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RESEARCH ARTICLE

A STUDY OF CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS OF MINOCA (MYOCARDIAL INFARCTION WITH ANGIOGRAPHICALLY NON OBSTRUCTIVE CORONARY ARTERIES) AMONG THE PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION

Dr. Kamlesh Goyal, Dr. Shashi Mohan Sharma, Dr. Dhananjay Shekhawat and Dr. Dinesh Kumar Gautam
Department of Cardiology, SMS Medical College, Jaipur.

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Abstract

Objective: Myocardial infarction (MI) with non-obstructive coronary arteries (MINOCA) is a relatively new term that is characterized by clinical evidence of MI with normal or near-normal coronary arteries on coronary angiography. The aim of this was to document the prevalence and demographics of MINOCA in an Indian population.

Methods: It is a single center study. All consecutive patients who were ≥18 years old, diagnosed with MI according to the Third Universal Definition of Myocardial Infarction, and had undergone coronary angiography were included in the study. Patients with stable coronary artery disease, unstable angina pectoris, a history of revascularization, and type 4/5 MI were excluded.

Results: A total of 548 patients who were diagnosed with MI and had undergone coronary angiography were enrolled. The prevalence of MINOCA was 6.2% in the overall study population. Compared with non-MINOCA patients, those with MINOCA were younger, had a higher prevalence of the female gender, and had a history of COVID 19 infection. Also, the median left ventricular ejection fraction as seen on echocardiography and the ratio of Killip Class I status at presentation was significantly higher in MINOCA patients than in non-MINOCA patients ($p<0.001$).

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Introduction:-

Acute myocardial infarction (MI), a severe condition often associated with obstructive coronary artery disease (CAD) characterized by >50% stenosis, is observed in over 90% of patients undergoing coronary angiography (1, 2). Earlier research has established a strong correlation between atherosclerosis and MI. Nonetheless, a significant proportion of MI patients recommended for CAG do not exhibit obstructive CAD, defined as <50% stenosis, leading to the diagnosis of myocardial infarction with non-obstructive coronary arteries (MINOCA) (1, 2).

Previous registries have reported varying prevalence rates of MINOCA, with estimates ranging from 2.6% to 15% (3-8). This variability underscores the substantial number of patients affected, especially when considering the broader population of CAD patients. A recent publication by the European Society of Cardiology (ESC) delved into the definition, clinical features, potential mechanisms, and treatment of MINOCA (2).

Corresponding Author:- Dr. Kamlesh Goyal
Address:- Department of Cardiology, SMS Medical College, Jaipur.

The study emphasized that diagnosing MINOCA is an ongoing process and underscored the importance of investigating both non-coronary and coronary causes. A wide array of potential causes underlies MINOCA, including myocarditis, vasospasm, thromboembolism, microvascular dysfunction, supply/demand mismatch, Takotsubo syndrome, myocarditis, acute pulmonary embolism, coronary thrombosis, and dissection. As a result, the diagnostic process may necessitate multiple steps, such as echocardiography, left ventriculography, intracoronary imaging, computed tomography, pulmonary angiography, and cardiac magnetic resonance imaging (CMRI). Given the absence of an established diagnostic algorithm, the selection of diagnostic tools should be contingent on the suspected cause. Additionally, clear treatment guidelines have not been established as of yet.

Considering India's population of nearly 1.5 billion and approximately 1.2 million annual cases of acute coronary syndrome (ACS) (9, 10), understanding the demographics and clinical characteristics of MINOCA patients becomes pivotal in shaping a new strategic plan and approach for these patients. These findings are anticipated to aid in the development of a novel scoring system for predicting MINOCA diagnosis before initiating CAG. This study concentrated on the demographic, clinical, and etiological attributes of MINOCA, with the aim of shedding light on this issue from a national perspective.

Methods:-

Study Population and Definition

This study was conducted as a single-center investigation at the Department of Cardiology, SMS Hospital, Jaipur, Rajasthan, which is a tertiary hospital located in North India. The protocol of this study was submitted to Institutional Ethics Committee, SMS Jaipur prior to the study and approval was obtained. The study focused on a cohort of patients who met specific criteria for Acute Myocardial Infarction (AMI) diagnosis, as outlined in the Third Universal Definition of Myocardial Infarction. These criteria entail the presence of a positive cardiac biomarker and supporting clinical indicators of AMI, including ischemic symptoms, new ischemic ECG changes, the development of pathological Q waves, and imaging evidence of new loss of viable myocardium or a new regional wall motion abnormality (1).

