Clinical and Experimental Health Sciences

Frequency of non-st elevation myocardial infarction in patient with normal electrocardiogram

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Abstract

Background: Non-ST elevation myocardial infarction (NSTEMI) may present without definitive electrocardiographic (ECG) abnormalities, posing a diagnostic challenge in emergency settings. Relying solely on ECG findings risks underdiagnosis of myocardial injury, particularly in patients with typical chest pain but normal ECG results.
Objective: To determine the frequency of NSTEMI in patients presenting with typical chest pain and normal electrocardiographic findings, using cardiac troponin I levels as the diagnostic standard.
Methods: This cross-sectional study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Karachi, over a period of six months. A total of 271 patients aged 18–70 years presenting with chest pain and normal ECG were enrolled using consecutive sampling. Patients with prior myocardial infarction, coronary interventions, or chronic kidney disease were excluded. Blood samples were collected to evaluate troponin I levels. NSTEMI was diagnosed if troponin I exceeded >0.05 ng/dL for males and >0.03 ng/dL for females. Data were analyzed using SPSS version 23, with statistical significance set at $p \leq 0.05$.
Results: Among the 271 patients, 168 (62%) were male, and the mean age was 47.8 ± 13.1 years. NSTEMI was diagnosed in 65 patients (24%), despite normal ECG findings. Higher NSTEMI frequencies were observed among diabetics (33%), hypertensives (28.4%), and urban residents (25.1%). The majority of patients with elevated troponin levels had no specific ECG changes at presentation.
Conclusion: A significant proportion of patients with chest pain and normal ECGs were diagnosed with NSTEMI, indicating that ECG alone is insufficient for ruling out myocardial infarction. Routine troponin testing is essential to prevent missed diagnoses and enable timely intervention.
Keywords: Acute Coronary Syndrome, Biomarkers, Chest Pain, Electrocardiography, Myocardial Infarction, NSTEMI, Troponin I

Introduction

Coronary artery disease (CAD) remains a leading global health concern, responsible for significant morbidity and mortality across both developed and developing nations. In 2016 alone, CAD accounted for 43.2% of deaths from cardiovascular disease in developed countries, surpassing stroke and hypertension, which were responsible for 16.9% and 9.8% of such deaths respectively (1). Cardiovascular diseases collectively caused approximately 17.6 million deaths globally in 2016, a figure that has remained consistent over previous years and is expected to rise to more than 23.6 million by 2030 (2,3). According to the World Health Organization, an estimated 31% of global deaths are attributed to cardiovascular causes, with CAD alone contributing to approximately 7.4 million deaths annually (4). Among the various clinical manifestations of CAD, acute coronary syndrome (ACS) presents as a medical emergency that necessitates immediate attention and intervention. ACS represents a spectrum of clinical presentations resulting from myocardial ischemia, primarily due to reduced coronary artery blood flow. This deprives portions of the myocardium of adequate oxygenation, leading to functional impairment and tissue damage (5,6). The diagnosis and classification of ACS are primarily guided by electrocardiographic (ECG) findings and cardiac biomarkers such as troponin and CK-MB. Based on these parameters, ACS is broadly categorized into ST-elevation ACS (STE-ACS) and non-ST-elevation ACS (NSTE-ACS) (7). While STE-ACS is characterized by ST-segment elevation and often leads to a swift diagnosis, NSTE-ACS presents a more complex diagnostic challenge. Patients with NSTE-ACS may show ST-segment depression, T wave inversions, or, in some cases, no definitive ECG abnormalities at all. This subset includes unstable angina (UA) with normal troponin levels and non-ST elevation myocardial infarction (NSTEMI) where troponin levels are elevated despite the absence of ST-segment elevation (8,9).

A critical concern arises when patients presenting with classic chest pain indicative of myocardial ischemia display normal ECG findings. Although a normal ECG may suggest a lower short-term risk of adverse outcomes, it does not reliably exclude the presence of myocardial injury or NSTEMI. In fact, numerous studies have emphasized the diagnostic limitations of ECG in isolation. For instance, research found that 24.67% of patients with normal ECG were later confirmed to have NSTEMI based on elevated troponin levels (10). Similarly, a study reported NSTEMI in 22.8% of patients who initially presented with a normal ECG (11). These findings underscore the need for heightened clinical vigilance and the routine assessment of cardiac biomarkers in all patients presenting with chest pain, regardless of initial ECG results. Despite these insights, routine clinical practice often overlooks the possibility of NSTEMI in patients with nondiagnostic ECGs, leading to potential underdiagnosis and missed opportunities for timely intervention. Given the high stakes of untreated myocardial injury, it is imperative to broaden diagnostic protocols to include troponin evaluation in patients with normal ECGs presenting with typical ischemic chest pain. The current study aims to address this diagnostic gap by determining the frequency of NSTEMI in patients presenting with chest pain and normal ECG findings, thereby reinforcing the necessity for comprehensive biomarker assessment in such cases. The objective of this study is to determine the frequency of non-ST elevation myocardial infarction in patients with normal electrocardiographic findings who present with chest pain, thus highlighting the importance of incorporating troponin testing into the diagnostic workflow for early detection and prevention of adverse cardiac outcomes.

