



# **Diabetes Mellitus with Silent Myocardial Ischemia: A Single-Center Cross-Sectional Study of Karachi, Pakistan**

**Muhammad Zohaib Siddiq<sup>1</sup>, Shahid Hussain Memon<sup>2\*</sup>, Anwar Ali<sup>2</sup>,  
Tabassum Almas<sup>3</sup>, Atiya Razzaq<sup>2</sup> and Farhan Ahmed<sup>2</sup>**

<sup>1</sup>NICVD Karachi, Pakistan.

<sup>2</sup>Department of Cardiology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan.

<sup>3</sup>Department of Cardiology, Al-Tibri Medical College, Isra University, Karachi Campus, Pakistan.

## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author MZS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript.*

*Authors SHM and AA managed the analyses of the study. Author TA managed the literature searches. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Background:** Previous studies have established the fact that diabetic patients are predominantly inclined towards silent myocardial infarction (SMI). The objective of the present study is to determine the incidence of SMI in diabetes mellitus (DM) patients.

**Methodology:** In this cross-sectional study, patient data was gathered on a predesigned proforma regarding the detailed history of dyspnea, DM and its duration, chest pain either present or not. Those patients who had normal ECG labeled negative for SMI, while those who had either ST-segment elevation or ST-segment deviation on resting ECG were positive for SMI. Study was conducted at the National Institute of Cardiovascular Diseases (NICVD) Karachi- Pakistan.

**Results:** The mean age of the enrolled patients was 54.21±8.65 (40-70) years. Out of 210, majority were female (51.90%). Overall, 94(44.76%) patients were obese, 122(58.09%) were hypertensive, 90(42.85%) had dyslipidemia and 98(46.66%) diabetic patients were smokers. There were 93

\*Corresponding author: E-mail: [shahidcrd2010@yahoo.com](mailto:shahidcrd2010@yahoo.com);

(44.3%) DM patients who had SMI. Moreover, 109(51.90%) patients had a family history of myocardial ischemia.

**Conclusion:** The SMI incidence among diabetic patients was found higher in local population. It is proposed that diabetic patients with demonstrated cardiovascular autonomic neuropathy must be screened for the manifestation of SMI.

*Keywords: Silent myocardial ischemia; diabetes mellitus; cardiovascular disease; ST-segment elevation; electrocardiogram.*

## 1. INTRODUCTION

Cardiovascular ailments can cause death in diabetic population [1,2]. Diabetic patients have a high risk of developing the cardiovascular disease with a high SMI frequency. Even though silent myocardial ischemia is asymptomatic, there is a great chance of poor diagnosis among patients with diabetes [3]. Patients with SMI and diabetes foremost require early detection. Numerous studies have addressed that the prevalence and incidence of diabetic patients with silent myocardial ischemia should be explored [1-4].

Milan et al. study showed the prevalence of silent coronary artery disease is 6.4% in non insulin-dependent Diabetes Mellitus, i.e. type 2 DM [4]. While latest studies also showed variation in Silent myocardial ischemia with Diabetes Mellitus as well as the non-consistent role of CVS risk status. Among the asymptomatic diabetic patients, this unpredictability highlights the trouble to have a proper evaluation and the need to describe a high CVS risk. Due to poor diagnosis in silent myocardial ischemia cases, it has enhanced the CVS events rate [4-5]. The incidence of SMI has significant inferences for the patient with diabetes, prospective as a result of cardiac autonomic dysfunction [3]. Clinicians/practitioners thoughtful for patients with diabetes need to know the possibilities and scientific explanations of silent ischemia. Findings of SMI in a diabetic patient may lead to additional events such as endeavored revascularization, thorough evidence that these proceedings progress prognosis in diabetics, with or without the history of any myocardial infarction [5,6].