The study's inclusion criteria encompassed consecutive patients aged 18 years or older who met the diagnostic criteria for MI and had undergone diagnostic coronary angiography. Patients who met the following exclusion criteria were not considered for the study: (1) individuals under 18 years of age, (2) those diagnosed with stable coronary artery disease (CAD), (3) individuals experiencing unstable angina pectoris, (4) patients with a history of revascularization through percutaneous coronary intervention (PCI) and/or coronary artery bypass grafting (CABG), (5) those who had experienced MI types 3–5, and (6) patients who had not provided informed consent (2).

A total of 548 patients were enrolled in the study, all of whom had previously undergone coronary angiography (CAG) and exhibited indications of ischemia. As part of the diagnostic criteria, all study participants demonstrated elevated cardiac troponin (cTn) levels, indicative of myocardial injury. Among these patients, three-quarters displayed new ischemic ECG changes, such as ST-segment elevation or depression, serving as evidence of ischemia. The remaining patients exhibited pathological Q-waves, new regional wall motion abnormalities in imaging, or presented with various ischemic symptoms (1, 2).

The diagnosis of MINOCA was based on the current opinion paper from the ESC working group, which focused on the clinical context of MINOCA (2). MINOCA was diagnosed when a patient, presenting with features consistent with those of acute MI, meets the following criteria,

1. As outlined in the AMI Criteria (Third Universal Definition of Myocardial Infarction) (12):
2. Non-obstructive coronary arteries on coronary angiography (CAG).
3. Lack of a clinically overt, specific cause for the acute presentation.

The AMI criteria necessitate the presence of a positive cardiac biomarker and supporting clinical evidence of an AMI, which may include ischemic symptoms, new ischemic electrocardiogram changes, and imaging evidence.

The term "non-obstructive coronary arteries on angiography" in this definition refers to the absence of obstructive coronary artery disease on angiography, which means there is no coronary artery stenosis of ≥50% in any potentially infarct-related artery. This encompasses angiographically normal coronary arteries (with no stenosis >30%) and mild coronary atheromatosis (with stenosis >30% but <50%).

Data collection involved the recording of patients' baseline clinical characteristics and medical history using case report forms after coronary angiography.

Coronary angiography was conducted in accordance with the specific protocols of the individual laboratory. Patients with angiographically normal coronary arteries (no stenosis >30%) and mild coronary atheromatosis (stenosis >30% but <50%) were identified. Digital copies of the coronary angiographies of these patients were gathered and independently evaluated by three invasive cardiologists who were unaware of the patients and the diagnosis of MINOCA was subsequently confirmed.

Statistical analysis was carried out using the Statistical Package for Social Sciences 20.0 software (SPSS Inc., IL, USA). Continuous variables were reported with mean and standard deviation (mean±SD) or median (25th–75th percentile) values, while categorical variables were expressed as proportions (%) and the number of cases. Nominal data were compared using the Chi-squared test or Fisher's exact test. The distribution of variables was assessed using the Kolmogorov-Smirnov test, and variance equality was evaluated with Levene's test. Variables with both normal and non-normal distributions were compared using the Student's t-test and the Mann-Whitney U test, respectively. Statistical significance was defined as a p-value of <0.05.

