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ORIGINAL ARTICLE *Volume 14 (Issue 4), 2025*

PAKISTAN JOURNAL OF MEDICINE & DENTISTRY

Assessing Risk Factors for Silent Myocardial Ischemia in Adults with Type 2 Diabetes: A Cross- Sectional Study

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ABSTRACT

Background: Silent myocardial ischemia (SMI) is an insidious but lethal form of coronary artery disease, especially in persons with type 2 diabetes mellitus (T2DM). It is often asymptomatic, which results in late diagnosis and risk of negative cardiac outcomes. The purpose of this study was to evaluate the prevalence and risk factors of SMI in adults having T2DM.

Methods: This cross-sectional study was conducted between February and July 2025 in the cardiology and endocrinology departments of a tertiary care facility. Non-probability purposive sampling was used to recruit 150 adults aged 35-70 years with a confirmed diagnosis of T2DM for more than five years. The participants were subjected to resting electrocardiography (ECG), treadmill stress test, and laboratory profiling of HbA1c, lipids, and renal tests. Statistical analysis with SPSS version 26.0 consisted of a chi-square test to compare categorical variables and logistic regression for confounder adjustment, where $p < 0.05$ was considered significant.

Results: The prevalence of SMI was 58 (38.6%). The most significant relations observed were the duration of diabetes (10 years or more) (OR: 3.75; CI: 1.87-7.53), poor glycemic control (HbA1c above 8%) (OR: 3.37; CI: 1.69 – 6.71), hypertension (OR: 2.57; CI:1.24 – 5.31), and microalbuminuria (OR: 2.95; CI: 1.45 – 6.01). Dyslipidemia was nearly significant, whereas gender, BMI, and smoking were not relevant to SMI.

Conclusion: SMI is widespread in asymptomatic T2DM patients. Metabolic and renal risk markers could be identified to facilitate earlier screening and intervention to lower the risk of unrecognized cardiac outcomes.

Keywords: Nerve Growth Factor, Flavonoids, Rats, Wistar, Neurodegenerative Diseases
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How to cite: Khan F, Akhtar B, Baloch MZ, Raza MT, Mal K, Ali F. Assessing Risk Factors for Silent Myocardial Ischemia in Adults with Type 2 Diabetes: A Cross-Sectional Study. Pak J Med Dent. 2025 September ;14(4): A-B. Doi: https://doi.org/10.36283/ziun-pjmd14-4/041.

Received: Sun, September 07, 2025 **Accepted:** Sun, September 28, 2025**. Published:** Mon, September 29, 2025

INTRODUCTION

Silent myocardial ischemia (SMI) among patients with type 2 diabetes mellitus (T2DM) is a clinically insidious phenomenon of the presence of objective evidence of MI in the absence of anginal symptoms, posing a high-risk condition due to autonomic neuropathy and hyperglycemia-mediated endothelial dysfunction [1]. SMI is a severe yet underestimated cardiovascular complication in diabetics that results in delayed diagnosis and an elevated risk of MI [2]. The prevalence of asymptomatic T2DM patients with SMI has been estimated to be 30-45% based on a pooled analysis of regional studies [3]. Long-term diabetes, poor glycemic management, hypertension, and premature renal dysfunction are risk contributors that are strongly prevalent and interconnected in this population. [4]

Treadmill test and stress electrocardiography (ECG) continue to be effective, non-invasive methods to identify SMI in asymptomatic people, especially those who have metabolic comorbidities [5]. SMI is also strongly related to microvascular complications of diabetes, including diabetic retinopathy and microalbuminuria, indicating a shared vascular pathology [6]. New recommendations proposed by cardiovascular societies now suggest that diabetics with known risks of cardiovascular disease, particularly end-organ damage or numerous metabolic risks, should be selectively screened [7].

Nevertheless, prospective screening of SMI is also underutilized in most clinical environments, leading to inadequate recognition and early interventions [8]. There is little regional information on how a combination of clinical indicators, such as glycemic control, hypertension, renal function, and diabetes duration, can inform proactive SMI identification among asymptomatic individuals [9]. With enhanced awareness of these predictors, clinicians may prioritize asymptomatic diabetics to seek timely cardiovascular evaluation and minimize the risks of cardiac events [10].

The objective of this study was to determine the prevalence of SMI and the relationship between clinical predictors, including diabetes duration, glycemic control, hypertension, and microalbuminuria among adults with T2DM. The goal was to facilitate the early diagnosis of high-risk, asymptomatic patients. Moreover, the purpose was to propose a practical screening protocol for early detection

METHODS

This cross-sectional study aimed to investigate the prevalence of SMI among individuals with T2DM and its association with selected clinical predictors, conducted at a tertiary care hospital that was a referral center to endocrine and cardiac patients PU and SZH Lahore from August to December 2022 (Ref: 1033/22). Adult patients in outpatient endocrinology and cardiology clinics were recruited

through a consecutive non-probability sampling approach. Participants were identified during regular clinical visits and enrolled after informed consent. The study comprised 150 participants. OpenEPI version 3.0.0 (released 2013, Atlanta, GA, USA) was used to determine the sample size based on the anticipated prevalence of SMI (35%), with a 95% confidence level, and a 7% margin of error [11].