MI in diabetic patients poses investigative and prognostic challenges for health care professionals, especially when patients are non-symptomatic throughout incidents of myocardial ischemia. As it is of collective health concern in low- and middle-income countries with a rise in potential hazards of smoking and obesity, that's

why causing higher morbidity and mortality across the globe [5-9]. This study aimed to determine the incidence of SMI in patients with diabetes mellitus presenting to a tertiary care hospital (NICVD), Pakistan's leading public sector cardiac hospital dealing with thousands of patients on a daily basis.

## 2. METHODOLOGY

A non-probability consecutive sampling was applied to conduct cross-sectional study at ER and OPD Department of NICVD, Karachi from August 2017 to January 2018. Keeping 95% confidence interval, 6.5% margin of error and 35.56% SMI prevalence with DM [10], the sample size of 210 was calculated using the WHO sample size calculator.

All consenting patients with dyspnea at rest, above age 40 and  $\leq 70$  years with type 2 DM of 3 years' duration or more, and patient without the previous administration of fibrinolytic therapy, platelet glycoprotein IIb/IIIa inhibitors assessed with history and previous reports were enrolled. While type 1 and type 2 DM with symptomatic heart disease, those with myocardial ischemia, thrombolytic therapy, coronary angioplasty, left bundle branch block, valvular heart disease, coronary artery bypass grafting, sepsis and chronic obstructive pulmonary disease (COPD) were excluded from the study.

After enrollment, data was gathered on a predesigned Proforma regarding the detailed history of dyspnea, DM and its duration, chest pain either present or not. A resting 12 leads ECG was performed for all the enrolled cases, those who had normal ECG were labeled as negative for SMI, while those having either ST-segment elevation or ST-segment deviation on resting ECG were labeled as positive for SMI.

The statistical analysis was carried out using SPSS version 21.0, the quantitative data like age, BMI, and DM duration was presented as

mean and standard deviation. Frequencies and percentages were calculated for qualitative variables like gender, hypertension, dyslipidemia, smoking, obesity, family history of myocardial infarction (MI), cardiogenic shock, socio-economic status, residence, and presence of SMI. Effect modifiers like age, duration of DM, gender, hypertension, dyslipidemia, smoking, obesity, family history of MI, cardiogenic shock, socio-economic status and residence were controlled by stratification. A Chi-square test was applied post-stratification to evaluate the effect of these modifiers on the outcome, taking  $p \leq 0.05$  as significant.

### 3. RESULTS

A total of 210 patients were included in the study, and of them 93 (44.3%) had SMI. The mean age of the patients was  $54.21 \pm 8.65$  years, BMI was  $22.98 \pm 6.57$  and duration of DM was  $6.1 \pm 6.31$  years (Table 1). Among them,

122(58.09%) patients were hypertensive, 90(42.85%) had dyslipidemia, 98(46.66%) diabetic patients were smokers. Stratification for silent myocardial ischemia with Obesity, Hypertension and Smoking showed a significant difference with P-values  $< 0.05$ .

### 4. DISCUSSION

The results of this study validated that there is an increased risk of SMI among patients with DM i.e.44.3% of the enrolled patients in the selected study group were observed having SMI (Table 1) and CVS risk factors relation was observed with the family history. The stratification for SMI with obesity, hypertension and smoking showed a significant difference with p-values  $< 0.05$  (Table 2). Various researches suggested that silent myocardial ischemia with significant lesions occurs in almost 20% of type 2 diabetic patients who mostly remain asymptomatic for CAD [9].

