ORIGINAL ARTICLE

MULTI-VESSEL CORONARY ARTERY DISEASE IN DIABETIC PATIENTS PRESENTING WITH ANTERIOR WALL MYOCARDIAL INFRACTION

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Objectives: This study aimed to determine the frequency of multi-vessel coronary artery disease (MVD) in diabetic patients presenting with anterior wall myocardial infarction (AWMI).

Methodology: In this descriptive cross-sectional study, we included diabetic patients with AWMI aged between 30-70 years. Patients with either a history of clinical diagnosis based on HbA1c >6.5% / fasting blood sugar > 126 mg/dL/ random blood sugar >200 mg/dL or taking anti-hyperglycemic treatment for at least six months were taken as diabetics. Patients with angiographic evidence of significant (>70%) stenosis in two major epicardial vessels were categorized for MVD.

Results: A total of 196 diabetic patients with anterior wall MI were included. Of which the mean age was 57.6±12.3 years, and 128 (65.3%) were male patients. MVD was observed in 91 (46.4%) patients. The MVD was found to be associated with a BMI ≥ 24 kg/m^2 with a frequency of 51.5% vs. 35%; p=0.033, as compared to a BMI < 24 kg/m^2. The frequency of MVD was higher among middle-class patients, with a frequency of 36.2%, 58.3%, and 39.5% (p=0.014) for patients in the low, middle, and upper classes, respectively. Similarly, the MVD frequency was higher among patients with hypertension (60.6% vs. 28.7%) and hyperlipidemia (62.1% vs. 38.5%) compared to non-hypertensive and non-hyperlipidemia, respectively.

Conclusion: It is to be concluded that MVD is highly prevalent in diabetic patients presenting with AWMI, and it was found to be associated with BMI ≥ 24 kg/m^2, middle class, hypertension, and hyperlipidemia.

Keywords: acute coronary syndrome, anterior wall myocardial infarction, diabetes, multi-vessel CAD, PCI, STEMI

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INTRODUCTION

Diabetes mellitus (DM) is an emerging modern-day global public health concern. It was estimated to affect around 451 million adults in the year 2017. The International Diabetes Federation (IDF) projected affected individuals to be 693 million by 2045.[1] It is a chronic metabolic disorder characterized by hyperglycemia due to impaired insulin secretion, insulin action, or both. It remains a well-established major risk factor for cardiovascular disease (CVD),[2] and patients with diabetes were reported to have 53%, 58%, and 10% higher risk of myocardial infarction, stroke, and coronary artery diseases, respectively, as compared to their non-diabetic counterparts.[2]

Myocardial infarction (MI) is a severe manifestation of CVD and a leading cause of morbidity and mortality worldwide.[3] DM in patients with MI is reported to be associated with higher disease severity with multi-vessel involvement,[4] and it is an independent predictor of short- and long-term adverse outcomes after an acute MI event.[5] Anterior wall myocardial infarction (AWMI) is a type of MI occurring due to decreased blood flow to the anterior wall of the heart due to occlusion of the left anterior descending artery (LAD), and it has been reported to have a worse prognosis when compared to inferior or posterior wall MI.[6]

The pathophysiological mechanisms behind the association of multi-vessel disease (MVD) with DM are complex and multifactorial, and several factors have been implicated in this strong association.[7] DM is associated with accelerated atherosclerosis and endothelial dysfunction, which can lead to diffuse coronary artery disease (CAD) involving multiple

coronary arteries. Chronic hyperglycemia promotes oxidative stress and endothelial dysfunction that can result in accelerated atherosclerosis and plaque rupture and promote inflammation.[8] Insulin resistance is a hallmark of DM, which either aggravates or results in the development of various metabolic disorders such as obesity, hypertension, and hyperlipidemia, in addition to the impairment of endothelial function, which all are established risk factors for the development of CAD.[8] An increased oxidative stress and impaired nitric oxide production can result in endothelial dysfunction, which can promote the adhesion of monocytes and platelets to the vessel wall, leading to the formation of atherosclerotic plaques.[9,10] The abnormal lipid metabolism is another possible pathway of an increased risk of CVD, which is also commonly observed in patients with DM.[11]

In recent years, the number of diabetic patients with CAD has increased due to changing lifestyles.[12] However, despite a wealth of findings and information in high-income countries regarding the prevalence and characteristics of MVD in diabetic patients presenting with anterior wall MI, there is a prominent scarcity of data and a knowledge gap in developing countries like Pakistan. Therefore, this study aimed to assess the frequency of multi-vessel CAD in diabetic patients presenting with AWMI at a tertiary care cardiac center in Karachi, Pakistan.

METHODOLOGY

This descriptive cross-sectional study was conducted between September 17, 2021, and March 16, 2022, at a tertiary care hospital in Karachi. The study was approved by the ethical review committee of the "NICVD (National Institute of Cardiovascular Diseases), Karachi, Pakistan" and verbal consent for participation was obtained from all the study participants. This study was conducted as part of the fellowship in adult cardiology (FCPS) from the "CPSP (College of Physicians and Surgeons Pakistan)."