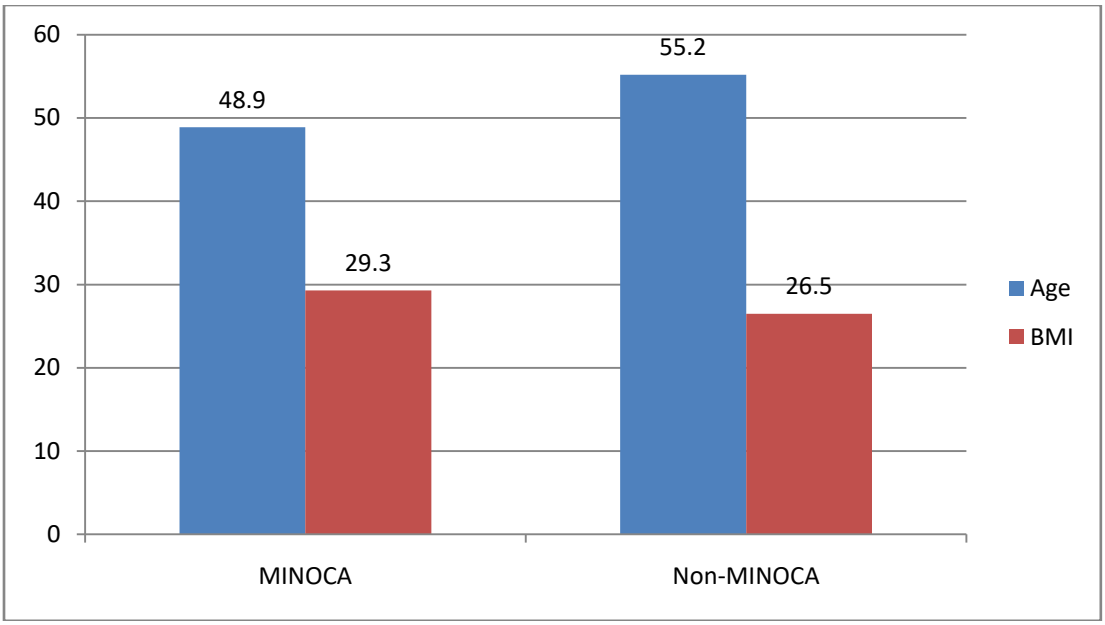
Results:-

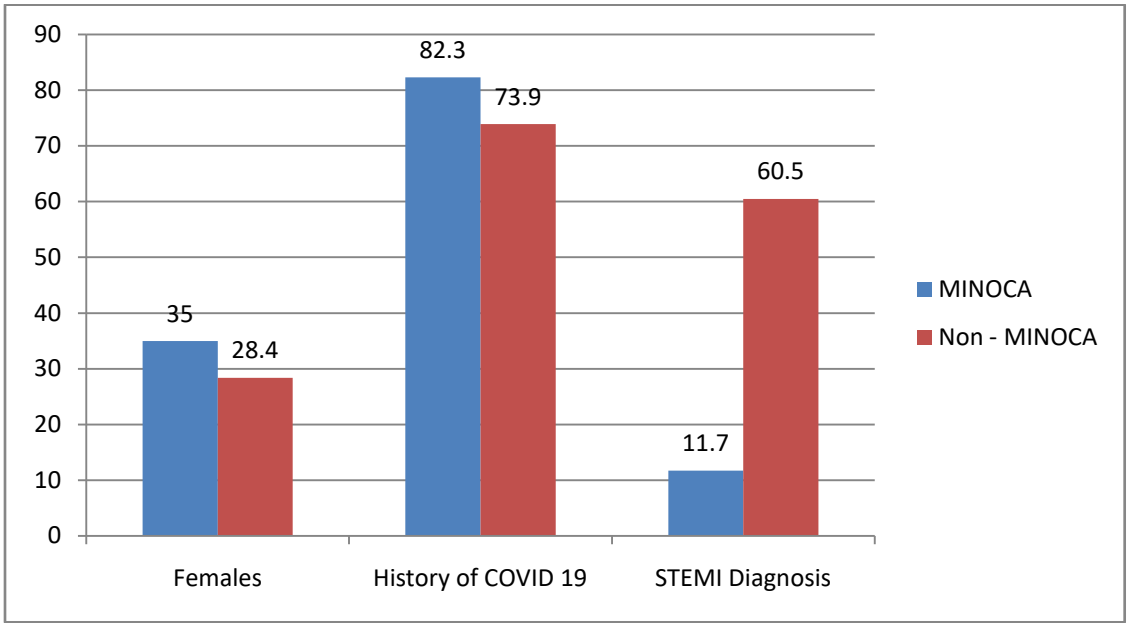
Baseline characteristics of the study population