Methods

This cross-sectional study was conducted in the Department of Cardiology at the National Institute of Cardiovascular Diseases (NICVD), Karachi, over a minimum period of six months following the approval of the research synopsis by the College of Physicians

and Surgeons Pakistan (CPSP) and the Institutional Review Board (IRB). Ethical clearance was obtained prior to initiation of the study, and written informed consent was taken from each participant after clearly explaining the study objectives, procedures, and voluntary nature of participation. Confidentiality and data privacy were strictly maintained throughout the study in accordance with ethical research standards. The study population included patients aged between 18 and 70 years who presented to the emergency department with chest pain fulfilling the operational definition of typical anginal pain lasting more than 20 minutes. Only those patients with normal electrocardiographic (ECG) findings at presentation were included. The diagnosis of a normal ECG was confirmed at the time of enrollment using standard 12-lead ECG interpretation. Both male and female patients were eligible for inclusion. Patients with a known history of myocardial infarction, prior coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), or chronic kidney disease requiring renal replacement therapy were excluded to minimize confounding effects on cardiac biomarker interpretation and overall cardiovascular risk profile (12).

A total sample size of 271 patients was calculated using the WHO sample size calculator, with a 95% confidence level, 5% margin of error, and an expected prevalence of NSTEMI in patients with normal ECG set at 22.8% based on previous literature (9). Participants were recruited through a consecutive nonprobability sampling technique to ensure practical feasibility while maintaining representative sampling within the study setting. Upon enrollment, each participant underwent detailed assessment including recording of baseline demographic and clinical data. This included age, gender, residential status (urban/rural), family monthly income, history of diabetes mellitus, hypertension, dyslipidemia, smoking status (current or ex-smoker), family history of cardiovascular disease (CVD), duration of chest pain, height, weight, and body mass index (BMI). All measurements were obtained using standardized instruments—digital weighing scales for weight and wall-mounted stadiometers for height. Smoking history was classified based on established criteria, where individuals who had smoked ≥100 cigarettes in their lifetime and within the past month were labeled current smokers, while those who had not smoked in the past month were considered ex-smokers.

A 5 cc venous blood sample was collected under aseptic conditions by trained phlebotomists for the measurement of cardiac troponin I levels. Troponin I was used as the diagnostic marker for NSTEMI, with a cutoff of >0.05 ng/dL for males and >0.03 ng/dL for females (13,14). All laboratory assessments were performed using validated assays in the hospital's central lab. Data entry and statistical analysis were conducted using IBM SPSS Statistics version 23. The Shapiro-Wilk test was applied to assess the normality of continuous variables. For normally distributed data, mean and standard deviation (SD) were reported, while non-normally distributed variables were presented as median with interquartile range (IQR). Quantitative variables included age, income, BMI, duration of chest pain, and troponin I levels. Categorical variables, such as gender, residence, smoking status, comorbidities, and NSTEMI diagnosis, were expressed as frequencies and percentages. Stratification was performed based on potential confounding factors including age, gender, residence, income, BMI, diabetes, hypertension, dyslipidemia, smoking, duration of chest pain, and family history of CVD. Chi-square or Fisher's exact test, as appropriate, was used post-stratification to evaluate associations, with a p-value ≤0.05 considered statistically significant.