Study inclusion criteria were diabetic patients of either gender admitted with anterior wall MI irrespective of the duration of diabetes and patients aged between 30-70 years. At the same time, exclusion criteria were patients with severe uncontrolled hypertension, acute stroke, active gastrointestinal bleeding, allergy to contrast agents, acute renal failure, and pregnant ladies. These conditions were considered confounders and, therefore, were excluded to avoid bias.

The AWMI was diagnosed based on the findings of a 12-lead ECG obtained at the time of presentation. The ECG criteria consisted of "ST segment elevation in the anterior leads (V3 and V4) at the J point or reciprocal ST-segment depression in the inferior leads (II, III, and aVF)". Similarly, patients with either a history of clinical diagnosis based on HbA1c >6.5% / fasting blood sugar > 126 mg/dL/ random blood sugar >200 mg/dL or taking anti-hyperglycemic treatment for at least six months were taken as diabetics. All patients were managed according to the standard of care received by patients with diabetes and anterior wall MI. All patients underwent a detailed history and clinical examination. An experienced interventional cardiologist performed coronary angiography. Patients with angiographic evidence of significant (>70%) stenosis in two major epicardial vessels were categorized for multi-vessel diseases.

All the mentioned information like age, gender, height (measured in meters), weight (measured in kg), body mass index (BMI, measured in kg/m^2), socioeconomic status, smoking status, family history of CAD, comorbidities (hypertension, chronic kidney disease, and hyperlipidemia) and presence of multi-vessel disease were recorded in a pre-designed proforma. We strictly followed exclusion criteria to control bias in study results. The socioeconomic status of patients was categorized based on monthly household income as low (≤ Rs. 50,000), middle (Rs. 50,001 to 100,000), and upper (> Rs. 100,000).

The minimum required sample size for the study was calculated to be 196; the WHO sample size calculator was used, and sample size calculation was based on the following assumptions: the estimated proportion of multi-vessel CAD in AWMI 48.6%,[12] margin of error 7%, and the confidence level was 95%. The sampling technique was non-probability consecutive sampling.

Data were analyzed using SPSS version 23.0. Mean and standard deviation (SD) were calculated for quantitative variables like age, height, weight, and BMI. Frequencies and percentages were calculated for categorical variables like gender and the presence or absence of multi-vessel CAD. The frequency of multi-vessel CAD was stratified by age, gender, and other confounding variables like height, weight, BMI, socioeconomic status, smoking, and comorbidities. Post-stratification, a Chi-square test was applied, keeping a p-value ≤ 0.05 as the criterion for significance.

RESULTS

A total of 196 diabetic patients with anterior wall MI were included. Of which the mean age was 57.6±12.3 years, and 128 (65.3%) were male patients. In the distribution of socioeconomic status, 69 (35.2%) were lower class, middle class 84 (42.9%), while upper-

class statuses were 43 (21.9%), and the distribution of risk factors is shown in Table 1.

Table 1: Composition of study sample in terms of various demographic and clinical characteristics

	Summary
Total (N)	**196**
Age (years)	57.6 ± 12.3
Height (m)	1.66 ± 0.82
Weight (kg)	65.3 ± 13.1
Body mass index (kg/m^2)	27.3 ± 5.9
Gender	
Males	128 (65.3%)
Females	68 (34.7%)
Socioeconomic status	
Lower class	69 (35.2%)
Middle class	84 (42.9%)
Upper class	43 (21.9%)
Comorbidities	
Smoker	87 (44.4%)
Hypertension	109 (55.6%)
Hyperlipidemia	66 (33.7%)
Number of vessels involved	
Single vessel disease	105 (53.6%)
Multi-vessel disease	91 (46.4%)

Multi-vessel CAD was observed in 91 (46.4%) patients. The multi-vessel CAD was found to be associated with a BMI ≥ 24 kg/m2 with a frequency of 51.5% vs. 35%; p=0.033, as compared to a BMI < 24 kg/m2. The frequency of multi-vessel CAD was higher among middle-class patients, with a frequency of 36.2%, 58.3%, and 39.5% (p=0.014) for patients in the low, middle, and upper classes, respectively. Similarly, the frequency of multi-vessel CAD was higher among patients with hypertension (60.6% vs. 28.7%) and hyperlipidemia (62.1% vs. 38.5%) as compared to non-hypertensive and non-hyperlipidemia, respectively. The frequency of multi-vessel CAD stratified by demographic characteristics and comorbidities is presented in Table 2.

