

Prevalence of Silent Myocardial Ischemia in patients with Type 2 Diabetes Mellitus attending Medical Outpatient Clinics

SAMIULLAH KHAN¹, SADULLAH SHAH², NAIMAT ULLAH SHAH³, SAEED MAQSOOD⁴, RADHIA KHAN⁵, MUHAMMAD SAAD JIBRAN⁶

¹Assistant Professor of Medicine, Medical Teaching Institution, Bannu

²Assistant Professor of Cardiology, Medical Teaching Institution, Bannu

³Assistant Professor of Medicine, Medical Teaching Institution, Bannu

⁴Assistant Professor of Cardiology, Medical Teaching Institution, Bannu

⁵Associate Professor of Biochemistry Bannu Medical College

⁶Assistant Professor Cardiology District Head Quarter Teaching Hospital, Medical Teaching Institution Dera Ismail Khan

Correspondence to: Dr. Saeed Maqsood, Email: drsaeedmaqsood@yahoo.com.

ABSTRACT

Background: Silent myocardial ischemia (SMI) is a disease that is well-known and yet frequently misdiagnosed as a cardiovascular complication of type 2 diabetes mellitus (T2DM). Ischemic symptoms can be hidden by autonomic neuropathy and distorted pain perception, coronary artery disease may develop without notice. Risk stratification and prevention of adverse cardiac events Risk stratification and prevention of adverse cardiac events are important in early identification of SMI.

Objective: To ascertain the occurrence of silent myocardial ischemia and its risk factors in patients with type 2 diabetes mellitus who visited medical outpatient clinics.

Methods: It was a cross-sectional study at the Medical Teaching Institution Bannu and Medical Teaching institution DI Khan during six months between November 2022 and April 2023. The patients that were enrolled were adult patients who had known T2DM and had no angina or any history of coronary artery disease. Demographic information, diabetes history and cardiovascular risk factors were taken. Each of the subjects was subjected to 12-lead electrocardiography at rest after which exercise stress testing or ambulatory ECG surveillance against individual indications to identify silent ischemia. Data analysis was done with the help of relevant statistical tests and significance level was taken to be $p < 0.05$.

Results: Silent myocardial ischemia had been found in 32 percent of the patients. Older age groups, longer duration of diabetes and coexisting hypertension and dyslipidemia were found to have higher prevalence. Resting ECG made the observation that a large percentage of cases were well diagnosed whereas stress testing enhanced the diagnostic accuracy among patients whose initial ECG showed normalcy.

Conclusion: Patients with type 2 diabetes mellitus have silent myocardial ischemia. Early intervention and minimization of cardiovascular morbidity in the future may be achieved by regular screening, especially among high-risk populations.

Keywords: Mute myocardial ischemia; Type 2 diabetes mellitus; Electrocardiography; Cardiovascular risk factors.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the significant metabolic diseases that cause chronic hyperglycemia due to the insulin insensitivity and comparative insulin deficiency. It is linked to the fact that it is associated with a much higher risk of macrovascular and microvascular form of problems such as coronary artery disease (CAD), cerebral vascular disease, and peripheral arterial disease. Of these, cardiovascular disease is the most significant contributor of morbidity and mortality among patients with T2DM¹.

Silent myocardial ischemia (SMI) is the objective evidence of myocardial ischemia that is absent with anginal symptoms. Autonomic neuropathy is a significant risk factor to patients with diabetes; it may dull pain, and it may not be able to detect ischemic events. As such, such patients could develop progressive coronary artery disease without any symptoms, subsequently resulting in late diagnosis and adverse prognosis².

Pathophysiology of SMI in T2DM refers to endothelial dysfunction, microvascular disease and accelerated atherosclerosis, which all implicate in the myocardial perfusion deficiency. Also, diabetic neuropathy is associated with the sensory fibers which relay pain sensations, which again add to the symptomless ischemia among these patients³.

Timely intervention which may include pharmacological intervention, lifestyle change, and the use of revascularization should be detected at an early stage of SMI as it is the only way to make sure that the intervention is timely. Screening of the high-risk patients will lower the rate of acute coronary events, as well as enhance the overall survival⁴.

