ORIGINAL ARTICLE

NON-OBSTRUCTIVE CORONARIES IN PATIENTS PRESENTING WITH THE NON ST-ELEVATION ACUTE CORONARY SYNDROME

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Background: Worldwide, cardiovascular diseases are the major cause of mortality and morbidity with acute coronary syndrome as the most common clinical manifestation. In a typical clinical setup, around 30% of the patients presented with "ST-segment elevation myocardial infarction (STEMI)" caused by the complete occlusion of the coronary artery and the remaining 70% with intermittent or partial occlusion of the coronary termed as non-ST elevation The aim of this study was to assess the prevalence and characteristics of non-obstructive coronary arteries among patients presenting with non ST-elevation acute coronary syndrome (NSTE-ACS) at a tertiary care cardiac center of Karachi, Pakistan. **Methods:** This was a descriptive cross-sectional study, conducted at a tertiary care hospital in Karachi. Study inclusion criteria were patients of either gender admitted with NSTE-ACS and aged between 30-70 years. A routine coronary angiogram was performed in all the patients and the absence of ≥50% stenosis in any major epicardial vessel was taken in non-obstructive coronaries. **Results:** A total of 174 patients (30–70 years) were included, of which 99 (56.9%) were male and the mean age was 59.43±11.24 years. In the distribution of socioeconomic status, 54 (31.0%) were lower class, middle class 81 (46.6%) while upper-class status were 39 (22.4%). Hypertension was observed in 76 (43.7%), chronic kidney disease in 20 (11.5%), and hyperlipidemia in 55 (31.6%). Non-obstructive coronary arteries were noted in 25 (14.4%) patients. **Conclusion**: It is to be concluded that non-obstructive coronary arteries are fairly prevalent in patients arriving in hospitals with NSTE-ACS in our population. Further research is needed to better understand the underlying pathophysiology and optimal management strategies for patients with NOCA in the setting of NSTEMI.

Keywords: Acute Coronary Syndrome; CAB; Non-Obstructive Coronaries; NSTEMI; PCI

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INTRODUCTION

Worldwide, cardiovascular diseases (CVD) are the major cause of mortality and morbidity with acute coronary syndrome (ACS) as the most common clinical manifestation. In a typical clinical setup, around 30% of the patients presented with "ST-segment elevation myocardial infarction (STEMI)" caused by the complete occlusion of the coronary artery and the remaining 70% with intermittent or partial occlusion of the coronary termed as non-ST elevation ACS (NSTE-ACS).[1] The presence of obstructive coronary artery disease (OCAD) on angiography is a major determinant of management and prognosis in patients with NSTE-ACS. However, approximately 30% of patients with NSTE-ACS have non-obstructive coronary arteries (NOCA) on angiography, defined as <50% stenosis in all epicardial vessels.[2,3]

The pathophysiology of MINOCA is not yet fully understood, and there may be several underlying mechanisms that can cause this condition.[4–6] Some of the proposed mechanisms include; coronary microvascular dysfunction: a condition where the small blood vessels in the heart do not function normally, which can lead to a decreased blood flow to the heart muscle.[7] Microvascular dysfunction has been shown to be more common in women and in patients with risk factors such as hypertension and diabetes.[8] Coronary artery spasm: a sudden, temporary narrowing of the coronary arteries, which can cause a decrease in blood flow to the heart muscle. Coronary artery spasms can be caused by several factors, including smoking, stress, and exposure to cold temperatures.[5] Plaque rupture with spontaneous healing: Plaque is a buildup of cholesterol and other substances in the walls of the coronary arteries. When a plaque ruptures, it can cause a clot to form, which can block blood flow to the heart muscle and cause a heart attack. In some cases, the body can spontaneously dissolve the clot, leaving no evidence of a blockage on angiography.[4] Coronary thromboembolism: a condition where a blood clot forms in another part of the body and travels to the coronary arteries, blocking blood flow to the heart muscle.[4,5]

Regardless of the underlying mechanism, MINOCA can cause damage to the heart muscle, leading to symptoms such as chest pain, shortness of breath, and fatigue.[9] It is important for patients with MINOCA to receive appropriate treatment to manage their symptoms and reduce their risk of future cardiovascular events.[10] In

2017 European Society of Cardiology (ESC) suggested a guideline for the first time and added a new section for MINOCA patients,[11] this guideline was for the management of STEMI patients, and suggested the use of additional diagnostic tools.[11] MINOCA is a heterogeneous clinical manifestation and despite a wealth of information regarding its prevalence and characteristics, there is a knowledge gap regarding the management and outcomes of MINOCA in developing countries like Pakistan, therefore the aim of this study was to assess the prevalence and characteristics of non-obstructive coronary arteries among patients presenting with NSTE-ACS at a tertiary care cardiac center of Karachi, Pakistan.

