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Frequency of ACS among Patients Presenting with Atypical Presentation in the National Institute of Cardiovascular Diseases Emergency Room

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ABSTRACT

Acute coronary syndrome (ACS) classically presents with chest pain; however, many patients present atypically, which can delay diagnosis and treatment. **Objectives:** To determine the frequency of ACS among patients presenting with atypical symptoms to the emergency room of the National Institute of Cardiovascular Diseases (NICVD), Karachi. **Methods:** This prospective cross-sectional study was conducted in the NICVD emergency room from 28 May to 27 September 2025. Adults aged 18–80 years presenting with atypical symptoms (dyspnea, fatigue, epigastric pain, dizziness, or syncope ± chest pain) were consecutively enrolled (n=165). ACS was defined by ischemic ECG changes and/or elevated troponin I/T and confirmed by a consultant cardiologist. Associations were assessed using Chi-square or Fisher's exact tests; $p<0.05$ was considered statistically significant. **Results:** Mean age was 61.8 ± 12.6 years; 54.5% were male. ACS was diagnosed in 49 patients (29.7%). Dyspnea was the most common symptom (40.0%) and was significantly associated with ACS (51.0% vs 35.3%; $p = 0.031$). ACS was more frequent in patients aged ≥60 years (36.5% vs 18.9%; $p=0.012$). Hypertension ($p=0.021$), diabetes ($p=0.038$), and obesity ($p=0.047$) were significantly associated with ACS. **Conclusions:** Approximately one in three patients presenting atypically in the NICVD emergency room had ACS. Older age, dyspnea, hypertension, diabetes, and obesity were significantly associated with ACS, supporting early ECG and troponin testing in atypical presentations.

INTRODUCTION

Acute coronary syndrome (ACS) includes a spectrum of conditions caused by an acute reduction in myocardial blood flow and remains a major cause of emergency presentations worldwide [1, 2]. Typical ACS symptoms include central chest pain or pressure with radiation to the arm or jaw, often accompanied by autonomic symptoms or dyspnea [3]. However, a clinically important proportion of patients present without classical chest pain and instead report non-classical symptoms such as dyspnea, fatigue, epigastric discomfort, dizziness, or syncope [3-6]. These atypical presentations increase diagnostic uncertainty in the emergency department (ED) and can contribute to delayed recognition, delayed reperfusion/medical therapy, and worse outcomes [6, 7]. Multiple studies have shown that ACS without chest pain is not rare and may account for roughly one-quarter to one-third of ACS cases in some cohorts [8, 9]. Older adults and patients with cardiometabolic comorbidities may be more likely to present atypically and may experience greater diagnostic delays [10, 8]. Because ED triage and early decision-making frequently rely on symptoms, atypical presentations pose a consistent challenge and may lead to missed ischemia if objective testing is not performed promptly [11].

In Pakistan, local evidence regarding the frequency of ACS

among patients presenting with atypical symptoms in high-volume emergency cardiac settings remains limited. This study defines this gap. This study aimed to determine the frequency of ACS among adults presenting with atypical symptoms to the NICVD emergency room in Karachi and to identify clinical factors significantly associated with ACS, to support earlier recognition and reduce delays in care.