The inclusion criteria were adults aged 35 to 70 years with confirmed diagnosis of T2DM for at least five years and no symptoms of prior cardiac disease. The exclusion criteria were coronary artery disease, angina, past myocardial infarction, arrhythmias, or severe renal disease. No intervention groups were used in the study; the natural clinical exposure to risk factors was explored. Age, duration of diabetes, Hemoglobin A1c (HbA1c), blood pressure, and microalbuminuria were the study variables. High-performance liquid chromatography (HPLC)-based assay was used to measure HbA1c. Urine albumin was determined by immunoturbidimetric method. SMI was detected by ECG and treadmill stress testing by the presence of myocardial ischemia without classic anginal manifestations, viewed by an expert in the field of cardiology.

SPSS version 26.0 (released 2019, IBM Corp., Armonk, NY) was used to analyze data. Categorical variables were analyzed using the chi-square test, and continuous variables using the independent t-test. The predictors of SMI were assessed with multivariable logistic regression. The p-value < 0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic Characteristics of Study Participants

Variable	Total (n=150)	SMI Present (n=58)	SMI Absent (n=92)	Test Value	p-value
Age (years, Mean ± SD)	56.2 ± 8.9	57.1 ± 9.3	55.7 ± 8.5	t = 1.03	0.30
Gender (Male%)	84 (56%)	34 (58.6%)	50 (54.3%)	$\chi^2 = 0.29$	0.59
BMI (kg/m², mean ± SD)	27.3 ± 3.8	27.8 ± 4.0	27.1 ± 3.7	t = 1.05	0.29
Duration of Diabetes ≥10 yrs	64 (42.7%)	36 (62.1%)	28 (30.4%)	$\chi^2 = 13.92$	<0.001*

*n = Number of participants, SMI = Silent Myocardial Ischemia, SD = Standard Deviation, % = Percentage, * = Significance at p-value <0.05*

The incidence and predictors of silent myocardial ischemia (SMI) in 150 adults with type 2 diabetes were assessed. ECG and stress testing identified 58 (38.6%) cases of SMI. The major risk factors identified were duration of diabetes (at least 10 years), HbA1c greater than 8%, hypertension, and microalbuminuria ($p < 0.05$). Early detection can be facilitated by screening of high-risk,

asymptomatic patients. Rapid response may avert serious cardiac incidents. Baseline demographic characteristics of the study population are indicated in **Table 1.**

Table 2: Clinical Characteristics and Laboratory Findings

Variable	Total (n=150)	SMI Present (n=58)	SMI Absent (n=92)	Test Value	p-value
HbA1c > 8%	76 (50.7%)	40 (69.0%)	36 (39.1%)	$\chi^2 = 13.1$	<0.001*
Hypertension (%)	94 (62.7%)	44 (75.9%)	50 (54.3%)	$\chi^2 = 6.53$	0.01*
Dyslipidemia (%)	88 (58.7%)	39 (67.2%)	49 (53.3%)	$\chi^2 = 2.86$	0.09
Microalbuminuria (%)	59 (39.3%)	32 (55.2%)	27 (29.3%)	$\chi^2 = 9.73$	0.002*
Smoking (%)	34 (22.7%)	17 (29.3%)	17 (18.5%)	$\chi^2 = 2.48$	0.11

*n = Number of participants, HbA1c = Hemoglobin A1c, SMI = Silent Myocardial Ischemia, % = Percentage, * = Significance at p-value <0.05*

The duration of diabetes of 10 years or more was strongly related to SMI (36 (62.1%) versus 28 (30.4%); p = 0.0002). There was no significant relationship with age (p = 0.30), gender (p = 0.59), or BMI (p = 0.29), suggesting that the presence of silent myocardial ischemia is highly associated with longer duration of diabetes. Clinical characteristics following laboratory tests are illustrated in **Table 2.**

Table 3: Significant Risk Factors for SMI

Risk Factor	Odds Ratio (95% CI)	Test Value	p-value
Duration of Diabetes ≥10 years	3.75 (1.87 – 7.53)	z = 3.69	<0.001*
HbA1c > 8%	3.37 (1.69 – 6.71)	z = 3.43	<0.001*
Hypertension	2.57 (1.24 – 5.31)	z = 2.53	0.011*
Microalbuminuria	2.95 (1.45 – 6.01)	z = 2.94	0.003*
Gender (Male)	1.16 (0.60 – 2.26)	z = 0.45	0.65

*n = Number of participants, SMI = Silent Myocardial Ischemia, CI = Confidence Interval, * = Significance at p-value <0.05*

Patients with SMI were more likely to have HbA1c of >8% (40 (69.0%) vs. 36 (39.1%); p = 0.0003), hypertension (44 (75.9%) vs. 50 (54.3%); p = 0.01), and microalbuminuria (32 (55.2%) vs. 27 (29.3%); p = 0.002). Dyslipidemia and smoking were insignificant factors (p = 0.09 and p = 0.11, respectively), highlighting that early nephropathy, poor glycemic control, and hypertension are separate predictors of SMI. **Table 3** shows the logistic regression of significant predictors of SMI.

