



## STUDY OF RISK FACTORS AND CLINICAL PROFILE OF ACUTE MYOCARDIAL INFARCTION IN FEMALES

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### ABSTRACT

Cardiovascular disease is the most important health issue facing mankind and continues to be major cause of morbidity and mortality. Women are disproportionately affected by coronary artery disease (CAD) compared with men. There are different clinical presentations of heart disease and acute myocardial infarction in women than in men. Also different studies show that there is difference in the major cardiovascular risk factors amongst men and women at younger age. The present study was undertaken with a view to understand the clinical profile of acute myocardial infarction in women and observe the variations in acute myocardial infarction between men and women. **Materials and methods**-This observational and analytical study includes 118 female cases of acute myocardial infarction admitted to ICCU and randomly selected 118 male cases of acute myocardial infarction admitted to ICCU during the same tenure. Various necessary investigations were carried out and risk factors of acute myocardial infarction were determined. All the cases were followed up on the 7<sup>th</sup> day of admission and one month after discharge from the hospital for various complications. Data thus collected was analysed at the end of study. **Results**-Maximum number of female cases were in age group 60-69 years (45.6%) while maximum number of male cases were in age group 50-59 years (33.05%). Anterior wall myocardial infarction was the commonest type of acute myocardial infarction in both groups. ST elevation myocardial infarction was more common in males (94.9%) as compared to females (83.89%) whereas non ST elevation myocardial infarction was common in females (10%) as compared to males (5%). Atypical chest pain was more common in female cases (50.8%) whereas typical chest pain was more common with male cases (52.4%). Also dyspnoea as presenting symptom was significantly more in female cases (51.6%) as compared to male cases (20.3%). Among the risk factors as Diabetes mellitus, significant difference was observed in female (45.7%) vs male cases (30.5%). Other risk factors like lack of physical activity was significantly more in female cases (84.7%) as compared to male cases (50%). Central obesity and family history of CAD were more common in female cases. 42 (35.6%) female cases had arrhythmias during hospital stay as compared to 50 (42.4%) male cases. Post MI angina was present in 21 (20.38%) female cases and 12 (11.11%) male cases during one month follow up. Mortality was more common in female cases (12.7%) compared with the male cases (8.47%) but it was not statistically significant. **Conclusions**-Females suffer from coronary artery disease slightly at older age as compared to males. Atypical chest pain and dyspnoea are more common presenting symptoms in females compared to males. Diabetes mellitus, central obesity, lack of physical activity and family history of CAD are most common risk factors in female cases for acute myocardial infarction. ST elevation myocardial infarction is less common in females as compared to males. Complications like congestive cardiac failure, arrhythmias are more common in females as compared to males. The overall mortality with acute myocardial infarction are common in females than males.

**KEYWORDS :** Acute myocardial infarction, coronary artery disease, risk factors, clinical profile

### INTRODUCTION

During 20<sup>th</sup> century there is major shift in the causes of illnesses throughout the world due to increase in the life expectancy and changes in lifestyle of people. Cardiovascular diseases (CVD) became the most common cause of death worldwide which was accounting for <10% deaths only a century ago but now accounts for nearly 40% of deaths in high income and about 28% in low and middle income countries, thereby having a greater economic impact on countries<sup>1</sup>. In India there is increasing incidence of CVD in recent years based on data from tertiary care hospitals and anecdotal physician experience. Acute myocardial infarction has historically been regarded as men's disease and for many years, women have been underdiagnosed and undertreated. As a result, women have poorer outcomes specially in socially isolated elderly women<sup>2</sup>.

Among women, estrogen is the predominant sex hormone which has influence on ischemic heart disease (IHD). The incidence of IHD was reported to be significantly lower in premenopausal women in comparison with men of similar age and postmenopausal women suggesting that endogenous estrogen have a protective effect on the development of IHD<sup>3</sup>. Considering conventional risk factors like diabetes, women with diabetes are at a greater risk for CAD than men with the same condition<sup>4</sup>. This gender disparity also relates to survival after myocardial infarction in which women with diabetes are less likely to survive than men with the same condition<sup>5</sup>. Thus clinical profile and outcome in respect of acute myocardial infarction differs in women from men in certain aspects due to difference in hormonal status, risk factors and gender inequality in treatment. In order to evaluate these aspects, this study was undertaken.