Research studies have also shown fluctuating occurrence of SMI in the diabetic population, which can be ascribed to the age, length of diabetes, glycemic control, and the diagnostic methods applied to diagnose diabetic patients including exercise stress

testing, ambulatory ECG, monitoring or myocardial perfusion imaging^{5,6}. Although the increasing awareness provides certain benefits, SMI continues to be underdiagnosed, particularly in outpatient care of developing states, which would indicate the necessity to have local epidemiological statistics⁷.

The knowledge of the burden and determinants of SMI among T2DM patients who use outpatient clinics can help clinicians to risk stratify and prevent those at risk. Besides, timely identification of silent ischemia could be beneficial in minimizing cardiovascular morbidity and mortality among this risky group⁸.

Objective: To identify the rate of silent myocardial ischemia in the patient group with type 2 diabetes mellitus visiting medical outpatient clinics at a tertiary care hospital.

MATERIALS AND METHODS

This was a cross-sectional and observational study that was based in a hospital and its objective was to establish the prevalence of silent myocardial ischemia (SMI) in patients with type 2 diabetes mellitus (T2DM). The cross-sectional design enabled an evaluation of the existence of ischemia at one time in the patients who were attending outpatient clinics.

The research was carried out in the Medical Teaching Institution Bannu and Medical Teaching institution DI Khan during six months between November 2022 and April 2023.

The population that was studied was comprised of adult patients diagnosed with type 2 diabetes mellitus and aged 30 years and above and visiting the medical outpatient department. Patients who had known coronary artery disease, a history of previous myocardial infarction, angina or heart failure or major valvular heart disease were excluded to make sure that silent ischemia was detected.

Sample Size and Sampling Technique: The enrollment of patients into the study was done using a consecutive non-probability sampling method to include patients that met the inclusion criteria within the study period. The sample was

Received on 28-05-2023

Accepted on 22-07-2023

determined to give a good estimate of SMI prevalence among the study population but in view of time and available resources.

Data Collection Procedure: Demographic and clinical information such as age, gender, diabetes duration, comorbidities, glycemic control, and cardiovascular risk factors were captured after giving informed written consent. All the participants were subjected to a standard 12-lead electrocardiogram (ECG) at rest, and participants with an absence of ECG abnormalities suggestive of overt ischemia were, as indicated, subjected to exercise stress testing or ambulatory ECG monitoring.

Outcome Measures: The first consequence was that there was the presence of silent myocardial ischemia where there is objective evidence of myocardial ischemia with no anginal symptoms. The secondary outcomes were links between SMI and patient demographics, diabetes duration, glycemic control, and comorbid conditions like hypertension or dyslipidemia.

Data Analysis: The data were inputted into statistical programs to analyze them. Continuous variables were provided in the form of a mean and standard deviation whereas categorical variables were provided in the form of frequencies and percentages. The appropriate tests were chi-square and t-tests, and a p-value less than 0.05 was regarded as statistically significant.

Ethical Considerations: The medical teaching institution ethics committee of Bannu gave ethical approval. All participants were informed and their consent was obtained before the study. Patient confidentiality was highly regarded during the research and all procedures were evaluated according to the ethical principle that is contained in the Declaration of Helsinki.

RESULTS

The study enrolled 200 patients suffering type 2 diabetes mellitus. The average age of the subjects was 52.4 ± 11.3 years with the range between 35-75 years. The study population (118 males and 82 females) was 59 and 41 percent respectively. The average years of diabetes were 8.6 ± 5.2 years. One hundred and forty-four (62) patients had hypertension and 96 (48) patients had dyslipidemia. Table 1 presents the baseline demographic and clinical characteristics.

Sixty-four (32) patients had silent myocardial ischemia. Sinus ECG changes were found in 38 (19 per cent) of individuals with SMI, with T-wave inversions and ST-segment depressions, and 26 (13 per cent) of individuals with ischemic changes on stress testing or ambulatory ECG monitoring and no resting ECG abnormalities. Table 2 shows the distribution of SMI with respect to diagnostic modality.

