

A Study of Angiographic Profile and Clinical Outcomes in Women with Acute Coronary Syndrome

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Abstract

Introduction: Cardiovascular disease (CVD) is the leading cause of mortality for women in India and globally. Coronary artery disease (CAD) has traditionally been considered a disease of men.

Aims and Objectives: The aim of the study was to study the clinical profile, risk factors, and extent of CAD in women with an acute coronary syndrome.

Materials and Methods: A total of 50 patients fulfilling the inclusion criteria will be a part of this study. Patients admitted in the Cardiology Department of Nizam's Institute Of Medical Sciences, Telangana.

Observations and Results: A total of 50 subjects were enrolled in the study after meeting the inclusion criteria. The enrollment period was from November 2018 to December 2018. Out of these 36 (72%) had ST segment elevation myocardial infarction (STEMI), 9 (18%) were non-STEMI, and 5 (10%) were diagnosed as unstable angina.

Conclusions: The incidence of CAD increases with age in females with more adverse outcomes in elderly females. Risk scoring systems such as Killip's Class and TIMI score were fairly accurate in female patients in predicting adverse outcomes and complications.

Key words: Acute Coronary Syndrome, Angiogram, Unstable angina

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of mortality for women in India and globally.^[1] Coronary artery disease (CAD) has traditionally been considered a disease of men. The Global Burden of Disease Study reported that the disability-adjusted life year lost by CAD in India during 1990 was 5.6 million in men and 4.5 million in women; the projected figures for 2020 were 14.4 million

and 7.7 million in men and women, respectively.^[2] The annual CVD mortality rate has remained greater for women than for men.

There are important sex differences in the pathophysiology, clinical presentation, and clinical outcomes of CAD in women.^[2] Women's health involves two aspects Sex differences resulting from biological factors and gender differences affected by broader social, environmental, and community factors.

Obstructive atherosclerotic disease of the epicardial coronary arteries remains the basic cause of acute myocardial infarction (AMI) in both sexes, plaque characteristics differ for women, and recent data have suggested a greater role of microvascular disease in the pathophysiology of coronary events among women.^[3]

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Women are often older when they present with their first AMI, at an average age of 71.8 years compared with 65 years for men.^[4] Recently, an increase in CAD incidence and deaths among women 45–54 years of age have been observed in various studies. Asian Indian women have greater proportionate mortality burden from CAD compared with non-Hispanic White women, particularly at a younger age because of more comorbidities (e.g., diabetes mellitus [DM], Hypertension [HTN], heart failure [HF], and obesity) at the time of presentation with AMI.^[5]

Certain risk factors are more potent in women, include tobacco abuse, type 2 DM, depression, and other psychosocial risk factors. The INTERHEART study data identified nine potentially modifiable risk factors (smoking, HTN, DM, waist-hip ratio, dietary patterns, physical activity, alcohol consumption, plasma apolipoproteins, and psychosocial factors) that account for 96% of the population attributable risk of AMI in women.^[6]

Compared with men, women are more likely to have high-risk presentations and less likely to manifest central chest pain.^[6] Women are undertreated with guideline-based recommendations, leading to worse outcomes and increased rates of readmission, reinfarction, and deaths in the 1st year after AMI.

Despite their substantial burden of CVD, women have been underrepresented in clinical trials of CVD, generally making up only ≈20% of enrolled patients. Thus, a considerable research gap exists in the knowledge of sex-specific examination of coronary pathophysiology; optimal diagnostic strategies; effective lifestyle, pharmacological, and invasive interventions.^[7]

Women's heart health is not only solely a medical issue but also involves economic, legal and regulatory, psychosocial, ethical, faith-based, cultural, environmental, community, health systems, and political and public policy issues locally and globally.

Considering the high burden of CAD in women there is a need for sex-specific data about pathophysiology of atherosclerotic disease, risk factor stratification, causes of treatment delay, rate of complications, angiographic profile, and treatment strategies.^[8] Hence, the present study is undertaken to improve the knowledge about presentation of acute coronary syndrome (ACS) in women in an urban tertiary care setting.

