



CLINICAL PROFILE AND 30-DAY OUTCOME OF WOMEN WITH ACUTE CORONARY SYNDROME

General Medicine

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ABSTRACT

INTRODUCTION: Gender differences existed in treatment and outcome of patients with acute coronary syndrome(ACS). Women hospitalized with ACS are at a higher risk for adverse outcomes as compared to men. The aim of the study was to evaluate the clinical profile, and short-term outcome in women presenting with ACS, as a first manifestation of Ischemic Heart Disease.

METHODS: Data regarding demographic and clinical status was collected among 100 female patients of ACS at ICCU, PGIMS, Rohtak. Descriptive results are displayed as subgroups of STEMI, NSTEMI and UNSTABLE ANGINA(UA). All the categorical data are presented as frequency and percentages. All the numerical data are presented as mean±standard deviation.

RESULTS: 57 had STEMI, 9 patients had NSTEMI and 34 had UA. Mean age at admission was 60 + 11.34 years. Atypical presentations were noted in 34% women and one or more risk factors in 58%. Among 57 STEMI patients, anterior location of infarct predominated (68.42%). Mortality of 10% was observed in STEMI patients and overall 47 % females had one or more major adverse cardiovascular event (MACE)

CONCLUSION: This study conducted in women presenting with ACS, demonstrated peculiar features like old age, atypical presentation which resulted in higher incidence of associated risk factors in postmenopausal groups. Complications and mortality were comparable with previous studies. Non-adherence to treatment and lack of desire to have coronary intervention also explained the decreased short-term outcome in women.

KEYWORDS

ACS, MACE

INTRODUCTION

Cardiovascular diseases(CVD) are one among the leading causes of mortality worldwide. Based on NHLBI's FHS (National Heart, Lung, and Blood Institute's Framingham Heart Study) data from 1980 to 2003, average annual rate of first cardiovascular events is 3 per 1000 men at 35 to 44 years of age and it rises to 74 per 1000 men at 85 to 94 years of age.¹ For women, comparable rates occur 10 years later in life.¹ Thus, although ACS occurs 3-4 times more in men than women among age group less than 60 years, but after 75 years women represent majority of patients.² Not only age, risk factor profile and clinical presentation also differs in women presenting with CVD. Diabetes mellitus(DM), a significant contributor to atherosclerosis increases a women's risk for coronary disease by three to sevenfold with only a two to threefold increase in diabetic men. Also risk for fatal outcome is higher in women with diabetes than men with diabetes.³ Dyslipidemia, aggravated by menopause associated hormonal disturbances increases the risk of thrombotic events in postmenopausal women. Sedentary behavior is more common in women than in men and it increases with age especially in developing countries like India. Women predominantly accumulate subcutaneous fat, whereas men accumulate significantly more visceral fat. Postmenopausal women have increased visceral fat accrual, which has implications for development of insulin resistance, inflammatory responses and lipolysis.⁴ Excess visceral fat and pericardial fat are prominent risk factors for cardiovascular morbidities independent of traditional measures of obesity.⁵ Hence have more chances of CVD. Metabolic syndrome and coronary disease association is also strongest in women, with a relative risk of 2.63 as compared with 1.98 in men. Additional factors include worse pregnancy outcomes like gestational diabetes and preeclampsia, anemia, autoimmune diseases, osteoporosis, polycystic ovarian syndrome and associated insulin resistance, depression and many more contribute to increased cardiovascular morbidity and mortality in women, although disease prevalence is more in men. Once viewed as a man's disease, CVD remains the leading cause of mortality for women worldwide, in both industrialized nations and developing economies.⁶ Apart from age and risk factors, atypical clinical presentation and increased incidence of microvascular disease, Syndrome X in women leads to diagnostic difficulties and delayed therapy in women. Evidence gained from the landmark WISE (Women's Ischemic Syndrome Evaluation) study⁷ indicates that the full spectrum of CVD

in women extends beyond atherosclerotic stenosis in the epicardial coronary arteries to dysfunction of the coronary microvasculature and endothelium. They create diagnostic challenges and limit the application of traditional testing strategies which, while adequate to detect obstructive epicardial coronary disease, may be insufficient for many women presenting with symptoms of chest discomfort. Few studies also state that suboptimal use of guidelines and underutilization of cardiac rehabilitation in women also contribute to this.