### MATERIALS AND METHODS

The study was carried out on 118 female cases of acute myocardial

infarction admitted to ICCU at Indira Gandhi Government Medical College, Nagpur. The cases were compared with randomly selected 118 male cases of acute myocardial infarction who were admitted to ICCU during same tenure. This study was conducted between January 2009 to August 2010. The study was approved by institutional ethical committee. Subjects admitted to ICCU within 24 hours from onset of symptoms and fulfilling any of the following two criteria out of the three were included in the study.

#### A) ST segment elevation myocardial infarction:

1. Typical symptoms-Acute onset chest discomfort lasting for more than 30 minutes and not relieved by sublingual nitrates.
2. Typical pattern of electrocardiogram (ECG): ST segment elevation  $\geq 0.1$  mV in at least two consecutive leads or fresh left bundle branch block.
3. Elevated enzyme levels: Serum creatine phosphokinase MB isoenzyme (CPK-MB) two times the upper limit of normal.

#### B) Non-ST segment elevated myocardial infarction:

1. Chest discomfort at rest lasting for more than 30 minutes and not relieved by sublingual nitrates.
2. ECG pattern: ST segment depression/transient ST elevation or T wave inversion.
3. Elevated levels of CPK-MB two times the normal.

#### Exclusion criterias:

1. Cases having past history of Ischemic Heart Disease (history of angina pectoris, history of positive treadmill test, positive ECG changes, positive angiographic evidence, angioplasty done, history of coronary artery bypass grafting (CABG) done).
2. Cases with Rheumatic heart disease, congenital heart disease.
3. Cases having other comorbid conditions like chronic kidney

disease,malignancies,chronic liver disease.

- Pregnancy.
- Cases who refused to participate in the study.

Subjects fulfilling the inclusion criteria were analysed.Baseline clinical history,complications,risk factors of acute myocardial infarction and past illness were documented.Personal history as regards to smoking and alcoholic habits were noted.Family history of ischemic heart disease was enquired,A detailed clinical examination was carried out including ECG,fasting and postmeal blood sugar,blood urea,lipid profile,SGOT level,CPKMB,chest X rays.

Hypertension was diagnosed if basal systolic blood pressure and/or diastolic blood pressure were above 140 mmHg and /or 90 mmHg or subject was taking antihypertensive treatment.

Smoking was studied by recording the duration and number of cigarettes/bidies smoked per day.

Diabetes mellitus was diagnosed on the basis of whether patient received insulin,oral hypoglycemic agents,restriction in a dietary sugar or random blood sugar  $\geq 200$ mg/dl or fasting blood sugar  $\geq 126$  mg/dl.

Central obesity was defined as waist circumference  $\geq 90$ cm in males and  $\geq 80$  cm in females.

Early menopause was defined as cases who attended their menopause before the age of 40 years.

Congest cardiac failure was considered to be present when following symptoms and sign were noted: breathlessness, orthopnea, cough, tachycardia, pulsus alternans,LV<sub>3</sub> gallop,end inspiratory rales on auscultation of chest.

**Cases were graded as per Killip's classification:**

**Class 1-** No signs of pulmonary venous congestion

**Class 2-** Moderate heart failure as evidence by rales at the lung bases, S3 gallop, tachypnoea or signs of failure of right side of heart including venous and hepatic congestion.

**Class 3-** Severe heart failure,pulmonary oedema

**Class 4-** Cardiogenic shock

Evidence of cardiogenic shock was determined in presence of cold clammy extremities,rapid thready pulse,fall of systolic blood pressure to 90 or below 90 mmHg with or without altered sensorium and oliguria.

Electrocardiographically as per the criteria,assessment was done and cases were graded into anterior wall MI,inferior wall MI,right ventricular MI,anterior wall MI with inferior wall MI,inferior wall MI with right ventricular MI with posterior wall MI and non Q MI.

The complications like cardiogenic shock,heart blocks, arrhythmias, left ventricular failure at the time of admission were recorded.