Aims and Objectives

The aim of the study was to study the clinical profile, risk factors, and extent of CAD in women with an ACS and to evaluate the in-hospital course and outcome of therapies in women with ACS.

MATERIAL AND METHODS

Study Site

Patients admitted to the Cardiology Department of Nizam's Institute of Medical Sciences, Telangana.

Study Population

The subjects will be female patients, who would present the first time with a diagnosis of ACS within a week of symptoms onset at our hospital. Once the patients will meet the inclusion and exclusion criteria as defined, they will be enrolled in the study after signing the informed consent.

Study Design

This was a prospective observational study.

Sample Size

A total of 50 patients fulfilling the inclusion criteria will be a part of this study.

Study Duration

The study will be performed from November 2018.

Inclusion Criteria

The following criteria were included in the study:

1. Female patients with symptoms of ACS within 7 days of presentation
2. Women with age 18 years or older
3. Women with first-time presentation with ACS
4. Women willing and able to provide informed, written consent.

Exclusion Criteria

Women with prior HF and prior ischemic heart disease were excluded from the study.

Methodology

Data is collected. During the in-hospital stay of the patient, and there will be no follow-up of patient after being discharged from the hospital. The data is collected from the patients and recorded in a prepared case report form. Demographic details, medical history, risk factors, investigations, complications rate, treatment, and hospitalisation details are collected.

ACS will be defined as a spectrum of conditions compatible with acute myocardial ischemia and/or infarction that are usually due to an abrupt reduction in coronary blood flow. Patients will be divided into three categories the diagnosis of acute MI will be done by third universal definition of acute myocardial infarction. As having unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI), or ST-elevation MI.

The absence of persistent ST-elevation is suggestive of NSTEMI/ACS. NSTEMI/ACS will be further subdivided on the basis of cardiac biomarkers of necrosis. If cardiac biomarkers are elevated, and the clinical context is appropriate, the patient is considered to have NSTEMI; otherwise, the patient is deemed to have UA.

The following data will be included for analysis:

1. Patients demographic profile:
2. Clinical presentation and physical examination Symptoms of ACS (Typical Symptoms or Atypical Symptoms) Time to presentation
3. CAD risk factor profile:
 - a. Current cigarette/bidi smoking or tobacco use
 - b. Dyslipidemia defined as the presence of any of the following Patients on lipid-lowering drugs or total cholesterol >240 mg/dl, TG >150 mg/dl, low-density lipoprotein (LDL) >130 mg/dl, and high-density lipoprotein (HDL) <50 mg/dl for females.

Diabetes mellitus Symptoms of diabetes and plasma glucose concentration ≥ 200 mg/dl or fasting blood sugar ≥ 126 mg/dl or 2-h postprandial ≥ 200 mg/dl.

- a. Hypertension (SBP ≥ 140 and/or DBP ≥ 90 mmHg and/or on anti-hypertensive treatment)
- b. Family history of CAD (first-degree relatives with CAD before the age of 55 years in men and 65 years in women),
- c. Obesity (defined using the body mass index (BMI) with a value >30 . BMI was calculated using Quetlet's formula (weight in kg/height in m^2).
- d. Psychosocial risk factors
- e. Physical inactivity (people who do not get the recommended level of regular physical activity).
4. Hematology investigations (CBC, renal function tests, lipid profile, and cardiac biomarkers)
5. ECG: On admission and regular intervals
6. Imaging studies
 - a. 2D echo was done within 24 hours of admission, chest Xray was done.
7. Coronary angiographic findings
 - a. Selective coronary angiogram will be done using the standard technique during hospital admission unless patient is not willing for CAG or has significant renal disease
 - b. Significant CAD is defined as diameter stenosis $>50\%$ in each major epicardial artery
 - c. Normal vessels were defined as the complete absence of any disease in the left main coronary artery (LMCA), left anterior descending (LAD), right coronary artery (RCA), and left circumflex (LCX) as well as in their main branches
 - d. Patients will be classified as having single-vessel disease (SVD), double-vessel disease (DVD) or triple vessel disease (TVD) accordingly.