**Table 1. Demographic and clinical characteristics of the enrolled subjects**

Variables	N=210	
Gender	Female	109(51.90)
	Male	101(48.09)
Socio-economic Status	Lower Class	73(34.76)
	Middle Class	80(38.09)
	Upper Class	57(27.14)
Silent myocardial ischemia in diabetic patients	Present	93(44.3)
	Absent	117(55.7)
Obesity		94(44.76)
Hypertension		122(58.09)
Dyslipidemia		90(42.85)
Smoking		98(46.66)
Cardiogenic Shock		58(27.61)
Family History of MI		109(51.90)
Age (years)		$54.21 \pm 8.65$
BMI ( $\text{kg}/\text{m}^2$ )		$22.98 \pm 6.57$
Duration of Diabetes Mellitus (years)		$6.1 \pm 3.1$

\*Values are given as mean $\pm$ SD or n(%)

**Table 2. Patient characteristics in association with Silent myocardial ischemia**

Variables	Silent Myocardial ischemia				p-value
	Present		Absent		
	N	%	n	%	
Obesity	54	57.4	40	42.6	$< 0.001^*$
Hypertension	64	52.5	58	47.5	$< 0.005^*$
Dyslipidemia	43	47.8	47	52.2	0.38
Smoking	58	59.2	40	40.8	$< 0.001^*$
Cardiogenic shock	23	39.7	35	60.3	0.40
Family History of MI	60	55	49	45	$< 0.001^*$

\* $p < 0.05$  is considered statistically significant

Based on these findings, it can be suggested that routine screening should be mandatory for diabetic population (type 2) with present CVS risk [8-11]. The clinicopathological studies showed correlations, supported by angiographic findings, i.e. patients with diabetes have more wide-ranging coronary arteries disease [12]. Moreover, the severity of myocardial infarction among diabetes mellitus population is more than in non-diabetes mellitus population [9,12]. Until now, it is believed that the diagnosis for CVS risks among type 2DM population remains poor, because of the catastrophe of existing management plans. In fact, before the actual diagnosis of diabetes, the vascular damage usually develops, i.e. usually in the pre-diabetic phase. So, the glucometabolic alarm often remains concealed until the time of a cardiovascular event and vice versa [11-13]. The notion that diabetes mellitus population have a high frequency of silent myocardial ischemia than the common population is proven by various studies justifying the reasons of silent or asymptomatic nature of the disease, like the different verge of pain or psychological renunciation but more significantly the role of cardiac autonomic neuropathy that has potential involvement in dysfunction at different point such as the afferent neurons, pain receptors or gate phenomenon of pain [12,13]. There is a reported catastrophe, angina develop at the beginning of ischemia and have an accommodating effect on the diabetic subjects' exercise tolerance [14,15]. Few research findings suggested a link between cardiac autonomic neuropathy and silent myocardial ischemia in patients with diabetes, reporting that irregularities in myocardial pain sensitivity in patients with diabetes are unswervingly related to sympathetic denervation [12-15]. The American diabetic association recommends that population with diabetes mellitus should be well-thought-out as a CVS disease equivalent. Moreover, the CVS disease risk factors among diabetic population should be evaluated and managed with or without known coronary artery disease [16,17]. There is an enduring argument on the usefulness of repetitive screening for CAD in diabetic patients and screening for myocardial ischemia is not usually recommended in diabetic patients since the result is not value-added as long as cardiovascular risk factors are under good control [16-18]. Equally, the European Society of Cardiology contemplates screening in high-risk patients of silent myocardial ischemia with DM but also emphasizes the essential to obtain

additional statistics to better classify diabetic patients will be benefitted from screening [19].

## 5. CONCLUSION

The incidence, prevalence and burden of SMI is very high among diabetes mellitus population. It is proposed that diabetic patients with demonstrated cardiovascular autonomic neuropathy must be screened for the manifestation of silent myocardial ischemia. Multicenter studies from Pakistan and linked countries are prerequisite as many aspects of diabetes complications are diverse from those described in studies from West mainly because of dissimilar population characteristics.

## CONSENT AND ETHICAL APPROVAL

Ethical approval was obtained from the Ethics Review Committee (ERC) of the College of Physicians and Surgeons of Pakistan (Reference no: CPSP/REU/CRD-2015-195-1172; Dated March 15, 2018) and written informed consent was taken from all the patients.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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