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Research Article

Impact of Gender on Clinical Characteristic, Treatment and Outcome in ST Elevation Myocardial Infarction: A Hospital Based Study from North-Eastern India

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ARTICLE INFO

Article history:

Received: 22 July, 2021

Accepted: 3 August, 2021

Published: 13 August, 2021

Keywords:

Gender

ST elevation myocardial infarction
north-eastern India

ABSTRACT

Background: Data on impact of gender on clinical presentation of ST Elevation Myocardial Infarction (STEMI) are sparse in our country. Gender related difference in STEMI has never been studied in North-Eastern India.

Aim: The present study was undertaken to study the impact of gender on clinical characteristic, treatment and outcome in STEMI.

Methods: We prospectively collected data of 510 STEMI patients from February 2011 to August 2012 in Gauhati Medical College, a tertiary care center in North-Eastern India. We evaluated data on impact of gender in clinical characteristic, treatment, and outcome in STEMI patients.

Results: A total of 510 cases of STEMI were included. Females in STEMI were older (53.6 years in males compared to 58 years in females, $P < 0.001$) and have greater atypical presentation (31.6% in females and 13.98% in males, $P < 0.001$). Females also have higher mean time to presentation and higher incidence of diabetes, dyslipidemia, hypertension and high BMI, whereas males had higher incidence of smoking. Females are less likely to undergo thrombolysis (28.73% in females compared to 44.34% in males, $p = 0.04$) and revascularization (17.5% in males and 9.1% in females $p = 0.01$) during index hospitalization, but standard medical therapy was similar. Women were also more likely to develop heart failure either at presentation or at 30 days and also had a higher 30-day mortality (15.5% in female and 9.8% in male, p value-0.06).

Conclusion: This study represents the first reported study on impact of gender on clinical presentation of STEMI from North-Eastern India and has observed that females have a higher mean age of presentation, higher incidence of atypical presentation, diabetes, dyslipidemia, hypertension and high BMI. Females also present later than males, though statistically not significant and also less likely to receive thrombolysis and revascularization than males. The 30-day mortality was also higher in females.

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Introduction

Cardiovascular disease has emerged as a major health problem in developing countries. It is the number one cause of death in India and accounted for approximately 21% of deaths in 2010, with 11.4% of these

deaths due to ischaemic heart disease [1]. Significant differences in the prevalence of coronary artery disease (CAD) exist with respect to gender, age, and ethnicity. The Acute Coronary Syndrome (ACS) comprises a wide spectrum of conditions that include unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI). ACS affects Indians at a

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younger age than counterparts in developed countries, as well as many other developing countries [2, 3]. CREATE registry, the largest data from Indian patients with ACS, has shown that the pattern of ACS among Indians is much different from that of the Western populations [3]. ACS occurs in Indians 5-10 years earlier than in other populations around the world and the major effect of this peculiar phenomenon is on the productive workforce of the country aged 35-65 years [3]. In our study on ACS, from North Eastern India, we have observed few key differences from national registry, CREATE with greater percentage of STEMI patients, greater delay in seeking treatment, greater 30-day mortality, and lesser percentage of patients receiving reperfusion therapy [4].

Gender related difference in myocardial infarction has been reported in various studies from western countries [5-8]. Specifically, women with ACS tend to be older than their male counterparts, are more likely to have a history of hypertension, and more often have atypical presenting symptoms [7]. There are limited studies on influence of sex on clinical presentation of myocardial infarction from our country. The national registry CREATE in India have not explored sex related differences in presentation, management, and outcomes in ACS [3]. The DEMAT registry, a multicenter registry from 10 tertiary care centers of our country has shown that women are more likely to be older and have greater co morbidities than men, though treatment and outcome did not differ after adjustment for potential confounders [9]. In Kerala ACS registry women were older and more likely to have previous MI, but there was no difference in in-hospital mortality, reinfarction, heart failure, or cardiogenic shock between sexes after adjustment for potential confounders [10]. Considering incredible diversity of our country, impact of gender on clinical characteristic, treatment and outcome in STEMI might be different in different regions. Gender related difference in STEMI has never been reported from North-Eastern India.

Therefore, the present study entitled "Impact of Gender on Clinical Presentation, Treatment and Outcome of STEMI-A Hospital Based Study from North-Eastern India" was undertaken in Cardiology Department of Gauhati Medical College, Guwahati with the aims of studying the gender related difference in clinical characteristics, treatment and outcome of STEMI.