8. Treatment received:
 - a. STEMI reperfusion strategies: Thrombolysis/percutaneous coronary intervention (PCI)/coronary artery bypass grafting (CABG) standard pharmacotherapy for STEMI as per guidelines
 - b. NSTEMI revascularization strategies: PCI/CABG Standard pharmacotherapy for NSTEMI as per guidelines.
9. Complications due to primary disease:
 - a. Cardiogenic shock
 - b. Mechanical complications (acute MR/ventricular septal rupture/left ventricular free wall rupture and tamponade)
 - c. Congestive cardiac failure/Left ventricular failure
 - d. Arrhythmias
 - e. Bleeding complications (major/minor bleeding)
 - f. In hospital death.

Statistical Methods

Continuous variables are presented as mean \pm SD or median if the data are unevenly distributed. Categorical variables are expressed as frequencies and percentages. The comparison of continuous variables between the groups was performed using student's *t* test. The data were summarized in the form of percent population.

RESULTS

A total of 50 subjects were enrolled in the study after meeting the inclusion criteria. The enrollment period was from November 2018 to December 2018. Out of these 36 (72%) had STEMI, 9 (18%) were NSTEMI, and 5 (10%) were diagnosed as UA.

Age

Most patients were in 61–70 years of age group across all ACS subtypes. The mean age was 62.1 ± 10 years.

Clinical Presentation

Chest pain

A total of 42 (84%) patients presented with chest pain Table 1. Out of these 31 (62%), patients presented with typical chest pain and 11 (22%) had atypical chest pain on presentation. Chest pain was absent in 8 (16%) patients. They had other associated symptoms.

Table 1: Associated symptoms in women

Symptoms	Number of patients	Percentage
Dyspnea	16	32
Sweating	13	26
Palpitations	2	4
Syncope	2	4
Vomiting	1	2

Time to Presentation

The average time from onset of symptoms to first medical contact was 24 h. In the STEMI group, patients who presented within 12 h were 27 (74.07%) and 9 (25.92%) patients came after 12 h of symptom onset.

Risk Factor Profile

Table 2: Risk factor distribution in ACS subtypes

	Overall (%)	UA (%)	NSTEMI (%)	STEMI (%)
HTN	35 (70)	3 (60)	8 (88.8)	24 (66.6)
DM	29 (58)	2 (40)	5 (57)	22 (60.6)
Obesity	17 (34)	1 (20)	2 (22.2)	14 (38.8)
Physical inactivity	19 (38)	2 (40)	4 (44.1)	13 (36.4)
Tobacco abuse	3 (4.3)	-	2 (22.2)	1 (4.1)
CVA/PVD	1 (3)	-	-	1 (7)
Family history	14 (30)	1 (20)	2 (6.7)	11 (33.3)

ACS: Acute coronary syndrome, HTN: Hypertension, DM: Diabetes mellitus, NSTEMI: Non-ST segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction, UA: Unstable angina, CVA: Cerebrovascular accident, PVD: Peripheral vascular disease

Type of ACS

Out of these, 36 (72%) had STEMI, 9 (18%) were NSTEMI, and 5 (10%) were diagnosed as UA.

Table 3: Type of ACS

Type of ACS	Total	Percentage
UA	5	10
NSTEMI	9	18
STEMI	36	72

ACS: Acute coronary syndrome, NSTEMI: Non-ST segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction, UA: Unstable angina

Echocardiography

Echocardiography revealed moderate mitral regurgitation (MR) in 3 (5.6%) patients, and all these patients had STEMI. Mild MR was present in 11 (22%) patients. The average ejection fraction was 47%.