According to recent reports of 3 large prospective studies from India suggest an age standardized CVD mortality rate of 255 to 525 per 100000 men and 255 to 299 per 100000 women.⁸ It's still an ongoing debate that women hospitalized with an ACS are at a higher risk for adverse outcomes as compared to men especially due to increased incidence of bleeding complications, heart failure and mechanical complications. There is a lack of gender-specific evidence due to the underrepresentation of women in clinical trials and a long-held myth that CVD is limited to men. Despite recent general improvements in health care, significant disparities persist in the cardiovascular care of women even when income, education level, and site of care are taken into consideration. Identifying factors that promote better cardiovascular knowledge, improved preventive health care, and prompt care-seeking behaviors represent important targets for women with ACS. A retrospective study conducted by Ayanian JZ et al⁹ showed that women who are hospitalized for CVD undergo fewer major diagnostic and therapeutic procedures than men and reflect their underuse in women and overuse in men. According to Sadowski et al¹⁰ who studied gender related differences in mortality after STEMI, women were older and had more risk factors. The incidence of in-hospital complications, in-hospital mortality and 12-month mortality was higher in women. The impact of non-traditional risk factors on CVD in women may be higher than in men due to increased prevalence of certain risk factors in women; however, the pathophysiologic relationship between CVD and non-traditional risk factors such as mental stress-induced ischemia, depression and anxiety in women is not clearly understood but is an active area of investigation.¹¹

This analysis reports the demographics, risk factor profiles, clinical presentation, complications and 30-day mortality in women with ACS.

MATERIALS AND METHODS

The study was carried out in 100 female patients of ACS admitted in ICCU, Dept. of Medicine, PGIMS, Rohtak from Dec 2016 to Dec 2017.

All participants were fully informed about the aim of research and were subjected to detailed investigations. Patients aged <18 yrs, prior heart failure or ischemic heart disease, underlying ECG abnormalities like WPW syndrome, left ventricular failure, patients on digoxin, amiodarone and having comorbid conditions like advanced chronic renal failure, cancer, physical disability, old cerebrovascular accident, valvular heart disease, already undergone coronary intervention-PTCA, CABG etc are excluded from the study. The study was approved by the ethical committee of the institution.

After inclusion, all the subjects at the time of ICCU admission, a detailed history, general physical examination and systemic examination was carried out. 12 lead ECG was done and blood samples were tested for blood urea, blood sugar, serum sodium, serum potassium, and CPK-MB. Patients were categorized as STEMI, NSTEMI and UA as per Universal Definition of Myocardial infarction⁸. All patients were treated as per uniform treatment protocol and STEMI patients underwent thrombolysis either by streptokinase/tenecteplase/ reteplase. Marker of successful thrombolysis like clinical improvement, relief of chest pain ST-segment settling at 90 mins and reperfusion arrhythmias were studied along with time lines. Patients were observed for any complications of MI and thrombolysis. Patients were re-evaluated after one month. Finally, descriptive results are displayed as subgroups of STEMI, NSTEMI and UA. All the categorical data are presented as frequency and percentages. All the numerical data were presented as mean±standard deviation.

RESULTS

100 patients were included in the study Mean age at admission was 60 + 11.34 years with range 32 to 85 years. 87% were postmenopausal. 66 patients out of 100 had typical chest pain, remaining 34 had atypical chest pain in the form of epigastric burning, jaw pain, back pain, shortness of breath, absence of chest pain, giddiness and syncopal attacks (TABLE 1). The mean Body mass index(BMI) was 25.06±2.377 Kg/m², 26 women were overweight (BMI 23-24.9 Kg/m²) and 55 women were obese (BMI >25 Kg/m²).

TABLE 1: ACS PRESENTATION DISTRIBUTION

PRESENTATION	NUMBER OF PATIENTS (34)
TYPICAL CHEST PAIN	66
EPIGASTRIC BURNING	18
JAW PAIN	3
BACK PAIN	4
SHORTNESS OF BREATH	7
SYNCOPE	2

Predominant risk factors include diabetes mellites (19%), hypertension (23%), smoking (20%), COPD (11%), family history of coronary artery disease (12%), thyroid disorder (4%). 58% of patients had one or more risk factors. 71% of females were anemic. Lipid targets in coronary artery disease described was exceeded as shown in Table 2A. Lipid abnormalities, therefore, were seen in 48 postmenopausal women and 7 premenopausal women. Glucose intolerance was observed in 51 patients, out of which 19 were diabetic and 32 were prediabetic. The mean CPKMB on Day 1 in STEMI group was 185.23±152.84 U/L, in NSTEMI group was 84.9±35.58 U/L and 37.97±12.24 U/L in UA group.