**Reinfarction was defined as presence of at least 2 of following 3 criteria.**

- New onset characteristic ischemic chest pain for >20 minutes requiring sublingual nitroglycerin or narcotic analgesia for relief of pain.
- Elevation of cardiac enzymes to twice the upper limit of normal reference range.
- ECG changes:ST elevation > 1mm in two contiguous leads,new Q wave or other persistent ECG changes consistent with MI.

All the cases were followed on the 7 th day of admission in hospital and one month after discharge from the hospital for various complications.

Statistical analysis was done at the end of the study.Continuous clinical characteristics in female and male groups were compared by unpaired t-test and categorical variables were compared by using Chi-square statistics.Data was presented in percentage and mean  $\pm$  SD.The statistical significance was considered as  $p < 0.05$ .

**OBSERVATIONS AND RESULTS**

118 female cases and 118 male cases of acute myocardial infarction

participated in the study.

**Table 1 :**Age distribution of cases

Age group in years	Females N=118(%)	Males N=118(%)
30-39	1(0.84)	4(3.38)
40-49	13(11.01)	37(31.35)
50-59	34(28.81)	39(33.05)
60-69	54(45.76)	26(22.03)
70-79	12(10.16)	10(8.47)
>80	4(3.38)	2(1.69)

Maximum number of female cases (54)belonged to the age group 60-69 years whereas maximum number of male cases (39)were in age group 50-59 years.Mean age at the time of presentation in female cases was  $58.75 \pm 9.32$  years,whereas in male cases ,it was  $53.43 \pm 10.99$  years.Females were found to be on an average 5.32 years older than males.

**Table 2 :** Distribution of cases of AMI according to type of infarction

Sr No.	Type of AMI	Females (%) (N=118)	Males (%) (N=118)
1	ST elevation MI	99 (83.89)	112 (94.91)
	A Anterior wall MI	52 (44)	70 (59)
	B Inferior wall MI	30 (25.4)	26 (22)
	C Right ventricular MI	0 (0)	0 (0)
	D Anterior wall+inferior wall MI	5 (4.2)	2 (1.7)
	E Right ventricular +inferior wall +Posterior wall MI	10 (8.6)	8 (6.8)
	F Acute onset LBBB	2 (1.7)	6 (5)
2	Non ST MI	19 (16)	6 (5)

ST elevation MI was more common in males with acute myocardial infarction when compared to females with statistical significant difference( $p=0.0111$ ).Anterior wall MI was the commonest type of AMI observed in both groups.Few cases presented with acute onset LBBB.Non ST MI was more common in females as compared to males with statistical significant difference( $p=0.01114$ ).

**Table 3:**Clinical presentation of acute myocardial infarction in females and males

Sr No.	Symptoms	Females (%) N=118	Males (%) N=118
1	Typical chest pain	38 (30.5%)	62 (52.4%)
2	Atypical chest pain	60 (50.8%)	40 (33.8%)
3	No chest pain	20 (16.9%)	16 (13.5%)
4	Sweating	99 (83.8%)	99 (83.8%)
5	Dyspnoea	61 (51.6%)	24 (20.3%)
6	Nausea and vomiting	82 (69.4%)	43 (37.3%)
7	Dizziness/Syncope	14 (11.8%)	6 (5%)
8	Palpitations	23 (19.4%)	10 (8.5%)

Typical chest pain was more common in males with acute myocardial infarction as compared to females with statistical significant difference( $p=0.0061$ ). Atypical chest pain was significantly high in females as compared to males.Few cases didn't have symptom of chest pain.Occurance of other symptoms like dyspnoea,nausea and vomiting,dizziness or syncope,palpitations were found to be more common in females as compared to males.None of the patient in both groups presented with altered sensorium,abdominal pain or focal neurological deficit.