Table 4: Echocardiographic findings in ACS subtypes

	UA	NSTEMI	STEMI
LVEF (%)	59.1 (SD±1.8)	57 (SD±3)	45 (SD±6)
Mild MR	-	4	7
Moderate MR	-	-	3
VSR	-	-	-

LVEF: Left ventricular ejection fraction, MR: Mitral regurgitation, ACS: Acute coronary syndrome, NSTEMI: Non-ST segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction, UA: Unstable angina, SD: Standard deviation

Coronary Angiography

Coronary angiogram was done in 50 (100%) patients as per standard protocol.

Table 5: Coronary angiogram findings in ACS subtypes

Findings	Total (%)	UA	NSTEMI	STEMI
Single vessel disease	22 (44.0)	2	2	18
Two vessel disease	13 (26)	1	2	10
Triple vessel disease	13 (26)	-	5	8
LMCA disease	4 (6.3)	-	2	2
Normal/mild disease	2 (4)	2	-	-

LCMA: Left main coronary artery, ACS: Acute coronary syndrome, NSTEMI: Non-ST segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction, UA: Unstable angina

Treatment Received

All 50 study patients received aspirin dose of 325 mg.

Furthermore, high dose statins (atorvastatin 40 mg/80 mg or Rosuvastatin 20 mg/40 mg) were used in all 50 study population. The second antiplatelet was used in 48 patients.

Clopidogrel was used in 20 (42%), prasugrel was used in 9 (18%), and ticagrelor was used in 19 (39%) study population.

Mortality

In the study population, 2 (4%) patients died during a hospital stay. Both women were above 60 years of age and average age was 71 years. Both patients had STEMI. The average time from onset of symptoms to first medical contact was 20 h. Out of these, both patients had DM, both patients had hypertension, and 1 patient was obese.

In both these patients, Killip’s class was >3 and TIMI risk score was >9. Both of these underwent coronary angiography. One patient had TVD and 1 patient had DVD with LMCA. One patient underwent primary PCI.

One patient had ventricular tachycardia, and the other had a complete heart block requiring temporary pacemaker support. Out of 2 patients, 1 died due to cardiogenic shock and 1 patient died due to ventricular tachycardia.

DISCUSSION

Gender disparity in cardiac diagnosis and treatment has been investigated thoroughly in multiple trials Table 2. This study highlights the clinical features of ACSs in women, an underemphasized study group.

Most patients in our study belonged to 61–70 years stratified age groups across all ACS subtypes. The mean age was 62.1 ± 10 years Table 3.

Older the age, higher was the odds of in-hospital mortality. Both the 2 patients who died were more than 60 years of age. The average age was 71 years Table 4.

Clinical Presentation

In all the ACS subtypes, 42 (84%) patients presented with chest pain. Out of these, 31 (62%) patients presented with typical chest pain and 11 (22%) had atypical chest pain on presentation. Chest pain was absent in 8 (16.0%) patients Table 5.

In a study by Canto *et al.*, 28.2% of women presented without typical chest discomfort and gender-specific differences in MI presentation without chest discomfort became progressively smaller with advancing age. The in-hospital mortality rate was 14.6% for women and 10.3% for men. Younger women presenting without chest pain had greater hospital mortality than younger men without chest pain, and these sex differences decreased or even reversed with advancing age, with adjusted OR for 65–74 years, 0.91 (95% CI, 0.88–0.95), and 75 years or older, 0.81. Out of 2 patients who died in our study both had typical chest pain Table 6.

Table 6: Comparison of patients with chest pain

	With chest pain %	Without chest pain %
Our study	84	16
Canto <i>et al.</i>	71.8	28.2
Milner <i>et al.</i>	83.4	16.6

In our study, dyspnea was the presenting symptom in 16 (32%) patients with 4 of them had only dyspnea without any chest pain. Other associated symptoms were sweating 13 (26%), palpitations 2 (4%), syncope 2 (4%), and vomiting 1 (2%).