On stratification by gender, SMI was found in 40 (33.9) males, and 24 (29.3) females; this was not significant ($p = 0.48$). The prevalence of SMI was higher among individuals with more than 50 years of age (38) than among those with 30-50 years of age (28) (Table 3).

Table 1: Baseline Demographic and Clinical Characteristics (n = 200)

Variable	Frequency (n)	Percentage (%)
Age (years), mean ± SD	52.4 ± 11.3	—
30-50 years	112	56
>50 years	88	44
Gender		
Male	118	59
Female	82	41
Hypertension	124	62
Dyslipidemia	96	48
Duration of diabetes (years), mean ± SD	8.6 ± 5.2	—

The prevalence of SMI was higher in patients with longer period of diabetes (>10 years) versus diabetes period 10 years or less (27%). Moreover, SMI (36 versus 25) was slightly more in those patients with comorbid hypertension. The trend on

associations with dyslipidemia was that above SMI prevalence was higher (34% vs 30%), but was not statistically significant.

Figure 1 represents graphical data of prevalence of SMI according to age and gender.

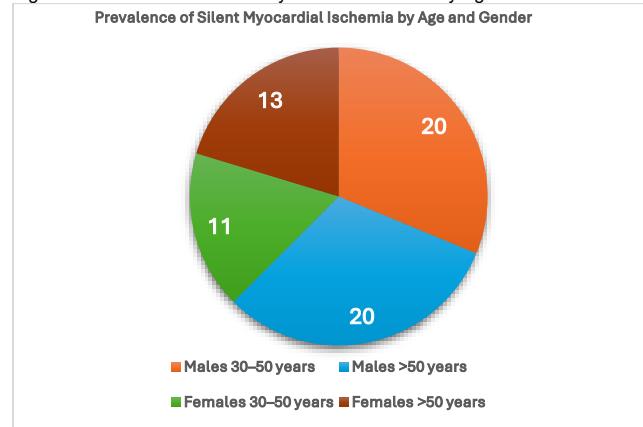
Table 2: Prevalence of Silent Myocardial Ischemia Based on Diagnostic Modality

Diagnostic Modality	Frequency (n)	Percentage (%)
Resting ECG changes	38	19
Stress testing / Ambulatory ECG	26	13
Total SMI	64	32

Table 3: Association of SMI with Age and Gender

Variable	SMI Present n (%)	SMI Absent n (%)	Total	p-value
Age				
30-50 years	31 (28)	81 (72)	112	0.12
>50 years	33 (38)	55 (62)	88	
Gender				
Male	40 (33.9)	78 (66.1)	118	0.48
Female	24 (29.3)	58 (70.7)	82	

Figure 1: Prevalence of Silent Myocardial Ischemia by Age and Gender



DISCUSSION

This paper discovered that silent myocardial ischemia (SMI) is widespread enough concerning the outpatient clinics dealing with type 2 diabetes mellitus (T2DM), where the prevalence is 32% among patients. The fact that SMI was detected in almost a third of the participants demonstrates the insidiousness of cardiovascular disease in diabetics, in which cases ischemic episodes can happen without any symptoms because of autonomic neuropathy. The fact that older patients and those with a history of diabetes longer than 20 years have a high prevalence rates underscores the cumulative effect of chronic hyperglycemia and metabolic derangements on the coronary vasculature⁹.

The preclinical myocardial involvement is observed in predominance of the resting ECG alterations, which include T-wave inversion, and ST-segment depressions, even before clinical manifestation. These results correlate with the prior research stating that diabetic patients often develop ECG signs of an ischemia without experienced angina, probably because diabetic autonomic neuropathy attenuates the pain sense¹⁰. Additional proof of the relevance of dynamic testing to detect occult ischemia was in the usage of stress testing and ambulatory ECG to determine SMI in patients with normal resting ECG¹¹.