**Table 4:**Comparison of risk factors for acute myocardial infarction in females and males

Sr. No.	Risk factors	Females (%) N=118	Males(%) N=118	Odds ratio	95% confidence	P value
1.	Hypertension	65(55%)	64(58.2%)	1.03	0.79-1.31	1.0
2.	Diabetes mellitus	54(45.7%)	36(30.5)	1.92	1.07-1.76	0.0227
3.	Smoking/ Tobacco chewing	29(24.6%)	79(67.8%)	0.16	0.28-0.54	0.0001
4.	Dyslipidemia	83(69.5%)	68(57.6%)	1.74	1.0-1.79	0.0576
5.	Central obesity	67(56%)	56(47.5%)	1.45	0.93-1.56	0.1926

6.	Lack of physical activity	100(84.7%)	59(50%)	5.56	1.76-4.10	0.0001
7.	Alcohol use	0	36(30.5%)	-	-	-
8.	Family history of CAD	36(30.5%)	20(16.9%)	2.15	1.10-1.82	0.0217
9.	Early menopause	17(13.6%)	-	-	-	-

Among the risk factors, hypertension was more common in female cases as compared to male cases of acute myocardial infarction. Diabetes mellitus was significantly more common in female cases as compared to male cases with p value 0.0227. 29 female cases used to practice tobacco chewing whereas 79 male patients used to smoke tobacco. Thus practice of using tobacco products was significantly

more common in male cases than female cases with p value 0.0001. Central obesity was more common in female cases than male cases. Lack of physical activity was observed significantly more in female cases vs male cases with p value 0.0001. Family history of CAD was significantly more common in female cases as compared to male cases with p value 0.0217

None of the female consumed alcohol whereas 36(30.5%) male patients used to consume alcohol. Early menopause was present in 17(13.6%) female cases in this study.

80(67.7%) female cases presented with congestive cardiac failure at the time of admission vs 50(42.5%) male cases (p=0.8773). Maximum cases were in Killip's class II in both the groups, 52(44%) female cases vs 29(25.4%) male cases.

**Table 5:** Complications and outcome of acute myocardial infarction during hospital stay

Sr. No.	Complications	Females(N=118)			Males(N=118)			P value
		No. of cases	Recovered	Death	No. of cases	Recovered	Death	
1.	Cardiogenic shock	10(8.47%)	2	8	4(3.3%)	2	2	0.162
2.	Reinfarction	3(2.5%)	3	0	2(1.7%)	2	0	1.00
3.	Arrhythmias	42(35.6%)	35	7	50(42.4%)	42	8	0.350
4.	Cerebrovascular episode	3(2.5%)	3	0	2(1.7%)	2	0	1.00
5.	Major/minor bleeding complications	0	0	0	2(1.7%)	2	0	-
6.	Death(total)	15(12.7%)	10(8.47%)			0.3975		

Arrhythmia was the most common complication in both groups having acute myocardial infarction with 42 female and 50 male cases. Out of 42 female cases, 35 recovered while 7 female cases died of cardiac arrest whereas out of 50 male cases, 42 recovered while 8 male cases died of cardiac arrest. Out of 10 female cases having cardiogenic shock, 2 cases recovered and 8 female cases died during 7 days stay in hospital. Out of 4 male cases having cardiogenic shock, 2 cases recovered and 2 died during same period of hospital stay. 3 female cases and 2 male cases had reinfarction with no mortality. 3 female cases and 2 male cases had cerebrovascular episode during 7 day hospital stay and there was no mortality. 2 male cases had bleeding complication in the form of hematemesis but none of the female cases had such complication during 7 day stay.

Mortality was more in female cases compared with male case i.e 15(12.7%) vs 10(8.47%), but there was no statistical significant difference.

**Table 6:** Complications, interventions and outcome of acute myocardial infarction in female and male cases on one month follow up

Sr. No.	Complications and interventions	Females(%) (N=103)	Males(%) (N=108)	P value
1.	Death(from day 8 to day 30)	2(1.69%)	2(1.85%)	0.6641
2.	Post MI angina	21(20.38%)	12(11.11%)	0.09593
3.	Congestive cardiac failure	8(7.76%)	2(1.85%)	0.04298
4.	Cardiogenic shock	2(1.69%)	2(1.85%)	0.6641
5.	Fresh myocardial infarction	0	0	-
6.	Cerebrovascular episode	0	0	-
7.	Coronary angiography	4(3.88%)	9(8.33%)	0.2903
8.	Percutaneous transcatheter angioplasty(PTCA)	0	3(2.77%)	-
9.	Coronary artery bypass graft(CABG)	0	0	-

15 female cases and 10 male cases died by the end of 1<sup>st</sup> week and hence 103 female and 108 male cases were followed at the end of one month.