Milner *et al.* studied 127 men and 90 women with CAD. They concluded, among patients presenting to the emergency department with symptoms of coronary disease other than chest pain, there were several sex-related differences in symptoms. Dyspnea, nausea/vomiting, indigestion, fatigue, sweating, and arm or shoulder pain as presenting symptoms in the absence of chest pain were more frequent among women than men. Many cases of myocardial infarction in women go unrecognized, particularly at younger ages due to these atypical symptoms.

Time to Presentation

The average time from onset of symptoms to first medical contact was 24 h.

In the STEMI group, patients who presented within 12 h were 27 (75%) and 9 (25%) patients came more than 12 h of symptom onset.

In a similar study done by Veena Nanjappa *et al.*,¹⁹ in South Indian women, 16.7% women presented within 4 h after symptom onset and 58.3% presented more than 12 h after

symptom onset in the NSTEMI group; 18.1% patients in STEMI group presented within 4 h of symptom onset and 38.6% after 12 h. About 64.3% patients in UA group presented 12 h after symptom onset Table 7.

Table 7 : Comparison of patients on time to presentation

	<12 h %	>12 h %
Our study	75	25
Veena Nanjappa <i>et al.</i>	61.4	38.6

Compared with young men with AMI in the VIRGO trial, young women who were eligible for and received reperfusion therapy were more likely to present >6 h after symptom onset (35% vs. 23%; $P = 0.002$).

In our study, the average time from onset of symptoms to the first medical contact was 24 h in patients who had in-hospital mortality. This delay in seeking medical attention likely contributes to adverse outcomes in women. This delay is often due to lack of awareness of risk, passivity, inaccurate symptom attribution, and barriers to self-care.

Risk Factor Profile

The percentage of subjects with diabetes mellitus (55.5% in NSTEMI, 61.1% in STEMI, and 40% in UA) was much higher than in both CREATE registry (30.4%) and the INTERHEART study (30.2%) Table 8.

The percentage of hypertensives (88.8% of NSTEMI, 66.6% of STEMI, and 60% of UA) was also high when compared to the CREATE registry (37.7%) and the INTERHEART study (53.6%).

Obesity and physical inactivity were the next most common risk factors found in this study.

The mean BMI was 28.9 ± 3.23 kg/m². About 65.33% patients had BMI between 25 and 30 kg/m² and 28.66% patients fell into the obese category (i.e., BMI > 30 kg/m²).

Physical inactivity was present in 9 (18%) patients. Physical inactivity is associated with higher blood pressure, worse cholesterol levels, poorer glucose metabolism, poorer mental health, and obesity. Physical inactivity, quantified by a prolonged sitting time, has been shown to be an independent risk factor for CVD in women beyond leisure-time physical activity.

Table 8: Comparison of risk factors between our study and interheart study

	Our study %	Interheart study %
HTN	70	58
DM	58	30.6
Smoking	4.3	20.1
Obesity	34	45.6

HTN: Hypertension, DM: Diabetes mellitus

Tobacco abuse was found in only 3 (6%) patients. This justifies the fact that the overall rate of smoking is low among Indian women, particularly in urban areas Table 9. Only 8% of the women in Asian countries smoke compared to 60% men who smoke.

Associated CVDs like Cerebrovascular accident (CVA)/ Peripheral vascular disease (PVD) were present in 1 (2%) patient that patient presented with STEMI. Associated CVDs have more severe presentation and poorer outcomes.

Dyslipidemia

The mean total cholesterol level was higher in our study (191.4 mg/dl) than that found among MI cases in Tirupati, India (177.07 mg/dl). The same was noticed for mean LDL level also (163.9 mg/dl). However, the levels of the protective HDL were also found to be lower in our study (40.6 mg/dl) than in the earlier study (46 mg/dl).