Methods

The study entitled "Impact of Gender on Clinical Presentation, Treatment and Outcome in STEMI-A Hospital Based Study from North-Eastern India" has been conducted in Department of Cardiology, Gauhati Medical College, Guwahati from February 2011 to August 2012. All patients presenting with STEMI were included in the study. Detailed history, physical examination and necessary investigation were done in all patients.

I Inclusion Criteria for Study

- (i) Patients must be greater than 18 years of age.
- (ii) Patients must fulfill the diagnostic criteria of Acute Coronary Syndrome as given below:
Diagnosis of myocardial infarction were made if there is: Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of

biochemical markers of myocardial necrosis with at least one of the following [11]:

- (a) Ischaemic symptoms;
- (b) Development of pathologic Q waves on the ECG;
- (c) ECG changes indicative of ischaemia (ST segment elevation or depression);

Cases of ischaemic symptoms with ST segment elevation were categorized as STEMI if their cardiac biomarkers are positive and were included in the study.

- (iii) Written consent must be given.

II Exclusion Criteria for Study

- (i) Patients who were initially treated elsewhere and referred to the study center only for additional management.
- (ii) Patients with proven non-cardiac chest pain and
- (iii) Patients who were discharged before completion of the treatment for any reasons.

The baseline clinical characteristics which were analysed were the age, gender, hypertension (blood pressure > 140/90 mm Hg and/or those already taking treatment for hypertension), diabetes mellitus (fasting blood glucose >126 mg/dL and/or postprandial blood glucose >200 mg/dL and those who were on treatment for diabetes mellitus), smoking status, dyslipidemia (cholesterol >200 mg/dL and/or triglycerides >200 mg/dL and/or, LDL>130 mg/dL and/or HDL<40 mg/dL) and Body Mass Index (BMI). Mode of presentation, time of occurrence of the STEMI, clinical course in the hospital, time to reach hospital, treatments in hospital, the mean duration of hospital stay, and complications related to the STEMI and its treatment and in hospital outcome were analysed. In our study patients were considered patients to have atypical presentation if they present with dyspnea, nausea/vomiting, indigestion, fatigue, sweating, and arm or shoulder pain as presenting symptoms in the absence of chest pain. Influence of sex on clinical parameters, treatment received in hospital and outcome were analysed.

III Statistical Methods

All baseline parameter, treatment and outcome were compared between male and female. Statistical analysis was performed using the online statistical calculator, (Link 1). Categorical variables were compared by Fisher's exact test and the continuous variables are presented as mean (+/- SD) and were compared by unpaired t test. A probability value of <0.05 was considered statistically significant.

Results

A total of 510 consecutive cases of STEMI admitted to cardiology department of Gauhati Medical College Hospital from February 2011 to August 2012 were included in the present study. In STEMI males outnumbered females, 336 (65.8%) were males and 174 (34.2%) were females. The age of the STEMI patients in this study ranged from 30-87 years. The mean age of STEMI was 55.8 years. Females in STEMI were older than males (53.6 years in males compared to 58 years in females, $P<0.001$). 57.7% of males and 45.4% of females were between 40-60 years, whereas 30.05% of males and 45.4% of females were between 60-75 years (Table 1). In STEMI, of the 510 patients 80% patients had predominant symptom as chest discomfort and 20% had atypical presentation. Overall atypical presentation was more common in

females. 31.6% of females presented with atypical presentation compared to 13.98% in males ($P<0.001$). In STEMI, mean time to presentation was 9.98 hours. Mean time to presentation was 9.51 hours in male and 10.46 hours in female. There was greater delay in presentation to hospital in case of females though statistically not significant ($P=0.26$). 118 (67.18%) of females and 163 (48.5%) of males presented to hospital from symptom onset at greater than 12 hours (Table

1). In this study, out of 510 patients, 262 (51.37%) patients had inferior wall infarction, 230 (45.0%) had anterior wall infarction. Of the remaining 18, 16 (3.13%) had isolated lateral wall infarction and 2 (0.3%) had posterior wall infarction. In 262 patients with inferior wall infarction 112 (42.74%) had associated RV infarction. There was no difference on the type of infarction between male and female.

Table 1: Clinical characteristic, treatment and outcome in STEMI.