A total of 548 patients were enrolled in this study. In this cohort the incidence of MINOCA was found to be 6.2% (n=34). The baseline demographic characteristics of the cohort are summarized in Table 1 and their comparison in the MINOCA versus the Non-MINOCA group. Significant differences were observed between the two groups. MINOCA patients, on average, were notably younger, with a median age of 48.9 years, compared to non-MINOCA patients, who had a median age of 55.2 years (P< 0.001). Furthermore, the MINOCA group had a higher mean BMI of 29.3 kg/m², while the non-MINOCA group had a lower mean BMI of 26.5 kg/m². Notably, a higher percentage of MINOCA patients were female (35.0%) compared to non-MINOCA patients (28.4%). The prevalence of active smoking was similar in the non-MINOCA group (32.2%) compared to the MINOCA group (35.0%). There was no significant difference in alcohol consumption between the two groups. A history of COVID-19 was more prevalent among MINOCA patients (82.3%) than non-MINOCA patients (73.9%). The diagnosis of ST-Elevation Myocardial Infarction (STEMI) was significantly less frequent among MINOCA patients (11.7%) than non-MINOCA patients (60.5%). Family history of CAD did not show a significant difference between the groups, and the prevalence of hypertension was similar in both groups.

The median left ventricular ejection fraction (LVEF) value on echocardiography was also higher in the MINOCA group [60% (25th–75th percentile, 58.5%–62%) vs. 50% (40%–55%); p<0.001].

Variables	MINOCA (n=34)	Non-MINOCA (n=514)	P-value
Age, median years (mean±SD)	48.9±10.7	55.2±13.1	<0.001
BMI (kg/m^2) (mean±SD)	29.3±4.4	26.5±5.7	0.004
Systolic blood pressure (mm Hg) (mean±SD)	130±22.6	129±11.1	0.583
Diastolic blood pressure (mm Hg) (mean±SD)	77.4±14.1	77.7±11.8	0.635
Sex (female) n, (%)	12 (35.0)	146 (28.4)	<0.001
Active smoker n, (%)	12 (35.0)	165 (32.2)	0.840
Alcohol n, (%)	8 (23.5)	128 (25.0)	0.909
History of COVID 19 n, (%)*	28 (82.3)	380 (73.9)	<0.001
Diagnosis STEMI n, (%)	4 (11.7)	311 (60.5)	<0.001
Family history of CAD n, (%)	6 (17.6)	140 (27.2)	0.092
Hypertension n, (%)	7 (20.5)	256 (18.2)	0.346





Discussion:-

As a single centre study, this showed that the prevalence of MINOCA was 6.7% in patients who were diagnosed with MI, without having a history of MI and revascularization. Prior research conducted on unselected patients with MI has indicated a wide range of prevalence for MINOCA, spanning from 2.6% to 15% (3-8). In our study, we found that MINOCA patients exhibited characteristics consistent with previous findings: they were generally younger, more frequently female, and presented with fewer conventional cardiovascular risk factors (1, 3, 13-15). Additionally, the occurrence of ST-Elevation Myocardial Infarction (STEMI) was less common in MINOCA patients, aligning with previous observations (3, 13-15). Our findings underscore the distinct characteristics of the Indian population compared to their European counterparts. India experiences approximately 1.2 million cases of ACS annually, and there is a notably higher prevalence of young MI patients (age <50 years) in India compared to Europe (9, 10). Given that MINOCA patients tend to be relatively younger than non-MINOCA patients, this underscores the significance of understanding and addressing MINOCA within the indian population. Moreover, nearly all patients receiving thrombolytic therapy undergo a diagnostic coronary angiogram within 3–24 hours of

their initial presentation at our centre. In light of these circumstances, the reported MINOCA prevalence in our study is less likely to be influenced by selection biases related to MI patients who did not undergo diagnostic CAG for various reasons.