MATERIAL AND METHODS

This was a descriptive cross-sectional study, conducted between September 29, 2021 and March 28, 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.

Study inclusion criteria were patients of either gender admitted with NSTE-ACS and aged between 30–70 years. The patients with acute stroke, active gastrointestinal bleeding, allergy to radiographic contrast, severe hepatic disease, severe infection, and pregnant ladies were excluded. These conditions are believed to be acted as confounders therefore should have been excluded to avoid bias.

A 12-lead ECG (electrocardiogram) was performed in all the patients with chest pain and NSTE-ACS was diagnosed based on the ECG findings such as ST-depression or T-wave inversions and development of pathologic Q waves, further, NSTE-ACS confirmed by troponin levels. Patients who were managed and received standard of care presented with NSTE-ACS. All patients underwent a detailed history and clinical examination. 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 coronary artery disease and co-morbidities (diabetes, hypertension, hyperlipidaemia, chronic kidney disease) were recorded in a pre-designed proforma. A routine coronary angiogram was performed in all the patients and the absence of ≥50% stenosis in any major epicardial vessel was taken is non-obstructive coronaries.

A sample size of 174 was calculated for the study based on the expected 13% rate of non-obstructive coronary arteries in patients with NSTE-ACS, 5% margin of error, and 95% confidence level. After data quality assessment SPSS Version 21.0 was used for the analysis, quantitative variables such as age, height, weight and BMI, were expressed as mean ± SD (standard deviation), while for the categorical variable's frequencies and percentages (%) were calculated. Patients were stratified by age, gender and other confounding variables like BMI, socioeconomic status, smoking status, and family history of CAD and co-morbidities. Post stratification Chi-square test was applied in which *p*-value ≤0.05 was taken as significant criteria.

RESULTS

Between September 29, 2021, and March 28, 2022, a total of 174 patients (30–70 years) were included to assess the prevalence and characteristics of non-obstructive coronaries in patients presenting with non-ST elevation acute coronary syndrome. Of which 99 (56.9%) were male and the mean age was 59.43±11.24 years.

In the distribution of socioeconomic status, 54 (31.0%) were lower class, middle class 81 (46.6%) while upper class statuses were 39 (22.4%) and the distribution of risk factor are shown in Table-1.

Non-obstructive coronary arteries were noted in 25 (14.4%) patients. The distribution of obstructive and non-obstructive coronary arteries by various demographic and co-morbid conditions are presented in Table-2. We have observed no specific statistical association between the various demographic and co-morbid conditions and the distribution of obstructive and non-obstructive coronary arteries.

Table-1: Demographic and clinical characteristics of study sample and distribution of non-obstructive coronaries

	Summary
Total (N)	**174**
Age (years)	59.43±11.24
Height (m)	1.68±0.08
Weight (kg)	79.26±10.49
Body mass index (kg/m^2)	28.13±4.81
Gender	
Males	99 (56.9%)
Females	75 (43.1%)
Socioeconomic Status	
Lower class	54 (31.0%)
Middle class	81 (46.6%)
Upper class	39 (22.4%)
Smoking status	
Smoker	50 (28.7%)
Non-Smoker	124 (71.3%)
Co-Morbidities	
Hypertension	76 (43.7%)
Chronic kidney disease	20 (11.5%)
Hyperlipidaemia	55 (31.6%)
Family history of coronary artery diseases	31 (17.8%)
Angiographic finding	
Non-obstructive coronary arteries	25 (14.4%)
Obstructive coronary arteries	149 (85.6%)

Table-2: The distribution of obstructive and non-obstructive coronary arteries by various demographic and co-morbid conditions

	Total (N)	Non-OCA	OCA	*p*-value
Age group				
30–60 years	66	8 (12.1%)	58 (87.9%)	0.509
>60 years	108	17 (15.7%)	91 (84.3%)	
Gender				
Male	99	13 (13.1%)	86 (86.9%)	0.593
Female	75	12 (16%)	63 (84%)	
Body mass index				
18–30 kg/m^2	114	13 (11.4%)	101 (88.6%)	0.124
>30 kg/m^2	60	12 (20%)	48 (80%)	
Socioeconomic status				
Lower class	54	5 (9.3%)	49 (90.7%)	0.419
Middle class	81	14 (17.3%)	67 (82.7%)	
Upper class	39	6 (15.4%)	33 (84.6%)	
Smoking status				
Smoker	50	10 (20%)	40 (80%)	0.179
Non-smoker	124	15 (12.1%)	109 (87.9%)	
Family history				
Positive	31	4 (12.9%)	27 (87.1%)	0.528
Negative	143	21 (14.7%)	122 (85.3%)	
Hypertensive				
Yes	76	14 (18.4%)	62 (81.6%)	0.179
No	98	11 (11.2%)	87 (88.8%)	
Chronic kidney diseases				
Yes	20	5 (25%)	15 (75%)	0.136
No	154	20 (13%)	134 (87%)	
Hyperlipidaemia				
Yes	55	7 (12.7%)	48 (87.3%)	0.675
No	119	18 (15.1%)	101 (84.9%)	