TABLE 2A: MEAN VALUES OF LIPID PROFILE IN THE POPULATION

Lipid Profile	Mean±SD	Range
Triglycerides(mg/dL)	132.86± 44.10	68-472
Cholesterol(mg/dL)	179.77± 39.50	91-284
HDL(mg/dL)	45.84± 9.26	14-73
LDL(mg/dL)	109.2± 34.72	43-184
VLDL(mg/dL)	27.82± 8.91	14-77

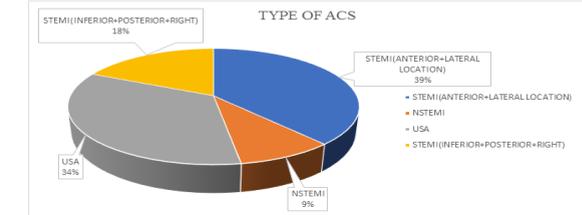
TABLE 2B: NUMBER OF PATIENTS WITH ABNORMAL LIPID PROFILE

ABNORMAL LIPID PROFILE	NUMBER OF PATIENTS (%)
INCREASED LDL (>100 mg/dL)	46
DECREASED HDL (<50 mg/dL)	40
INCREASED CHOLESTEROL (>180 mg/dL)	31
INCREASED TRIGLYCERIDES (>160 mg/dL)	19

Among 57 STEMI patients, anterior location of infarct predominated (GRAPH 1). All patients were registered and followed up in cardiovascular clinic of the department. There was no dropout and 10 patients died within one month and mortality was seen in only STEMI patients. Table 3B shows compilation of events after discharge till 30 days after ACS in all patients. It was observed that 13 out of 100 women were non-compliant to treatment. 2 patients had reinfarction and 5 went into heart failure after discharge. 9 patients were re-hospitalized for post MI angina, reinfarction and heart failure.

TABLE 3: THE COMPARISON BETWEEN CLINICAL PARAMETERS AMONG WOMEN WITH STEMI, NSTEMI AND UA.

VARIABLE	STEMI	NSTEMI/UA
NUMBER OF PATIENTS	57	43
RISK FACTORS		
SMOKING (20)	14(24.5%)	6(14%)
DIABETES MELLITUS (19)	9(15.8%)	10(23.25%)
HYPERTENSION (23)	11(19.2%)	12(28%)
DYSLIPIDEMIA (55)	30(52.6%)	25(58.13%)
MORTALITY (10)	10(17.5%)	0



GRAPH 1: TYPE OF ACS

TABLE 4 shows the complications in female patients during the entire study period. Forty seven percent, that is almost half of the study population had one or the other complication. Among which post MI angina and hypotension were the most significant. Mortality of 10% was observed in STEMI patients. Factors significantly observed with MACE include Age > 65 yrs, Atypical presenting symptoms, high BMI, Anterior location of MI & chronic smoking. 13% of patients had non-adherence to treatment.

TABLE 4: COMPOSITE RATE OF COMPLICATIONS IN STUDY POPULATION (0-30 DAYS)

COMPLICATIONS (0-30 DAYS)	NUMBER OF PATIENTS (%)
POST MI ANGINA/ ANGINA	23
REINFARCTION/EXTENSION OF INFARCT	5
HYPOTENSION/SHOCK	24
HEART FAILURE	19
MAJOR ARRYTHMIAS	3
AV BLOCKS	5
BLEEDING (NO MAJOR BLEEDS)	10
ISCHEMIC MR	4
SEPTAL RUPTURE	3
PULMONARY EDEMA	2

TABLE 5: SUBGROUP ANALYSIS OF COMPLICATIONS AMONG PATIENTS WITH HYPERTENSION, DM AND SMOKING

	HTN	DM	SMOKING
NUMBER OF PATIENTS	23	19	20
COMPLICATIONS			
REINFARCTION	1(4.3%)	2(10.5%)	2(10%)
POST MI ANGINA	3(8.6%)	7(36.8%)	7(35%)
HEART FAILURE	2(13)	7(36.8%)	6(30%)
MORTALITY	1(4.3%)	3(15.7%)	5(25%)

DISCUSSION

The difference in outcome between women and men with CVD are due to specific risk factors, atypical presentation, differences in treatment and management strategies, and pathophysiologic differences in women.

Age is one of the significant factors since females with ACS present approximately 10 years later than males, and in this study, mean age was 60±11.43 years, which was comparable with other studies from India (TABLE 6).