Results

The study enrolled a total of 271 patients presenting with chest pain and normal electrocardiography (ECG) findings. The mean age of participants was 47.8 ± 13.1 years. Of the total, 168 (62%) were male and 103 (38%) were female. The mean body mass index (BMI) was 26.3 ± 4.7 kg/m². Regarding socioeconomic distribution, 80 patients (29.5%) belonged to the lower-income group, 143 (52.8%) to the middle-income group, and 48 (17.7%) to the upper-income group. Most of the participants, 187 (69%), resided in urban areas, while 84 (31%) were from rural backgrounds. In terms of occupational status, 159

(58.7%) were employed, and 112 (41.3%) were unemployed. The median duration of chest pain prior to presentation was 2.5 hours, with an interquartile range (IQR) of 1.0 to 5.0 hours. Comorbidity profiles revealed that 94 patients (34.7%) were diabetic, 102 (37.6%) were hypertensive, and 89 (32.8%) had dyslipidemia. Smoking was reported in 76 patients (28%), while 58 patients (21.4%) had a documented family history of cardiovascular disease (CVD). Evaluation of cardiac biomarkers showed that 65 patients (24%) had elevated troponin I levels (≥ 0.03 ng/dL for females and ≥ 0.05 ng/dL for males), confirming the diagnosis of non-ST elevation myocardial infarction (NSTEMI), while the remaining 206 patients (76%) had normal troponin I levels. The overall frequency of NSTEMI in patients with normal ECG findings and typical chest pain was therefore 24%. Stratified analysis indicated a higher frequency of NSTEMI among diabetic patients compared to non-diabetics (31 vs. 34), with NSTEMI being present in 33% of diabetic individuals and 19.2% of non-diabetics. A similar trend was observed in hypertensive patients, among whom 28.4% were diagnosed with NSTEMI, compared to 20.1% in non-hypertensives. The occurrence of NSTEMI was slightly higher in males (25.6%) compared to females (21.4%), although this difference was not statistically significant. Urban residents had a marginally higher frequency of NSTEMI (25.1%) than rural residents (21.4%). The findings suggest that a notable proportion of patients with normal ECGs presenting with chest pain may still have underlying myocardial injury, reinforcing the need for routine troponin evaluation in such presentations to prevent missed diagnoses of NSTEMI.

Table 1: Demographic Characteristics of Study Participants (n = 271)

Variable	Categories	Values
Age (years)		47.8 ± 13.1
Gender	Male	168 (62%)
	Female	103 (38%)
BMI (kg/m²)		26.3 ± 4.7
Socioeconomic Status	Lower	
	Middle	
	Upper	
Occupation Status	Employed	
	Unemployed	
Residence	Urban	
	Rural	

Table 2: Clinical Characteristics of Participants

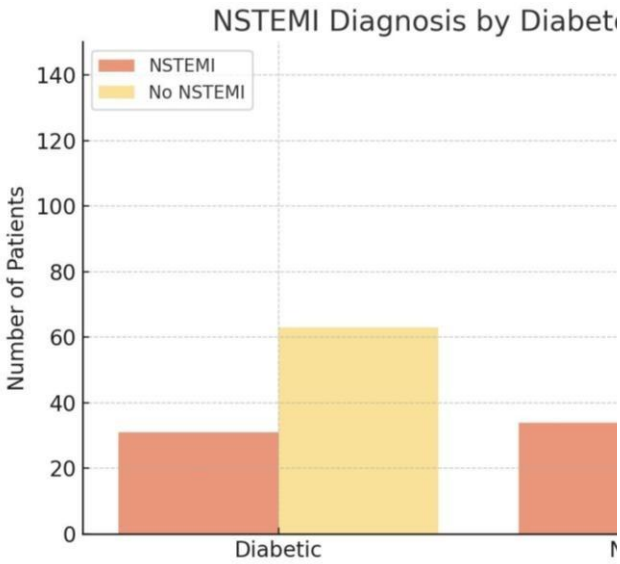
Variable	Categories
Duration of Chest Pain	
Diabetes	Yes
	No
Hypertension	Yes
	No
Dyslipidemia	Yes
	No
Smoking	Yes
	No
Family History of CVD	Yes
	No

Table 3: Troponin I Levels

Troponin I Level
< 0.03 ng/dL (Normal)
≥ 0.03 ng/dL (Raised)