The analysis of the age of patients showed that SMI was more prevalent among patients older than 50 years (38) than among young patients (28). This is in line with the previous literature that has shown that aging and prolonged exposure to

hyperglycemia leads to progression of atherosclerotic coronary artery disease and abnormally higher risks of having silent ischemic events¹². We did not find statistically significant gender differences in our cohort, though the prevalence was slightly higher in males, which is also similar to other previous studies¹³.

Higher SMI prevalence was linked to comorbid hypertension and dyslipidemia, which implies an additive cardiovascular risk of these patients. Hypertension may increase endothelial dysfunction and atherosclerosis, and dyslipidemia may accelerate the progress of the plaque, both of which may impair myocardial perfusion without causing anginal symptoms¹⁴. The tendency in our study is in line with the past reports which stressed the importance of combined risk factors in silent ischemia among diabetic individuals¹⁵.

The second determinant of importance was duration of diabetes; patients had a significantly high prevalence of SMI (42%); with diabetes over 10 years compared to patients with shorter disease duration (27%). Prolonged hyperglycemia favors the formation of end-products of glycosylation, microvascular dysfunction, and coronary atherosclerosis that proceeds silently, predisposing to silent ischemic attacks¹⁶. The findings were in concurrence to available evidence that associates chronic exposure to diabetes with subclinical coronary disease¹⁷.

Stress testing and ambulatory ECG among diabetics have shown comparative studies are prevalent with SMI of 20-40 percent, as is the case with our study. The minor difference can also be explained by the difference in sample size, population and diagnostic modalities, and glycemic control between cohorts¹⁸⁻²⁰. Notably, our research supports our view that symptoms or resting ECG is insufficient to predict the actual burden of ischemic heart disease in T2DM.

Limitations: The research is limited in a number of ways. Its cross-sectional nature does not allow the examination of causality or time dynamics of ischemic alterations. The study is a single-center case, which could restrict the generalizability to the other population. There was no detailed analysis of the coronary anatomy with the help of such imaging techniques as CT angiography or coronary angiography, and no analysis of long-term cardiovascular outcomes was conducted. Lastly, glycemic variability and microvascular complications were not entirely examined and this may contribute to the prevalence of SMI.

CONCLUSION

Patients with type 2 diabetes mellitus frequently experience silent myocardial ischemia, an underappreciated consequence that is more common in older people, those with longer disease durations, and those with co-occurring hypertension or dyslipidemia. While ambulatory ECG or stress testing greatly improves diagnostic yield, resting ECG may identify certain conditions. For risk assessment and prompt action to avoid serious cardiovascular events, early detection of SMI is essential. To enhance clinical results and lower morbidity and mortality, high-risk diabetes patients should be routinely screened for silent ischemia.