VARIABLE		TOTAL	MALE	FEMALE	P VALUE
N		510	336 (65.8%)	174 (34.2)	<0.001
CLINICAL CHARACTERISTIC					
MEAN AGE		55.8 yrs	53.6 yrs	58 yrs	<.001
SMOKER		235 (46.07)	227 (67.5%)	8 (4.5%)	<0.001
HYPERTENSION		210 (41.1%)	122 (36.3%)	88 (50.5%)	<0.001
DIABETES		174 (34.1%)	91 (27.08%)	83 (47.7%)	<0.001
BMI $\geq$ 25		135 (26.4%)	66 (19.6%)	69 (39.6%)	0.003
H/O OF PREVIOUS MI		88 (17.25%)	45 (13.3%)	33 (18.91%)	0.11
DYSLIPIDEMIA		170 (33.3%)	89 (26.4%)	81 (46.5%)	0.001
MEAN TIME TO PRESENTATION		9.98 hrs	9.51 hrs	10.46 hrs	0.26
ATYPICAL PRESENTATION		102 (20%)	47 (13.98%)	57 (31.6%)	<0.001
TREATMENT IN HOSPITAL					
ASPIRIN		506 (99.2%)	334 (99.4%)	172 (98.8%)	0.6
CLOPIDOGREL		502 (98.4%)	332 (98.8%)	170 (97.7%)	0.45
STATINS		506 (99.2%)	334 (99.4%)	172 (98.8%)	0.6
ACEI/ARB		459 (90.1%)	301 (89.5%)	158 (90.8%)	0.75
Beta blockers		456 (89.4%)	300 (89.2%)	156 (89.6%)	1.00
LMWH		496 (98.4%)	327 (97.3%)	169 (97.1%)	1.00
Thrombolysis		199 (39.1%)	150 (44.34%)	50 (28.73%)	0.04
PCI		75 (14.7%)	59 (17.5%)	16 (9.1%)	0.01
OUTCOME AT 30 DAYS					
HEART FAILURE/ CARDIOGENIC SHOCK		65 (12.7%)	35 (10.41%)	30 (17.2%)	0.03
REINFARCTION		34 (6.66%)	18 (5.35%)	16 (9.1%)	0.13
CARDIAC ARREST (resuscitated)		33 (6.47%),	17 (5.05%)	16 (9.1%)	0.08
STROKE		3 (0.58%)	3 (0.89%)	0%	0.55
DEATH		60 (11.76%)	33 (9.8%)	27 (15.51%)	0.06
Cause of death	Pump failure	27 (45%)	14 (42.4%)	13 (48.1%)	0.14
	Asystole	10 (18.51%)	6 (18.1%)	4 (14.81%)	0.74
	VF	10 (18.51%)	6 (18.1%)	4 (14.81%)	0.74
	Multifactorial	13 (24%)	7 (21.21%)	06 (22.2%)	0.38

In this study, out of 510 patients, 235 (46.07%) were smokers (past or present), 210 (41.1%) were hypertensives, 174 (34.1%) were diabetic, 88 (17.25%) had history of previous myocardial infarction, 170 (33.3%) had dyslipidemia and 135 (26.4%) had BMI $\geq$ 25. There was higher incidence of diabetes, hypertension, dyslipidemia and high BMI among females whereas males had higher incidence of smoking (Table 1). In this study, of the 510 patients, 199 (39%) patients received thrombolysis and 9 (1.76%) patients received Primary PCI. Lesser percentage of females received thrombolysis (28.73% in females compared to 44.34% in males, $p=0.04$). Overall females are less likely to undergo revascularization with 17.5% of males and 9.1% of females undergoing revascularization during index hospitalization ($p=0.01$). However, in terms of standard medical therapy there was not much of difference between males and females, with high percentage of both groups receiving standard medical therapy (Table 1). On observing the outcome at 30 days, we observed that females were also more likely to develop

heart failure either at presentation or at 30-days and also had a higher 30-day mortality. The 30-day mortality was found to be 11.76% (15.5% in female and 9.8% in male, $p=0.06$). The most common cause of death was pump failure which was observed in 45% of all death. Females had higher incidence of pump failure as mode of death in STEMI (Table 1).