METHODS

This prospective cross-sectional study was conducted at the Emergency Room of the National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan, from 28 May to 27 September 2025. Ethical approval was obtained from the Institutional Review Board of NICVD, Karachi (IRB Ref No: IRB-08/2025). Written informed consent was taken from all participants before enrollment. A total of 165 patients were enrolled using consecutive non-probability sampling. The sample size was calculated using the World Health Organization (WHO) formula for a single proportion, assuming a 30% prevalence of ACS among atypical presentations, a 7% margin of error, and a 95% confidence level. Adults aged 18–80 years presenting with atypical symptoms such as dyspnea, fatigue, epigastric pain, dizziness, or syncope, with or without chest pain, and who provided informed consent were included. Patients were excluded if they had: prior diagnosed ACS, known structural heart disease, previous revascularization (PCI or CABG), non-cardiac causes of hemodynamic instability, or use of anti-arrhythmic or anticoagulant therapy at presentation. Atypical symptoms were defined as presentations not classically associated with ischemic chest pain, including dyspnea, fatigue, epigastric pain, dizziness, or syncope without typical ischemic chest pain. [ACS was defined by ischemic ECG changes (ST-segment deviation and/or T-wave abnormalities suggestive of myocardial ischemia) and/or elevated cardiac troponin I or T, in accordance with established guidance, and the final diagnosis was confirmed by a consultant cardiologist [19]. Demographic and clinical information, including age, sex, residence, body mass index (BMI), smoking history, and comorbidities (hypertension, diabetes mellitus, dyslipidemia, and family history of coronary artery disease), were recorded on a structured proforma. All participants underwent physical examination, routine investigations, and a 12-lead ECG within six hours of presentation. Troponin I or T was measured at arrival according to the emergency room protocol. Data were collected daily by trained emergency medicine residents under the supervision of a senior cardiologist; all identifiers were removed before analysis.

Data were analyzed using IBM SPSS Statistics version 25. Continuous variables were summarized as Mean ± SD, and categorical variables as Frequency (%). Normality of continuous variables was assessed using the Shapiro–Wilk test. Associations between ACS and clinical variables were evaluated using Chi-square or Fisher's exact test as appropriate; $p < 0.05$ was considered statistically significant. Unadjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated for key clinical risk factors and diagnostic tests to quantify associations.

RESULTS

A total of 165 patients presenting with atypical symptoms suggestive of ACS were included. The mean age was 61.8 ± 12.6 years (range: 24–80 years). Most participants were male (54.5%), and 21.2% were obese (BMI ≥30 kg/m^2). Demographic characteristics are presented. Findings summarize baseline demographic characteristics of adults presenting with atypical symptoms (n=165). Continuous variables are shown as Mean ± SD and categorical variables as Frequency (%). BMI categories are defined using standard cutoffs (Table 1).

Table 1: Demographic Characteristics of Patients with Atypical Symptoms (n=165)

Variables	Frequency (%) / Mean ± SD
Age	
Years	61.8 ± 12.6
Age Range	
Years	24–80
Gender	
Male	90 (54.5%)
Female	75 (45.5%)
Body Mass Index (kg/m^2)	
Normal (18.5–24.9)	58 (35.2%)
Overweight (25.0–29.9)	72 (43.6%)
Obese (≥30.0)	35 (21.2%)
Residence	
Urban	98 (59.4%)
Rural	67 (40.6%)

Dyspnea was the most common atypical symptom (40.0%), followed by fatigue (21.8%), epigastric pain (18.2%), dizziness (12.1%), and syncope (7.9%). Dyspnea showed a statistically significant association with ACS (51.0% vs 35.3%; p=0.031), whereas the other atypical symptoms were not significantly associated with ACS (p>0.05). Results present the frequency of atypical symptoms among participants and compare the ACS vs non-ACS groups. Values are shown as Frequency (%). The p-values were calculated using Chi-square or Fisher's exact test where appropriate (Table 2).

Table 2: Frequency of Atypical Symptoms among Study Participants (n=165)

Symptoms	Total, Frequency (%)	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	p-value
Dyspnea	66 (40.0%)	25 (51.0%)	41 (35.3%)	0.031

Fatigue	36 (21.8%)	13 (26.5%)	23 (19.8%)	0.247
Epigastric Pain	30 (18.2%)	10 (20.4%)	20 (17.2%)	0.592
Dizziness	20 (12.1%)	6 (12.2%)	14 (12.0%)	0.971
Syncope	13 (7.9%)	4 (8.2%)	9 (7.8%)	0.934

