modality, and individuals who satisfied the predetermined inclusion criteria were chosen as subjects for the investigation. The data collection encompassed the acquisition of demographic data, medical history records, ECG findings, and outcomes of the TMT. The primary aim of this investigation was to acquire a comprehensive understanding of the cardiovascular health status of asymptomatic individuals diagnosed with diabetes within the designated cohort.

Statistical analysis.

The determination of the sample size was conducted using a 95% confidence interval, allowing for a maximum permissible error of 10%. The estimated prevalence of TMT positivity among asymptomatic individuals with diabetes mellitus was determined to be 37%. The determination of

the sample size was conducted employing the formula for estimation of sample size within the framework of determining a single sample proportion.
The formula for calculating the sample size (N) in a medical study can be expressed as follows:

$$N = Z_{1-\alpha/2}^2 \, P \, (1 - P) / E^2$$

The requisite sample size was determined to be a minimum of 93 subjects. Considering a non-response rate of 10%, the sample size was increased and rounded to approximately 120 participants.

RESULTS.

Within the confines of the current investigation, it was determined that the average age of subjects who received a diagnosis of diabetes was calculated to be 47.89 years. Furthermore, the male-to-female ratio was found to be 1.62:1, indicating a higher proportion of males in the sample population. The prevalence of Silent MI in individuals with diabetes, as evidenced by a positive TMT, was determined to be 11.8%.

Table 1: Factors associated with silent MI among diabetic patients.

Variables	TMT Negative	TMT Positive	P value
Age group			
40 - 50 years (S)	93.2%	4.8%	0.003
50 - 60 years	77.6%	20.4%	
Gender			
Female	84.5%	13.5%	0.083
Male	87.6%	10.4%	
Duration of diabetes			
<5 years (S)	94.7%	3.3%	<0.001
5-9 years	92.3%	5.7%	
10-15 years	43.4%	54.6%	
BMI (Kg/m²)			
18.5 - 22.9 Kg/m²	92.1%	5.9%	0.554
23 - 24.9 Kg/m²	84.4%	13.6%	
≥25 Kg/m²	84.5%	13.5%	

The study revealed a notable increase in the occurrence of asymptomatic myocardial infarction (MI) in individuals aged 50 to 60 years (20.4%) in comparison with those aged between the ages of 40 and 50 (4.8%), as indicated by positive results on the treadmill test (TMT).
The study revealed a notable increase in the incidence of TMT positivity among individuals with a documented history of diabetes exceeding 10 years (54.6%) in comparison to those with diabetes duration ranging from 5 to 9 years (5.7%) and less than 5 years (3.3%).
Furthermore, the prevalence of TMT positivity exhibited a statistically significant elevation in individuals presenting with dyslipidemia (49%) in comparison to those without dyslipidemia (3%). The prevalence of the aforementioned condition was observed to be significantly elevated in individuals exhibiting HbA1c levels exceeding 10% (58%) in comparison to those with HbA1c levels ranging from 7% to 10% (9.1%) and below 7%.
The study revealed a notable increase in the incidence of asymptomatic MI among the study population with elevated BMI, increased waist circumference, active smokers, alcohol consumers, and those who reported low levels of physical activity. Moreover, it was observed that TMT-positive patients exhibited notably elevated levels of total cholesterol, LDL, and TGRs in comparison to TMT-negative patients. The amount of HDL was found to be notably diminished in patients who tested positive for the TMT (Table 2). The average level of HbA1c was found to be significantly elevated in individuals who tested positive for TMT (9.19%) in comparison to those who tested negative for TMT (6.74%).

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Table 2: Laboratory characteristics in connection to TMT outcomes.

	TMT positive	TMT negative
TC (mg/dl)	375	263.6
LDL (mg/dl)	139.2	114.6
HDL (mg/dl)	28.69	37.27
TG (mg/dl)	225.8	139.1
FBS (mg/dl)	155.2	134.7
HbA1c (%)	9.19	6.74
Blood urea	30.38	31.2
Serum creatinine	0.83	0.75

DISCUSSION.

In this study, the incidence of silent myocardial infarction (MI) in individuals with diabetes mellitus was assessed using exercise treadmill testing (TMT). The mean age of the study population was 47.89 years, with a significant proportion falling within the age range of 45 to 49 years. Males constituted the majority of the study subjects, consistent with previous research. The majority of patients had a documented history of diabetes for 5 to 9 years. The TMT results indicated that 11.8% of the patients exhibited evidence of silent MI. However, the prevalence of silent MI varied across different studies.