Conflict of interest: None

Funding: None

REFERENCES

1. Davis TM, Coleman RL, Holman RR, et al. Prognostic significance of silent myocardial infarction in newly diagnosed type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS 79). *Circulation*. 2013;127(9):980-987.
2. Atlas D. International diabetes federation. IDF diabetes atlas. Brussels: international diabetes federation. 2015.
3. Zabeen S, Hoque M, Rahman R. Silent myocardial ischemia and its association with microalbuminuria in type 2 diabetes mellitus. *BSMMU J*. 2012;5(1):42-45.
4. Prasad DS, Kabir Z, Devi KR, Peter PS, Das BC. Prevalence and Risk factors for Silent Myocardial ischemia (PRISM): A clinico observational study in patients of type 2 diabetes. *Indian Heart Journal*. 2019 Sep 1;71(5):400-5.
5. Hussain AM. *Analysis of Treadmill Test for Asymptomatic Cad in Type 2 Diabetes Mellitus* (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
6. Pop-Busui R. Cardiac autonomic neuropathy in diabetes: a clinical perspective. *Diabetes care*. 2010 Feb;33(2):434.
7. Tavares CA, Wajchjenberg BL, Rochitte C, Lerario AC. Screening for asymptomatic coronary artery disease in patients with type 2 diabetes mellitus. *Archives of Endocrinology and Metabolism*. 2016 Apr;60(2):143-51.
8. Dun Y, Wu S, Cui N, Thomas RJ, Olson TP, Zhou N, Li Q, Liu S. Screening for asymptomatic coronary artery disease via exercise stress testing in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Frontiers in Cardiovascular Medicine*. 2021 Nov 1;8:770648.
9. Hernández C, Candell-Riera J, Ciudin A, Francisco G, Aguadé-Bruix S, Simó R. Prevalence and risk factors accounting for true silent myocardial ischemia: a pilot case-control study comparing type 2 diabetic with non-diabetic control subjects. *Cardiovascular Diabetology*. 2011 Jan 21;10(1):9.
10. Chauhan S, Ghosh M, Agrawal PK, Singh MP, Alam W. Prevalence of silent myocardial ischemia in type 2 diabetes mellitus with microalbuminuria. *Int J Adv Med*. 2017;4(1):40-46.
11. Kamperidis N, Kamperidis V, Zegkos T, Kostourou I, Nikolaidou O, Arebi N, Karvounis H. Atherosclerosis and inflammatory bowel disease—shared pathogenesis and implications for treatment. *Angiology*. 2021 Apr;72(4):303-14.
12. Zia N, Aftab S, Butt NI, Ashfaq F, Anser A, Saeed S. Prevalence of silent cardiac ischemia in type II diabetes mellitus. *Pakistan Heart Journal*. 2021 Jun 24;54(2):162-6.
13. Fokoua-Maxime CD, Lontchi-Yimago E, Cheuffa-Karel TE, Tchato-Yann TL, Pierre-Choukem S. Protocol for prevalence of asymptomatic or "silent" myocardial ischemia in diabetic patients: a systematic review and meta-analysis. *PLoS ONE*. 2021;16(6):e0252511.
14. Wackers FJ, Young LH. Lessons learned from the detection of ischemia in asymptomatic diabetics (DIAD) study. *Journal of nuclear cardiology*. 2009 Dec;16(6):855-9.
15. Emami T, Naeimei Z, Salehfard A, Azizmohammadi Z, Iranpour D, Kalantarhormozi M, Jafari E, Gholamrezanezhad A, Assadi M. Significance of microalbuminuria in predicting silent myocardial ischemia in patients with type 2 diabetes using myocardial perfusion imaging. *Molecular Imaging and Radionuclide Therapy*. 2019 Jun 24;28(2):62.
16. Care D. Cardiovascular disease and risk management: Standards of medical care in diabetes. 2021. *Diabetes Care*. 2021 Jan;44(January):S125-50.
17. Yahagi K, Kolodgie FD, Lutter C, Mori H, Romero ME, Finn AV, Virmani R. Pathology of human coronary and carotid artery atherosclerosis and vascular calcification in diabetes mellitus. *Arteriosclerosis, thrombosis, and vascular biology*. 2017 Feb;37(2):191-204.
18. Rawshani A, Rawshani A, Franzén S, Sattar N, Eliasson B, Svensson AM, Zethelius B, Miftaraj M, McGuire DK, Rosengren A, Gudbjörnsdóttir S. Risk factors, mortality, and cardiovascular outcomes in patients with type 2 diabetes. *New England journal of medicine*. 2018 Aug 16;379(7):633-44.
19. Young LH, Wackers FJ, Chyun DA, et al. Cardiac outcomes after screening for asymptomatic CAD in patients with type 2 diabetes: the DIAD study outcomes. *JAMA*. 2009;301(14):1547-1555.
20. Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, Kosiborod M, Leiter LA, Lipska KJ, Newman JD, Welty FK. Clinical management of stable coronary artery disease in patients with type 2 diabetes mellitus: a scientific statement from the American Heart Association. *Circulation*. 2020 May 12;141(19):e779-806.

This article may be cited as: Khan S, Shah S, Shah NU, Maqsood S, Khan R, Jibran MS; Prevalence of Silent Myocardial Ischemia in patients with Type 2 Diabetes Mellitus attending Medical Outpatient Clinics. *Pak K Med Health Sci*, 2023; 17(8): 210-212.