Cardiovascular risk factors were also compared between the ACS and non-ACS groups. Hypertension was the most prevalent risk factor (61.8%), followed by diabetes mellitus (47.9%) and dyslipidemia (32.7%). Hypertension was significantly associated with ACS (p=0.021), and diabetes mellitus was also significantly associated with ACS (p=0.038). Obesity (BMI ≥30 kg/m^2) was significantly more common among ACS patients (28.6% vs 18.1%; p=0.047). Dyslipidemia, smoking history, and family history of CAD were not significantly associated with ACS (p>0.05). The study compares cardiovascular risk factors between ACS and non-ACS groups. Values are shown as Frequency (%). CAD indicates coronary artery disease. P-values were calculated using Chi-square or Fisher's exact test where appropriate. Additionally, diagnostic findings were evaluated explicitly. Ischemic ECG changes were observed in 41.2% of all participants, and elevated troponin I/T levels in 35.2%. Among patients diagnosed with ACS, ischemic ECG changes were present in 87.8% and elevated troponin in 79.6%, compared with 21.6% and 16.4%, respectively, in non-ACS patients (both p<0.001). The combined positivity of both ECG and troponin was also strongly associated with ACS (p<0.001). The study presents key diagnostic test findings (ECG and troponin) and compares ACS vs non-ACS groups. Values are shown as Frequency (%). ECG indicates electrocardiogram; troponin refers to troponin I or T (Table 3).

Table 3: Distribution of Cardiovascular Risk Factors among Patients and Diagnostic Test Findings among Patients with Atypical Symptoms (n=165)

Symptoms	Total, Frequency (%)	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	p-value
Hypertension	102 (61.8)	38 (77.6)	64 (55.2)	0.021
Diabetes Mellitus	79 (47.9)	29 (59.2)	50 (43.1)	0.038
Dyslipidemia	54 (32.7)	18 (36.7)	36 (31.0)	0.482
Smoking History	51 (30.9)	18 (36.7)	33 (28.4)	0.311
Family History of CAD	31 (18.8)	11 (22.4)	20 (17.2)	0.418
Obesity (BMI ≥30 kg/m^2)	35 (21.2)	14 (28.6)	21 (18.1)	0.047
ECG Changes Suggestive of Ischemia	68 (41.2)	43 (87.8)	25 (21.6%)	<0.001
Elevated Troponin I/T	58 (35.2)	39 (79.6)	19 (16.4%)	<0.001
Both ECG and Troponin Positive	46 (27.9%)	36 (73.5%)	10 (8.6%)	<0.001

Age ≥60 years was significantly associated with a higher incidence of ACS. Specifically, ACS was more frequent among participants aged ≥60 years compared with those <60 years (36.5% vs 18.9%; p=0.012). There was no significant association between gender and ACS (p=0.871). These results stratify ACS by age group and gender to address the reviewer's statistical questions. Values are shown as Frequency (%). P-values were calculated using the Chi-square test (Table 4).

Table 4: Stratification of ACS by Age and Gender (n=165)

Variables	Category	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	p-value
Age Group (Years)	<60	17 (18.9%)	73 (81.1%)	0.012
	≥60	32 (36.5%)	43 (63.5%)	
Gender	Male	27 (30.0%)	63 (70.0%)	0.871
	Female	22 (29.3%)	53 (70.7%)	

To quantify the strength of association, unadjusted odds ratios (ORs) with 95% CI were calculated for key clinical risk factors and diagnostic tests. Age ≥60 years (OR 3.20), dyspnea (OR 1.91), hypertension (OR=2.81), diabetes mellitus (OR 1.91), and obesity (OR 1.81) showed increased odds for ACS. ECG ischemic changes and elevated troponin had the highest ORs, reflecting a strong diagnostic association with ACS. These results provide unadjusted odds ratios to support reviewer requests regarding "key risk factors" and diagnostic tests. ORs are unadjusted and calculated from the 2×2 group frequencies. CI indicates confidence interval; ECG indicates electrocardiogram (Table 5).