OCA=obstructive coronary artery

DISCUSSION

The clinical significance of non-obstructive coronaries in patients with NSTE-ACS is an area of active research and debate and it is a major determinant of management and prognosis in NSTE-ACS. Hence, we conducted this study to assess the prevalence and characteristics of non-obstructive coronary arteries in patients with NSTE-ACS. In this study, we observed non-obstructive coronary arteries in 25 (14.4%) patients with NSTE-ACS. We have observed no specific statistical association between the presence of non-obstructive coronary arteries and various demographic and co-morbid conditions such as age, gender, body mass index, socioeconomic status, smoking status, family history, hypertension, chronic kidney diseases, and hyperlipidaemia.

The prevalence of NOCA varies greatly from 5% to 25% depending on the type of population under study.[12-16] Multiple studies have identified several factors that may affect the likelihood of NOCA in patients with NSTEMI. Some of these factors include age, older age is associated with a higher prevalence of obstructive coronary artery disease (OCAD) in patients with NSTEMI, and therefore a lower likelihood of NOCA,[17] in a study conducted by Kılıç S *et al*.[12] the mean age for the patients with and without NOCA 54.9±15 years vs. 61.9±12.1 years, respectively. Female gender is another commonly observed factor found associated with an increased likelihood of NOCA,[3,12,15–17] in VIRGO study the likelihood of NOCA was observed to be 5-fold higher among females as compared to male patients.[18] This may be due to differences in the underlying pathophysiology of coronary artery disease in women compared to men, including differences in the severity and distribution of atherosclerotic plaques.[14] Patients with NOCA diseases are less likely to have the prevalence of conventional risk factors of CAD such as hypertension, diabetes, and hyperlipidaemia. However, a study by Pasupathy *et al*.[19] reported no statistically significant differences in the prevalence of conventional risk factors, except for the hyperlipidaemia which was found to be less likely among patients with NOCA disease. Additionally, the presence of non-cardiac comorbidities such as chronic obstructive pulmonary disease (COPD) and cancer has been associated with a higher likelihood of NOCA in patients with NSTEMI, possibly due to the presence of non-cardiac causes of chest pain.[20]

The management of patients with NOCA in the setting of NSTEMI is a complex issue, as these patients may have a different underlying pathophysiology and clinical course. It is important to note that the management of NOCA should be individualized based on the patient's specific

presentation and underlying risk factors.[21] Regardless of the underlying mechanism, NOCA can cause damage to the heart muscle, leading to symptoms such as chest pain, shortness of breath, and fatigue.[10] There is currently no universally accepted guideline for the management of patients with NOCA, but several organizations have published recommendations based on the available evidence.[11] Some patients with NOCA in NSTEMI may benefit from aggressive medical therapy, including antiplatelet agents, beta-blockers, and statins, to reduce the risk of future cardiovascular events.[4,22] It is also important to consider repeat angiography in some patients, to rule out any technical or interpretive errors, especially for patients with recurrent symptoms or signs of myocardial ischemia.[13] Additionally, invasive testing such as cardiac magnetic resonance imaging should be considered to evaluate coronary microvascular dysfunction.[13,23] Last but not least, these patients benefit from a multidisciplinary approach to care, including close follow-up with a cardiologist, management of comorbidities, and involvement of other specialists, such as a psychologist, to address potential psychological factors that may contribute to persistent symptoms and lifestyle modifications, such as smoking cessation, weight loss, and regular physical activity, can help improve cardiovascular health and reduce the risk of future cardiovascular events in patients with NOCA.[22,24]

Our study has certain limitations that need to be addressed in future studies, it was a single-center observational study and data regarding the management and outcomes of patients with NOCA are not recorded. Hence, considering the significant proportion of patients with NOCA, it is important to conduct multicenter studies and evaluate the effectiveness of various management options and outcomes of these patients.

CONCLUSION

It is to be concluded that non-obstructive coronary arteries are fairly prevalent in patients presenting with non-ST-elevation acute coronary syndrome in our population. Based on the available literature it has been observed that NOCA may represent a distinct clinical entity with a lower risk of adverse outcomes compared to OCAD, further studies are needed to better understand the underlying pathophysiology and optimal management strategies for these patients.

AUTHORS' CONTRIBUTION

SZ, KIB: Conceived the idea. MZ, RP: Study design. SZ, KIB, DM: Data collection. SZ, KIB, AURM: Write-up. SZ, KIB: Review. AS: Supervised the entire project.

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