The lipid abnormalities were present in 61.5% in the INTER-HEART study and in 38.75% in a study by Bhasin *et al.* It suggests a high prevalence of dyslipidemia in the female population.

Type of ACS

In our study, 36 (72%) had STEMI, 9 (18%) were NSTEMI, and 5 (10%) were diagnosed as UA.

In our study, the majority of patients were STEMI (72%) which is different from the data from developed countries, in which NSTEMI was the predominant presentation Table 10.

In the STEMI subgroup, 18 (50% of STEMI population) had anterior wall myocardial infarction (AWMI), 15 (41.3% of STEMI population) had inferior wall myocardial infarction (IWMI), 1 (2.9% of STEMI population 2.3%) had Living with Mental Illness (LWMI), and 2 (5.8% of STEMI population) had people LWMI (PLWMI).

In a similar study done by Veena Nanjappa *et al.*, 45% had AWMI, 34% had IWMI, and 17 % had LWMI/PLWMI.

Table 9: Comparison of ACS in developed and developing countries

	STEMI %	NSTEMI %
Our study	72	18
Veena Nanjappa <i>et al.</i>	62.4	27.1
Create128	61	39
Global registry of ACS	30–40	60–70
European heart surveys	42	51

ACS: Acute coronary syndrome, NSTEMI: Non-ST segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction

Risk Assessment

Killip's class

In our study, 4.6% of STEMI patients presented in Killip's Class III and 4.2% of STEMI patients presented in Killip's Class IV. The majority of STEMI patients were in Killip's Classes I or II (76.4% and 14% of STEMI population, respectively). In all the patient death patients, Killip's class was more than 3.

In a similar study by Veena Nanjappa *et al.*, 12% of STEMI presented in Killips Class III and 15.7% of STEMI patients presented in Killips Class IV.

About 21.7% in Kerala ACS registry had Killips Class >1. About 38.6% of women had Killips Classes II–IV in SWEDEHEART study.

TIMI Score

The mean TIMI score across all subtypes were 5. The mean TIMI risk score in UA was 3 (SD ± 1) and 4.3 (SD ± 1.4) in NSTEMI subgroups.

The mean TIMI score for STEMI patients was 5.2 (SD ± 2).

The TIMI risk score was a good predictor of disease severity, as most complications were associated with higher scores. In STEMI patients who died during hospital stay, TIMI risk score was >9.

As these scores were developed in patient populations that were at least two-thirds male, so their performance in women is not well established. However, still, the TIMI risk score has performed well in both men and women for the prediction of death or MI at 30 days.

Echocardiography

Echocardiography revealed moderate mitral regurgitation in 3 (6%) patients and all these patients had STEMI. In VeenaNanjappa *et al.* study, echocardiogram finding of moderate MR is seen in 6% of STEMI population.

The average ejection fraction was 47 %.

The STEMI group showed the worse left ventricular ejection fraction (45 ± 6%).

Coronary Angiography

Coronary angiogram was done in 50 (100%) patients out of the study population. Single vessel disease was most commonly found across the spectrum of ACS 22 (44%).

Triple vessel disease was found in 13 (26%) patients. About 4% in NSTEMI, 22.2% in STEMI, and none in UA group had TVD.

Left main involvement was seen in 4 (8%) patients of which 2 patients had STEMI and 2 patients had NSTEMI.

Normal or mild disease was found in 2 (4%) patients. All were having UA.

UA was more commonly associated with normal coronaries as compared to NSTEMI and STEMI. In UA group, many patients may have been over diagnosed, false-positive as ACS. In a similar study by Veena Nanjappa *et al.*, single-vessel disease was most common finding. About 13.9% in UA group had NSTEMI, 10.8% in UA group had STEMI, and 14.3% in UA group had TVD. Left main involvement was seen in 3 patients each of STEMI and NSTEMI group.