Post infarction angina was the most common complication among both groups during one month follow up period. 21 female cases and 12 male cases experienced post infarction angina during follow up period. 8 female cases and 2 male cases had congestive cardiac failure during this period. 2 female cases and 2 male cases went into cardiogenic shock during one month follow up period but none of the patient with cardiogenic shock survived. None of the patient from both groups had fresh myocardial infarction or cerebrovascular episode during follow up period.

4 female cases underwent coronary angiography but none of them had angioplasty or CABG done while 9 male cases underwent coronary angiography and out of them 3 patients had done coronary angioplasty.

## DISCUSSION

In this study the clinical presentation, risk factors, complications, interventions and mortality rates of females with acute myocardial infarction were compared with males. Although women are principally subject to the same risk factors as men, the significance and the relative weighting of these factors are different. Coronary artery disease in females is often difficult to diagnose because it may present with a mix of typical and atypical symptoms.

In this study, maximum number of female cases belonged to the age group 60-69 years whereas maximum number of male cases were in age group 50-59 years. 48(40.7%) female cases were <60 years age whereas 80(67.8%) male cases were <60 years age group. 70(59.3%) female cases belonged to >60 years of age while 38(32.2%) male cases were >60 years age group. Mean age at the time of presentation in female cases was 58.75 ± 9.32 years, whereas in male cases, it was 53.43 ± 10.99 years. Females were found to be on an average 5.32 years older than males. In Interheart study(2004)<sup>5</sup>, mean age of females with AMI was 65 years while 56 for male cases with significant difference, p<0.0001. 67.3% female cases were of age >60 years while 37.3% male cases were of age >60 years. 32% female cases were <60 years age group vs 59% male cases. Thus female patients with AMI were older than male cases. In other words male patients presented earlier at younger age than female patients. Thus our observations were similar as in above study. In similar study by Toba et al(2007)<sup>7</sup>, out of 918 patients of acute myocardial infarction, 71.9% were males and 28.1% were females. Women and men had mean ages of 65.62±10.56 years and 58.98±12.11 years respectively.

In our study, STEMI was more common in males(94.9%) as compared to females(83.89%) with p value 0.011. Anterior wall MI was the commonest type of MI observed in both groups. Next common type was inferior wall MI in both groups. Non ST elevation MI was more common in females (16%) vs men (5%) with p value 0.0114. Typical chest pain was more common in males(52.4%) than females(30.31%) with p value 0.0061. Atypical chest pain was common in females (50.8%) than males(33.8%). 20(16.9%) females and 16(13.5%) males presented without chest pain. Occurrence of other atypical symptoms was found to be more in females as compared to males like dyspnoea 51.6% in females vs 20.3% in males with p value 0.0001. Other symptoms like nausea and vomiting was more in females (69.4%) vs males (37.3%) with p value 0.0001, palpitations in 19.4% females vs 8.5% males with p value 0.024. Similar observations were made in study by Milner KA, Richards S, et al(1999)<sup>8</sup> where they studied AMI in 127 male cases and 90 female cases. Typical chest pain was observed in 36(57%) female cases and 63(70%) male cases of AMI. Atypical chest pain was observed in 27(43%) female cases vs 27(30%) male cases of AMI. Occurrence of other atypical symptoms was found to be more in female cases as compared to male cases of AMI.

## Comparison of risk factors for AMI in female and male cases

Significant difference was observed in risk factors like diabetes mellitus, lack of physical activity and family history of CAD amongst

female and male cases. These risk factors were significantly more in female cases than male cases of AMI. Diabetes mellitus in 54(45.7%) females vs 36(30.5%) males, lack of physical activity in 100(84.7%) females vs 59(50%) male cases, whereas family history of CAD in 36(30.5%) female cases vs 20(16.9%) male cases of AMI. Tobacco use was significantly more in male as compared to female cases, 79(67.8%) male vs 29(24.6%) female cases. 36(30.5%) male used to consume alcohol whereas none of the female consumed alcohol. No significant difference observed in risk factors like hypertension, dyslipidemia and central obesity amongst male and female cases.