Table 4: NSTEMI Diagnosis

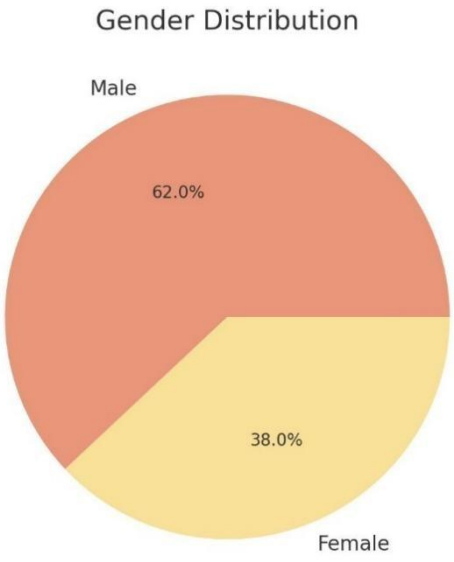
NSTEMI Diagnosis
Yes
No



Discussion

The present study found that 24% of patients with typical chest pain and normal electrocardiography (ECG) were diagnosed with non-ST elevation myocardial infarction (NSTEMI) based on elevated troponin I levels. This finding aligns closely with previously reported frequencies of 22.8% in a similar Pakistani cohort (13), suggesting a consistent prevalence of myocardial injury in patients with ACS who present with non-diagnostic ECGs. Electrocardiography remains a cornerstone in the early evaluation of acute coronary syndromes; however, its sensitivity in NSTEMI is limited due to the absence of definitive ST-segment elevations (14). Several studies have emphasized that a significant proportion of NSTEMI patients may present with either non-specific ECG changes or entirely normal tracings (15,16). A recent cross-sectional analysis confirmed that normal ECG findings may not exclude underlying myocardial damage, especially when used in isolation without biomarker correlation (17). This highlights a critical diagnostic gap where reliance solely on ECG may delay identification and management of at-risk individuals. Several pathophysiological mechanisms may explain normal ECGs in NSTEMI patients, including infarctions in electrically silent myocardial territories, transient ischemia with reperfusion, and well-developed collateral circulation minimizing electrical disturbance (18). Moreover, novel diagnostic tools such as ischemiamodified albumin and oxidative stress markers have shown promise in detecting subtle myocardial injury when traditional methods fall short (19).

This study's observation that diabetics and hypertensives had a higher frequency of NSTEMI further reinforces established evidence linking these comorbidities to greater cardiovascular risk. Echo findings and advanced ECG markers like T/QRS ratio have also demonstrated value in earlier diagnosis of NSTEMI when standard ECG findings are inconclusive (20). Combining these diagnostic modalities with highsensitivity troponin assays could dramatically enhance early detection and management, as shown in a recent multinational trial (21). From a clinical



perspective, these findings underscore the necessity for integrating cardiac biomarker testing in all patients presenting with chest pain, irrespective of ECG findings. This approach is vital for early detection of myocardial necrosis, timely initiation of therapeutic interventions, and improved prognostic outcomes. Delay or failure to diagnose NSTEMI due to overreliance on a normal ECG can result in missed opportunities for guideline-directed therapy, as highlighted by a study that nearly one-third of clinically misdiagnosed NSTEMI cases led to premature cardiovascular mortality (22).

One notable strength of this study was its focused inclusion criteria and prospective data collection, which minimized confounding from prior cardiac interventions. The use of a single-center tertiary care setting ensured procedural consistency in ECG interpretation and troponin measurement. However, certain limitations must be acknowledged. First, the absence of serial troponin measurements could have led to underestimation of late-rising biomarkers. Second, exclusion of patients with renal dysfunction may limit generalizability, as such individuals often present with elevated troponin and cardiovascular risk. Third, echocardiographic correlation, which could have strengthened diagnostic validity in ECG-silent cases, was not performed. Future research should focus on multi-modality diagnostic algorithms that combine ECG, cardiac biomarkers, and imaging. Larger multicenter studies are also warranted to evaluate population-level trends, particularly in high-risk groups such as the elderly, diabetics, and patients with atypical symptoms. Machine learning applications may further enhance diagnostic prediction models using subtle ECG and biomarker data, as recently explored in emerging AI-based studies (23). In summary, the current study confirms that a significant proportion of patients with ACS and normal ECGs may have underlying NSTEMI, justifying the inclusion of cardiac biomarker assessment in all chest pain protocols. Failure to do so risks underdiagnosis and adverse clinical outcomes. Emphasizing an integrated approach combining ECG, troponins, and potentially point-of-care imaging could enhance diagnostic accuracy and optimize patient care pathways.

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Conclusion

This study demonstrated that nearly one in four patients presenting with chest pain and a normal ECG had elevated troponin levels confirming NSTEMI, underscoring the diagnostic limitations of ECG alone. Routine assessment of cardiac biomarkers is therefore essential for accurate detection of myocardial injury. These findings advocate for a more comprehensive and vigilant diagnostic approach in emergency settings to prevent missed diagnoses and improve patient outcomes.

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