STUDY	AGE
Sahni M et al (Himachal Pradesh) ¹²	62.7±13.6 years
Raihanathul MKJ et al (Kerala) ¹³	69 years
Present study	60±11.43 years

34% women presented with atypical symptoms in this study, similar to a study of National Registry of Myocardial Infarction (United States) where the proportion of MI patients who presented without chest pain was significantly higher for women than men (42.0 versus 30.7 percent).¹⁴ The absence of chest pain or discomfort with ACS was noted more commonly in women than in men in the cumulative summary from large cohort studies (37% vs 27%).¹⁵

The prevalence of hypertension and diabetes in current study was lower than reported in south Asian cohort of INTERHEART study¹⁶ (TABLE 7). The proportion of STEMI patients in our study was higher than NSTEMI/UA patients (57 vs 43), and the prevalence of hypertension and diabetes mellitus was higher among NSTEMI/UA group than STEMI group (TABLE 3), like what was observed in CREATE registry.¹⁷

TABLE 7: COMPARISON OF PREVALENCE OF RISK FACTORS WITH INTERHEART STUDY

Risk Factor	Prevalence In Interheart Study ¹⁶	Prevalence In Current Study
Hypertension	28.9%	23%
Diabetes	20.5%	19%
Smoking	7.1%	20%
Dyslipidemia	52%	55%

After China, India accounts to be the 2nd largest consumer of tobacco in the world. Overall prevalence of tobacco usage in men is 48% and women is 20%. Haryana is among those states in India which is at higher tobacco consumption in women. Many socio cultural and ritual factors play role in this and in present study, there were around 20 women who use tobacco either in the form of bidi or hookah or pan, which was significantly high compared to INTERHEART south Asian cohort.¹⁶

Dyslipidemias were seen associated more with postmenopausal group. Increased LDL (46%) and decreased HDL (40%) were the ones seen in majority of patients than increased triglycerides (19%), though dyslipidemias among Indians includes abnormal triglycerides and HDL more often than increased LDL. Though BMI correlation with visceral adiposity and CVD is less than waist circumference in Indian population, 55% of women in this study were obese (>25 Kg/m²).

In present study, 20 women developed heart failure, majority of them were anemic and 6 of them expired. This signifies heart failure increases mortality in failure patients. Women with CHD more frequently have or develop symptomatic HF than men.⁹

Reinfarction was seen in 5 women. All 3 women who developed reinfarction during hospital stay expired. Previous studies shown that women with early reinfarction following fibrinolysis for MI had more frequent early death and were managed less aggressively. These findings suggest the need for increased awareness and timely intervention in these patients. However, bleeding complications were more frequent after either repeat fibrinolysis or urgent revascularization

Three patients developed major arrhythmias. 2 patients with AWTMI had VT and recovered with therapy. One patient with extensive ALWTMI had recurrent VF with was resistant to defibrillator therapy also and she died. None had atrial fibrillation. 5 patients had AV blocks, all those 5 had inferior wall MI, which recovered with thrombolysis. With the introduction of intensive cardiac care unit in the management of acute myocardial infarction (AMI), arrhythmias have become one of the most modifiable complications of AMI.

Ten patients in the present study had bleeding complications in the form of local hematoma, hemoptysis. None had major bleed like intracranial and massive hemoptysis or gastrointestinal bleed after thrombolysis.

With respect to mechanical complications, four patients with ASMI developed ischemic mitral regurgitation (MR), HTN was common feature in 2 patients among them. One patient had reversal of MR after

thrombolysis within 2 days. There was no mortality among these patients. And septal rupture was found in 3 patients (3%) (2 had AWTMI and 1 had IWTMI). All the 3 died within 25 days. Women are at a higher risk of developing mechanical complications after MI, but sex-specific data on treatment are sparse.

In present study 30-day mortality was 10%, with 5% in hospital mortality and remaining 5% within 30 days. All belonged to STEMI group, which was comparable to CREATE study and other studies in developed nations.

In a study by Sahni M et al¹², in 2013, reinfarction (0-5 days) was seen in 2.5%, heart failure in 35%, stroke in 2%, arrhythmias in 8.7% and in-hospital mortality in women 13.75%.

Among factors which affect mortality and morbidity in females, old age and higher prevalence of comorbidities like hypertension, diabetes, dyslipidemia and obesity in women compared to men are most significant according to a study by Mohamad IJ et al, in 2017.²¹ In present study also, older age, late presentation, atypical presentation, obesity, higher clustering of comorbidities were the factors responsible for high morbidity and mortality. Smoking and the site of infarct i.e. anterior wall ischemia/infarction were also associated with significant MACE in the current study.

CONCLUSION

This study conducted in women presenting with ACS, demonstrated peculiar features like old age, atypical presentation which resulted in delay in treatment and higher incidence of associated risk factors in postmenopausal groups. Anemia also contributed to overall mortality and morbidity in women. Complications and mortality were comparable with previous studies. Non-adherence to treatment and lack of desire to have coronary intervention also explained the decreased short-term outcome in women.

LIMITATIONS

1. Since the study population include only 100 patients, larger studies are needed to exactly delineate these findings so that effective strategies can be worked out and applied to women population in general.
2. The present study included patients who underwent thrombolysis as mode of treatment in STEMI group, so doesn't reflect the mortality and morbidity in patients undergoing primary percutaneous coronary intervention (PCI).

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