Table 2: Frequency of multi-vessel coronary artery diseases stratified by various demographic and clinical characteristics

	Total (N)	Number of Vessels Involved		P-value
		MVD	SVD	
Total (N)	196	91 (46.4%)	105 (53.6%)	-
Gender				
Male	128	63 (49.2%)	65 (50.8%)	0.283
Female	68	28 (41.2%)	40 (58.8%)	
Age (years)				
30 to 50 years	40	18 (45%)	22 (55%)	0.839
>50 years	156	73 (46.8%)	83 (53.2%)	
Body mass index (kg/m^2)				
≤ 24	60	21 (35%)	39 (65%)	0.033
> 24	136	70 (51.5%)	66 (48.5%)	
Socioeconomic Status				
Lower class	69	25 (36.2%)	44 (63.8%)	0.014
Middle class	84	49 (58.3%)	35 (41.7%)	
Upper class	43	17 (39.5%)	26 (60.5%)	
Smoking Status				
Smoker	87	39 (44.8%)	48 (55.2%)	0.688
Non-smoker	109	52 (47.7%)	57 (52.3%)	
Hypertension				
Hypertensive	109	66 (60.6%)	43 (39.4%)	<0.001
Non-hypertensive	87	25 (28.7%)	62 (71.3%)	
Hyperlipidemia				
Hyperlipidemia	66	41 (62.1%)	25 (37.9%)	0.002
Non-hyperlipidemia	130	50 (38.5%)	80 (61.5%)	

MVD=multi-vessel disease, SVD=single vessel disease

DISCUSSION

The prognostic role of DM is a well-established fact for patients with CAD and its strong association with the development of multi-vessel diseases further makes management of these patients challenging.[4,5] We conducted this study to evaluate the frequency of MVD among diabetic patients presented with AWMI. In a sample of 196 diabetic patients with AWMI, the multi-vessel disease was found in 91 (46.4%) patients, and it was found to be associated with a BMI ≥ 24 kg/m^2, middle class, hypertension, and hyperlipidemia. Multi-vessel disease has been reported to be 32 to 65% in various studies.[4,12]

In addition to diabetes, several risk factors have been reported as potential confounders in the association between diabetes and the development of multi-vessel coronary artery diseases. Such factors included duration of DM,[13] the longer duration of type II DM is not only a significant risk factor for the development of multi-vessel disease, but it has been reported to be a significant independent predictor of 1-year major adverse cardiovascular events rate after percutaneous coronary intervention.[14] Addition to the duration of DM, poor glycemic control is another important clinical determinant found to be strongly associated with a higher risk of MVD, as observed by Pathak SR et al.[13] 72.2% vs. 10% multi-vessel diseases among patients with poor (HbA1c > 8.5%) and good glycemic control (HbA1c < 7.0%), respectively. Older age is the

most commonly reported factor among other clinical predictors of multi-vessel disease. A study by Mir A et al.[15] reported age (years) as an independent predictor of multi-vessel disease with an adjusted odds ratio of 1.1 [95% CI: 1.02-1.17]. Similarly, obesity, hypertension, and dyslipidemia increase the risk of multi-vessel diseases, as observed in the current study and multiple other past studies.[15-17] Additionally, elevated levels of inflammatory markers, such as C-reactive protein (CRP), are associated with a higher risk of multi-vessel disease.[18] Presence of renal impairment, as indicated by elevated serum creatinine levels or reduced estimated glomerular filtration rate (eGFR), is also associated with a higher risk of multi-vessel disease.[19]

It is important to note that these predictors are not independent of each other and often coexist in diabetic patients with anterior wall MI. Identifying these predictors can help clinicians tailor their management accordingly. Furthermore, multi-vessel disease in diabetic patients with AWMI is often associated with more extensive myocardial damage, larger infarct size, and impaired left ventricular function, which can further increase the risk of adverse outcomes.[20] Hence, the management strategies involve a comprehensive approach, including both medical therapy and revascularization procedures. The primary goals of management in these patients are to alleviate symptoms, reduce the risk of recurrent MI, and improve long-term outcomes.[20] Mechanical revascularization has been reported to lower the risk of adverse cerebrovascular and cardiovascular events in these patients.[21] However, the cardiovascular community has debated for over 20 years whether percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is the preferred revascularization strategy, particularly for diabetic patients with multi-vessel CAD.[22] In addition to revascularization, lifestyle modifications (smoking cessation, regular exercise, and a heart-healthy diet) and medical therapy in diabetic patients with anterior wall MI and MVD should include antiplatelet therapy, beta-blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARBs), and lipid-lowering therapy with statins. These medications have been shown to improve outcomes in patients with MI and should be prescribed according to current guidelines.[23, 24]

Even though, to the best of our knowledge, this is the first study reporting multi-vessel disease among diabetic patients with AWMI from our population. However, single-center coverage and limited sample size are the key limitations of the current study. Secondly, we cannot establish the prognostic role of multi-vessel diseases in these patients due to a lack of management and outcome data. Further large-scale studies are warranted to elaborate the prognostic role of multi-vessel disease among diabetic patients presented with AWMI.

CONCLUSION

It is to be concluded that MVD is highly prevalent in diabetic patients presenting with AWMI, and it was found to be associated with BMI $\geq$ 24 kg/m^2, middle class, hypertension, and hyperlipidemia. Patients with AWMI should be worked up for the presence of multi-vessel CAD to ensure adequate treatment.

AUTHORS' CONTRIBUTION

SZ, AA, IH, RP, and SK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. , AURM, MF, and ZJ: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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