In a study done by Rajni Sharma *et al.*, single-vessel disease was present in 127 (46.02%) of female patients whereas 603 (51.67%) of male patients ($P < 0.001$). 2VD was present in 44 (15.94%) female patients in comparison to 220 (18.85%) male patients. TVD was seen in 27 (9.78%) female patients but 89 (7.62%) male patients. LMCA disease was seen in 3 (1.09%) female patients whereas in 20 (1.71%) male patients ($P > 0.05$). Normal or mild disease was present in 75 (27.17%) of female patients compared with 235 (20.15%) of male patients.

Treatment

All 50 study patients received aspirin and statins during hospitalization or on discharge. The second antiplatelet was used in 48 patients. Clopidogrel was used in 20 (40%), prasugrel in 9 (18%), and ticagrelor in 19 (38%).

In a similar study by Veena Nanjappa *et al.*, all patients received aspirin across all ACS groups. Ticagrelor use was 11.1% in NSTEMI, 8.4% in STEMI, and 21.4% in UA group. About 42.2% of STEMI patients received prasugrel and 30.6% in NSTEMI group. Clopidogrel was used in 94.4% NSTEMI and 94% of STEMI patients. About 39.9% of patients had a switch over. All patients initially received statins, and in 1 patient, it was later discontinued because of raised liver enzymes in patient with normal coronaries.

The use of ticagrelor as a second antiplatelet agent is steadily increasing due to its superior efficacy and better safety profile.

A total of 44 (88%) patients received adjuvant anticoagulation in our study. LMWH was most commonly used 29 (58%). Unfractionated heparin was used in 15 (30%) patients, especially in patients who had associated AKI.

Emergency Revascularization

Of the 36 patients who were eligible for primary revascularization, 20 patients (55.5%) underwent either thrombolysis or primary PCI.

Thrombolysis

Thrombolysis was done in 8 (22.2%) STEMI patients. Most patients had time to presentation < 12 h. All 8 patients received streptokinase. No patient had a risk of IC bleed during or post-thrombolysis with streptokinase.

In a similar study by Veena Nanjappa *et al.*, 10.8% received thrombolysis in STEMI group.

Primary PCI

In our study, 12 (33.3% of STEMI population) underwent primary revascularization with PCI.

Out of these, primary PCI to RCA was the most common with 6 patients. Primary PCI to LAD was done in 5 patients and 1 patient had primary PCI to LCx.

In a similar study by Veena Nanjappa *et al.*, 68.7% of patients in STEMI group underwent primary angioplasty.

A pooled analysis of 22 trials that randomized 6763 STEMI patients to primary PCI versus thrombolytics found that women had lower 30-day mortality with primary PCI. Despite this beneficial effect, women are less subjected to primary PCI, especially in Indian scenarios.

In a study by Mady Moriel *et al.* in STEMI-patients, acute reperfusion was less frequent in women than in men (53% vs. 63%, respectively, $P = 0.01$); reperfusion by thrombolysis was done in 30% patients and PAMI in 70% of STEMI.

Elective Revascularization

Out of the 50 women, 36 patients received elective revascularization. The majority underwent PCI 30 (60%), while 6 (12%) patients had CABG surgery.

In the PCI group, single-vessel PCI was most common in all ACS subtypes. Most of the two vessels or multivessel PCI was done in NSTEMI and STEMI group.

In a study done by Veena Nanjappa *et al.*, 69.4% in NSTEMI group underwent PCI, 42.9% patients in UA group underwent PCI. Multivessel PCI was done in 8.3% NSTEMI and 6% STEMI patients and none in UA group.

In our study population, around 96% received revascularization, either in the form of primary revascularization (thrombolysis or primary PCI) or elective revascularization (PCI or CABG surgery). In the study done by Veena Nanjappa *et al.*, 83.6% patients had received revascularization. The higher cumulative percentage found in both studies may be related to the fact that both studies were conducted in a tertiary cardiac care hospital.