The independent predictors of SMI were diabetes duration of at least 10 years (OR: 3.75; CI: 1.87-7.53), HbA1c >8 % (OR: 3.37; CI: 1.69-6.71), hypertension (OR: 2.57; CI: 1.24-5.31), and

microalbuminuria (OR: 2.95; CI: 1.45-6.01). Gender was also not significant (p = 0.65), implying that these variables may help to screen meticulously to detect early asymptomatic cardiac risk.

DISCUSSION

This study aimed to investigate the clinical risk predictors of SMI, including longer diabetes duration, elevated HbA1c, hypertension, and microalbuminuria in T2DM patients. The results validate that these variables are closely linked to SMI, which supports that metabolic and vascular markers play a critical role in subclinical cardiac ischemia. Poor Glycemic control (HbA1c >8%) was also identified as a significant factor in SMI, suggesting that hyperglycemia is a predictor of endothelial dysfunction, autonomic neuropathy, and pro-inflammatory states that adversely affect myocardial perfusion without eliciting symptoms of chest pain [12]. Prospective studies have strengthened this connection, and possible HbA1c measurements have been seen to predict subclinical ischemia and poor cardiac remodeling in diabetics [13]. The presence of diabetes (10 or more years) has also been an independent predictor of SMI. These acute metabolic stresses induce progressive coronary artery degradation and subsequent insufficient myocardial oxygen supply [14,15]. This observation is consistent with previous cohort studies that identified diabetes duration as a critical time-varying risk factor of silent ischemic changes [16].

The association between hypertension and SMI was also significant, as hypertension contributes to left ventricular hypertrophy and vascular remodeling, which aggravate the contribution of atherosclerosis in diabetes [17,18]. A meta-analysis study demonstrated that hypertensive diabetics are more likely to have unrecognized MI than normotensive controls [19]. The other significant predictor was microalbuminuria, which represents extensive microvascular damage and endothelial impairment [20]. A potential cardiovascular risk marker, frequently viewed as a precursor of diabetic nephropathy and independently associated with cardiovascular death and subclinical ischemia in multiple recent trials [21]. Interestingly, the study did not record any statistically significant relationships between SMI and dyslipidemia or smoking. Although these are already proven cardiovascular risk factors, their predictive ability is weakened in the population in which glycemic and hypertensive control has a stronger pathological effect [22]. A recent meta-analysis validates these findings, indicating that classic lipid abnormalities may contribute less to silent ischemia when baseline lipid risk is lowered by integrated care [23,24]. These findings are consistent with emerging data on the importance of selective screening for asymptomatic diabetics, especially those with persistent hyperglycemia, renal impairment, or chronic disease [25]. Structured screening systems may enhance the early identification of cardiovascular risk, guide modifications to therapy, and possibly decrease morbidity of SMI [26].

Study limitations are a single-center design and a small sample size, which affect generalizability and limit subgroup analysis. Ischemia of low sensitivity is not necessarily detected during stress testing in some patients, and subclinical neuropathy may change symptom perception, interfering with the identification of SMI. Moreover, unmeasured confounding factors, including medication adherence, lifestyle, and socioeconomic parameters, may affect the noted relationship. Future research should focus on larger, multicenter trials and cost-benefit analyses to determine the viability of screening SMI in diabetic care models.

CONCLUSION

In this study, the prevalence of SMI was found to be high in asymptomatic adults with T2DM, especially in individuals with poor glycemic control, hypertension, microalbuminuria, and prolonged duration of diabetes. The findings establish the crucial role of targeted clinical predictors in enhancing SMI risk within this group.

These findings highlight the need for selective cardiovascular screening in high-risk asymptomatic diabetic patients. Early identification may prevent adverse cardiac outcomes. The incorporation of these predictors in the routine evaluation may improve management in diabetic patients.

ACKNOWLEDGEMENT

None

FUNDING

None

CONFLICT OF INTEREST

None

ETHICAL APPROVAL

This cross-sectional study was conducted at a tertiary care hospital that was a referral center to endocrine and cardiac patients PU and SZH Lahore from August to December 2022 (Ref: 1033/22).

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE.

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