Nonetheless, it's essential to recognize that the prevalence of MINOCA can be influenced by factors associated with the study population. Primarily, not all patients who present with STEMI undergo CAG. Instead, those with a higher likelihood of having obstructive CAD are often chosen for CAG. Conversely, individuals with a higher probability of having MINOCA, particularly those characterized by a lower presence of traditional cardiovascular risk factors, a younger age, and a female gender, may not undergo CAG. These differences in patient selection may contribute to the observed lower frequency of MINOCA in certain studies. While our study included all consecutive patients diagnosed with ACS who underwent CAG, it is plausible that individuals at lower risk might not have undergone CAG or may have been directed to the cardiology department through emergency services. It is noteworthy that the ESC guidelines recommend the use of high-sensitivity cardiac troponin (hs-troponin) assays over standard troponin tests. This shift has resulted in an increased detection of myocardial infarctions (MIs) and a concurrent reduction in the diagnosis of unstable angina. Consequently, the adoption of hs-troponin for MI diagnosis has the potential to raise the prevalence of MINOCA. Importantly, all the participating patients in our study underwent hs-troponin for MI diagnosis.

MINOCA represents an initial diagnosis and can encompass one or more causes with diverse underlying pathophysiologies (1, 2). It is imperative to discern the etiopathologies of patients initially categorized as having MINOCA (2). The relatively low prevalence of traditional cardiovascular risk factors and the younger age of MINOCA patients suggest that mechanisms beyond atherosclerosis and thrombosis may underlie MINOCA pathology.

Coronary pathologies exhibit various mechanisms, with the most common coronary causes of MINOCA encompassing coronary dissection, thromboembolism, coronary artery spasm, plaque rupture, erosion, and other types of type 2 MI (2, 3, 17-20). Factors such as plaque rupture, erosion, ulceration, and intraplaque hemorrhage can lead to plaque disruption, subsequently causing thrombosis. Additionally, coronary artery spasm is a prevalent phenomenon, attributed to both endogenous and exogenous triggers (21). Given that certain non-coronary causes are treatable, meticulous employment of diagnostic tools is crucial for precise diagnosis and treatment. The current guidelines from the ESC on STEMI emphasize the importance of identifying the underlying cause of MINOCA patients to prevent inappropriate therapy and unfavorable outcomes (22). The ESC working group's position paper on MINOCA has suggested the use of both non-invasive methods (such as echocardiography, cardiac magnetic resonance imaging, coronary CT angiography, and CT scan) and invasive techniques (including ventriculography, intravascular ultrasonography, optical coherence tomography, ergonovine/acetylcholine testing, and endomyocardial biopsy) based on the suspected diagnosis (2).

Consistent with prior studies, our findings demonstrate that MINOCA patients exhibit a lower cardiovascular risk profile compared to non-MINOCA patients (1, 2). Furthermore, MINOCA patients tend to be younger and more frequently female than their non-MINOCA counterparts. These results hint at the potential influence of sex-related hormonal factors in the pathogenesis of MINOCA, a subject deserving further investigation. Similarly, akin to previous studies, we noted that the LVEF of MINOCA patients was significantly higher than that of non-MINOCA patients. This discrepancy might be attributed to the presumption of less extensive myocardial damage in MINOCA patients relative to their non-MINOCA counterparts (1, 14).

In our population people with history of COVID-19 infection had a significantly higher incidence of MINOCA. In a previous study by Popovic et al [10], there was a statistically significant increase in the proportion of MINOCA in COVID-19 patients compared to a historical cohort (54.5% vs 1.4%, $P < 0.001$). Due to the heterogeneity in case definitions and evaluation protocols between centers, the actual proportion of MINOCA among COVID-19 patients is difficult to estimate.

The outlook for MINOCA patients is contingent on the specific underlying cause. While many studies have indicated a more favorable prognosis for MINOCA patients, this conclusion is not uniformly consistent in all research reports (1, 2). Additionally, there is a notable absence of long-term prognostic data for MINOCA patients (14). A systematic review of MINOCA trials disclosed a mortality rate as substantial as 4.7% within one year (3). Despite the fact that MINOCA patients are typically younger and exhibit a lower prevalence of cardiovascular risk

factors, these findings underscore the significance of MINOCA, and thus more studies are needed on MINOCA patients.

Conclusions:-

In the present study, we showed that the prevalence of MINOCA in North India is 6.2% in patients who were admitted with MI. Also, as compared to non-MINOCA patients, the MINOCA patients were exposed to fewer traditional risk factors of CAD.

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