The findings of this study highlight several important factors related to TMT positivity. Advanced age, particularly individuals aged 50 years and above, showed a significantly higher prevalence of TMT positivity. Females exhibited a slightly higher rate of TMT positivity compared to males, although this difference was not statistically significant. Patients with middle socioeconomic status (SES) displayed a slightly higher prevalence of TMT positivity compared to those with lower SES, although again, this difference was not statistically significant.

Patients with a longer duration of diabetes, exceeding 10 years, had a markedly higher prevalence of TMT positivity compared to those with shorter durations. Similarly, individuals with higher body mass index (BMI) values, specifically equal to or exceeding 25 Kg/m2 and ranging from 23 to 24.9 Kg/m2, exhibited a higher prevalence of TMT positivity compared to those with lower BMIs. Increased waist circumference (WC) was also associated with a higher prevalence of TMT positivity, although this difference did not reach statistical significance.

Furthermore, the study revealed a significant increase in the incidence of TMT positivity among individuals diagnosed with dyslipidemia, with a rate of 50%. Patients with TMT positivity demonstrated elevated concentrations of total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TGRs), along with reduced levels of high-density lipoprotein (HDL) compared to those with TMT negativity.

Elevated levels of hemoglobin A1c (HbA1c) were significantly associated with an increased rate of TMT positivity. Individuals with HbA1c levels greater than 10% exhibited a notably higher prevalence of TMT positivity compared to those with HbA1c levels ranging from 7% to 10% and HbA1c levels below 7%. These findings align with previous research investigating similar associations between these variables and TMT outcomes.

The demographic characteristics, such as age and gender distribution, in this study, align with findings from prior investigations. In the investigation carried out by Dipankar Deb *et al*., [7] the predominant demographic consisted of individuals aged 35-44 years. In the study conducted by Amit Daphale *et al*. [8], the average age of the participants was found to be 46.20 years. Males comprised the majority of study subjects, which aligns with the findings in other studies [8, 9, 10].

The patient cohort predominantly consisted of male individuals, a finding consistent with previous investigations in the field [11, 12]. The majority of patients had a documented history of diabetes spanning a duration of 5 to 9 years [13]. The observed prevalence exhibited inter-study variability, with certain investigations documenting elevated proportions [12, 13]. The association between diabetes duration, BMI, waist circumference, dyslipidemia, and HbA1c levels with TMT positivity is consistent with existing literature [13, 14, 15, 16]. However, it's important to note that the prevalence of silent MI varied across studies, suggesting potential differences in study populations or

methodologies. Further research is warranted to explore these variations and confirm the identified associations.

GENERALIZABILITY.

The findings of this study cannot be generalized for a larger sample population.

CONCLUSION.

A notable portion of individuals diagnosed with T2DM exhibited instances of silent MI or asymptomatic CAD. Individuals diagnosed with diabetes mellitus who are of advanced age, possess an elevated BMI, exhibit abdominal obesity, suffer from dyslipidemia, experience unregulated blood glucose levels, engage in smoking habits, and consume alcohol are more susceptible to an increased risk of silent MI. The exercise stress test, also known as the TMT, may serve as a straightforward, non-invasive, and economically efficient method for the timely detection of silent MI or asymptomatic coronary artery disease. Furthermore, the recognition of the correlated variables aids in the prompt assessment of these individuals, particularly to avert any impending cardiovascular incident.

LIMITATIONS.

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

RECOMMENDATIONS.

Early screening for silent myocardial infarction using treadmill testing (TMT) should be considered in asymptomatic individuals with type 2 diabetes, especially those who are older, obese, have a history of diabetes for more than ten years, or exhibit dyslipidemia and high HbA1c levels. TMT can serve as a valuable non-invasive tool for the timely detection of silent MI in this population.

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LIST OF ABBREVIATIONS.

ADA- American Diabetes Association
LBBB- Left Bundle Branch Block
ECG- Electrocardiogram
HDL- High-density lipoprotein
LDL- Low-density lipoprotein
TGRs- Triglycerides
SES- Socioeconomic status
WC- Waist circumference
BMI- Body mass index
TC- Total cholesterol
HbA1c- Hemoglobin A1c
MI- Myocardial Infarction
TMT- Treadmill test
T2 DM- Type 2 diabetes mellitus
CAD- Coronary artery disease
DKA- Diabetic ketoacidosis
HHNK- Hyperosmolar hyperglycemic nonketotic coma
PAD- Peripheral Arterial Disease
CHD- Coronary Heart Disease
CVD- Cardiovascular disease
NO- Nitric oxide

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CONFLICT OF INTEREST.

The author declares no conflict of interest.

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