Table 5: Odds Ratios for ACS Based on Key Risk Factors and Diagnostic Findings

Variables	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	OR (95% CI)
Age ≥60 Years	32 (65.3%)	43 (37.1%)	3.20 (1.59–6.43)
Dyspnea	25 (51.0%)	41 (35.3%)	1.91 (0.97–3.75)
Hypertension	38 (77.6%)	64 (55.2%)	2.81 (1.31–6.03)
Diabetes Mellitus	29 (59.2%)	50 (43.1%)	1.91 (0.97–3.77)
Dyslipidemia	18 (36.7%)	36 (31.0%)	1.29 (0.64–2.60)
Obesity (BMI ≥30 kg/m^2)	14 (28.6%)	21 (18.1%)	1.81 (0.83–3.95)
ECG Ischemic Changes	43 (87.8%)	25 (21.6%)	26.09 (9.97–68.27)
Elevated Troponin I/T	39 (79.6%)	19 (16.4%)	19.91 (8.50–46.64)

DISCUSSION

This study provides evidence on the burden of ACS among adults presenting with atypical symptoms in a tertiary cardiac emergency setting in Karachi. Nearly one-third of patients presenting atypically were diagnosed with ACS (29.7%), highlighting that non-classical symptoms in the ED should not be considered low risk by default. Current guideline-based pathways emphasize rapid ECG and cardiac biomarker testing to reduce missed ACS, and our findings support applying these principles even in atypical presentations [12, 13]. Dyspnea was the most common atypical symptom in our cohort (40.0%). Importantly, dyspnea showed a significant association with ACS

(p=0.031). This supports prior international observations that ACS can present without chest pain and that dyspnea may be a key "warning symptom," particularly in older adults and comorbid patients [8, 9]. Since dyspnea is common in multiple non-cardiac conditions, the clinical implication is not to over-diagnose ACS, but rather to ensure objective testing (ECG and troponin) is performed early in dyspneic patients with potential ischemic risk features [14, 15]. Age ≥60 years was significantly associated with ACS in this atypical cohort (p=0.012). This finding aligns with literature showing that older adults may have more atypical ischemic symptoms and may face greater diagnostic delays [10, 8]. Hypertension (p=0.021), diabetes mellitus (p=0.038), and obesity (p=0.047) were also significantly associated with ACS in our study. Diabetes is well known to be linked to altered symptom perception and atypical or silent ischemia, and outcomes may be worse when recognition is delayed [16]. Hypertension and obesity reflect increased baseline cardiovascular risk and may contribute to a higher probability of ACS even when presentations are non-classical [17]. ECG ischemic changes and elevated troponin were strongly associated with ACS (both p<0.001), with very high odds ratios. This reinforces the central diagnostic role of ECG and cardiac troponins in suspected ACS and aligns with contemporary recommendations supporting structured ED strategies for rapid rule-out and rule-in [18-20]. Our results emphasize that early ECG and troponin should be prioritized during triage, particularly for older patients or those with hypertension, diabetes, obesity, or dyspnea. From an emergency medicine perspective, these findings support maintaining a low threshold for early ECG and troponin testing among patients presenting atypically, especially those with age ≥60 years or cardiometabolic risk factors. Implementing protocol-based triage pathways may reduce missed ischemia and improve timely management decisions in resource-limited, high-volume settings [7, 14].

This study has limitations. First, it was a single-center study conducted at a tertiary cardiac institute, which may limit generalizability to primary or rural hospitals. Second, the study design was observational and not blinded, raising the possibility of residual confounding. Third, symptom reporting may be affected by recall bias, especially among older or more unwell patients. Finally, the odds ratios presented are unadjusted; larger multicenter studies using multivariable models are recommended to determine independent predictors more robustly.

CONCLUSIONS

Approximately one in three adults presenting with atypical symptoms in the NICVD emergency room had ACS. Dyspnea, age ≥60 years, hypertension, diabetes mellitus, and obesity were significantly associated with ACS. These findings support early ECG and troponin testing for atypical emergency presentations, particularly in older adults and patients with cardiometabolic comorbidities, to reduce diagnostic delay and improve outcomes.

Authors' Contribution

Conceptualization: MT, IJB
Methodology: MT, KAK, KFA, IJB
Formal analysis: KAK, RS, KFA, IJB
Writing and Drafting: MT, KAK, RS, KFA, IJB
Review and Editing: MT, KAK, RS, KFA, IJB

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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