PCI was done in only 11.9% of patients in Kerala ACS registry and in 7.5% in CREATE registry. About 47.8% underwent PCI in a study by Sadowski *et al.*

About 6 (12 %) patients underwent CABG surgery, of which about half of them had NSTEMI.

IN HOSPITAL COMPLICATIONS

Among the study cohort, CCF (14%), hypotension (4%) and cardiogenic shock (2%) were the most common complications. They were predominantly present in STEMI group.

Table 10: Complications in ACS subtypes

	Overall (%)	UA	NSTEMI	STEMI
CCF/LVF	7 (13.9)	1	2	4
Hypotension	2 (4)	-	-	2
Cardiogenic shock	1 (2)	-	-	1
Free wall rupture	-	-	-	-
CHB	3 (5.3)	-	-	3
Ventricular tachycardia	1 (2)	-	-	1
AKI	4 (8)	1	1	2
PV bleeding	-	-	-	-
CIN	1 (2)	-	-	1
Intracranial bleeding	-	-	-	-
IN-Hospital death	2 (4)	-	-	2

CHB was observed in 3 (6%) and ventricular tachycardia in 1 (2%) patients. They were present only in STEMI group.

Acute kidney injury was the most common extracardiac complication. It was mostly secondary to cardiogenic shock or contrast-induced nephropathy.

In CADILLAC trial, female gender was an independent predictor of MACE and bleeding complications.

Mortality

In the study population, 2 (4%) patients died during hospital stay. Most of them were elderly; most of them presented with STEMI, had delayed presentation and had higher Killip's class and TIMI risk scores. Out of 2 patients, 1 died due to cardiogenic shock and 1 patient died due to ventricular tachycardia.

Eleven deaths (8.3%) were noted; 8 (6%) in hospital and 3 (2.3%) in the follow-up period in study done by Veena Nanjappa *et al.* All of them belonged to STEMI group.

In Kerala, ACS registry had in-hospital mortality with 8.2% in STEMI group. In AMI-FLORENCE registry the in-hospital mortality for women was 16%.

CONCLUSIONS

1. The incidence of CAD increases with age in females with more adverse outcomes in elderly females
2. There is a significant delay in seeking treatment after symptoms onset due to various medical and social reasons causing a delay in delivering guideline-directed treatment and consequently more complications
3. Although the majority of the females have typical symptoms of ischemia, percentages of females having atypical symptoms are also significant, and this may cause delay in seeking treatment, appropriate diagnosis, and treatment
4. Traditional risk factors such as diabetes mellitus, hypertension, dyslipidemia, obesity and physical inactivity, and family history of CAD were most common in study population. Tobacco abuse is less significant risk factor in Indian females than in the western population
5. Risk scoring systems such as Killip's Class and TIMI score were fairly accurate in female patients in predicting adverse outcomes and complications
6. Single vessel disease was the most common coronary angiographic finding in study population. Nearly one-fourth of the patients had triple vessel disease. UA was more commonly associated with normal coronaries as compared to NSTEMI and STEMI
7. Only one-third of the patients received primary revascularization from the eligible population, and about two-thirds of whole study cohort received elective revascularization. This signifies that there is treatment bias toward female population
8. Patient characteristics such as elderly age, diagnosis of STEMI, delayed presentation, and higher Killip's class and TIMI risk scores were associated with significant morbidity and mortality

Limitations

The limitations of our study include the following

1. This being a single center prospective and observational study with a limited time period, the results cannot be extrapolated in a larger population
2. Sample size is small and further studies including a larger sample size are recommended
3. There was no direct comparison between males

and females in their clinical profiles, treatment, and outcomes to ascertain gender bias in clinical presentation and management

4. As there was no follow-up, so short-term and long-term mortality and morbidity and adherence to treatment were uncertain
5. As ours was a tertiary cardiac care center, the majority of patients were referred from peripheral hospitals causing difficulty in interpreting some clinical data

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