Similar observations were made in Interheart study(2004)<sup>5</sup> including 27098 participants from 52 countries, 6787 of whom were female. In this study, hypertension, diabetes, physical activity and moderate alcohol use were more strongly associated with AMI among women than men. The association of abnormal lipids, current smoking, abdominal obesity, high risk diet and psychosocial stress with AMI were similar in men and women. Similar study by Yavagal ST, Rangarajan R, Prabhavati et al(1994)<sup>9</sup> observed AMI in women occurred mostly (80%) in postmenopausal period. Common risk factors in Indian women were hypertension in 49% cases and diabetes mellitus in 34% cases.

#### Complications and outcome of acute myocardial infarction during hospital stay

In our study 80(67.7%) female cases and 50(42.5%) male cases had congestive cardiac failure at the time of admission. More female cases 10(8.47%) had cardiogenic shock, out of which 2 cases recovered and 8 female cases died. 4(3.3%) male cases had cardiogenic shock of whom 2 cases recovered and 2 died. Arrhythmias were seen in 42(35.6%) females vs 50(42.4%) male cases. Reinfarction observed in 3 female cases and 2 male cases without any adverse outcome. 3 females and 2 males suffered cerebrovascular episode during 7 days stay in hospital without any mortality. 2 male cases and none of the female cases had bleeding manifestation in the form of hematemesis. Mortality during hospital stay was more in the female cases compared with the male cases, 15(12.7%) in females vs 10(8.47%) in males without statistical significant difference ( $p=0.3975$ ).

Similarly Sawaya J., Ijazra C., Sabara R.F.(1999)<sup>10</sup> studied 433 cases, 99 were females. They observed that women developed more heart failure, arrhythmias and had significant higher incidence of recurrent ischemia or myocardial infarction. The overall mortality rate was higher in females than males, 16.2% vs 8.1% with  $p=0.037$ .

#### Complications, interventions and outcome of AMI in females and males on one month follow up

15 female cases and 10 male cases died by the end of 1<sup>st</sup> week, hence 103 female and 108 male cases followed up at the end of one month. Overall mortality at the end of one month was 17(14.4%) in female cases vs 12(10.16%) male cases with  $p=0.427$ . Out of 17 female cases, 7(41.17%) female cases died of ventricular fibrillation compared to 8 (66.66%) male cases ( $p=0.329$ ). 10(58.83%) female cases died of cardiogenic shock compared to 4(33.33%) male cases. ( $p=0.329$ )

Though we found increased mortality in female cases as compared to male cases, when age was adjusted for mortality, there was no significant difference observed. Increased age found to be a strong predictor for mortality.

Similar study by Nicod P. et al.(1989)<sup>11</sup> having 2089 cases with 1551 men and 538 women with AMI observed women had an increased mortality compared to men with  $p<0.003$ . Fabijanic D et al.(2006)<sup>12</sup> studied 3382 cases of AMI with 1184 women and 2198 men. They reported unadjusted in hospital mortality was higher in women (OR 1.77, 95% CI 1.47-2.15). Women died more often because of refractory pulmonary edema and cardiogenic shock ( $p=0.02$ ) or electromechanical dissociation and men died mostly by primary ventricular tachycardia or fibrillation ( $p=0.002$ ).

In our study 4(3.88%) female cases underwent coronary angiography but none of them had angioplasty or CABG done whereas 9(8.33%) male cases underwent coronary angiography and 3(2.77%) of them underwent PTCA. In study by Kudenchuk PJ et al(1996)<sup>13</sup> of 1096 cases of AMI with 846 men and 246 women observed that women were half as likely as men to undergo acute catheterization, angioplasty or coronary bypass surgery (odds ratio 0.5[0.3 to 0.7]). They reported

AMI in women was not as aggressively treated and resulted in less favourable outcome than in men.

#### CONCLUSIONS-

Females with AMI presented at older age than men. AMI with atypical chest pain was common in females. Conventional risk factors like diabetes mellitus, lack of physical activity, family history of CAD were significantly higher in females than men cases. Females had more mortality as compared to men but after adjustment for age it was not significant. Increased age at presentation in both the genders served as a strong predictor for mortality.

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