Discussion

In this study, we have studied the impact of gender on clinical presentation, treatment and outcome of ST Elevation Myocardial infarction in Gauhati Medical College, which is a tertiary care Hospital of Assam. This is the first reported study on impact of gender on clinical presentation in STEMI from North-Eastern India. In this study, males outnumbered females, 336 (65.8%) were males and 174 (34.2%) were females ($p<0.001$). Similar observation has also been made in other studies with males outnumbering females in STEMI [3, 12-15]. In

GRACE registry 72% of STEMI were males and in EHS (European Heart Survey) I there was male dominance of 71.6% in STEMI [12, 13]. In CREATE Registry, from our country 81.5% of STEMI were males [3]. In our study, females were older than males (53.6 years in males compared to 58 years in females, $P < 0.001$). Similar observation has been made in various western and Asian studies [3, 8, 14, 15]. In study by Hochman *et al.*, the median age of females in STEMI was 69 years compared to 61 years in male. Another registry from Thailand of 1,223 patients, mean age of females was 67.5 years compared to 59.7 years in male [15]. In an Indian study by Misiriya *et al.*, the mean age of females in STEMI was 69 years compared to 56 years in male [14].

The mean time to presentation of STEMI from symptom onset to arrival in hospital is 9.98 hours in our study. In our study, the mean time to presentation to hospital was higher in females, though statistically not significant ($p = 0.26$). Similar observation has also been made with various western and Indian studies [7, 11, 14]. In study by Misiriya *et al.*, mean duration of symptom before hospitalization was 3.3 hours in male and 5.2 hours in female [14]. In our study, there was higher incidence of diabetes, hypertension, dyslipidemia and high BMI among females whereas males had higher incidence of smoking. There was also a trend towards higher incidence of history of previous MI in females, though statistically not significant. Similar observation has also been made in various other studies [8, 14]. In study by Hochman *et al.* 54% of females and 36% of males with STEMI had hypertension and 22% of females and 14% of males with STEMI had diabetes [8]. Similar to our study, an Indian study by Misiriya *et al.*, has also observed higher incidence of diabetes, hypertension and dyslipidemia in females [14]. In our study, atypical presentation was more common in females. 31.6% of females presented with atypical presentation compared to 13.98% in males ($P < 0.001$). Similar observation has also been made in various other studies [16, 17].

On observing the treatment pattern in our study, we noted that females are less likely to undergo thrombolysis (28.73% in females compared to 44.34% in males, $p = 0.04$) and revascularization (17.5% in males and 9.1% in females $p = 0.01$) during index hospitalization. Other studies have also made similar observation [14, 15, 18, 19]. In Thai registry, thrombolysis, and PCI were used less frequently in women [15]. The CRACE (Chinese Registry of Acute Coronary Events), which consisted of 1,301 patients from 12 medical centers in China, found that female patients less often received reperfusion therapies [18]. The GULF RACE-2 (2nd Gulf Registry of Acute Coronary Events) of 7,930 patients from 6 Arabian Gulf countries with ACS found that women were less likely to undergo angiography, percutaneous coronary intervention (PCI), and reperfusion therapy [19]. In our study, use of key medical treatments (anticoagulant, antiplatelets, β blockers, ACE inhibitors and statins) was comparable between men and women. This shows increased awareness of evidence-based treatments by our medical fraternity. Since, it is a single center, tertiary care hospital most of the costly medicines including low molecular weight heparin was available free of cost to our patients. So, it was easy on our part to provide evidence-based treatment to our patients. Since percutaneous coronary intervention or bypass surgery was not free of cost to our patients, we observed that females are less likely to undergo revascularization. This reflects lack of intention to provide treatment to female patients by their family members. In contrast to our study, CRACE and Thai registry observed significant difference in in-hospital treatment between male and female [15, 18]. However

Indian study, DEMAT registry and Kerala registry failed to observe significant differences in in-hospital medical treatment [9, 10].

On analysing the outcome at 30-days, we observed that women were also more likely to develop heart failure either at presentation or at 30-days and also had a higher 30-day mortality. Higher incidence of heart failure and mortality in females has also been noted in few other studies [14, 15]. In the Thai registry, the total in-hospital mortality was 24% in women and 14% in men [15]. The DEMAT and Kerala registry, however failed to observe sex related difference in 30-day outcome after adjustment for confounding factors [9, 10]. Contrary to above registry, an Indian study by Misiriya *et al.*, observed higher mortality in (22.8% vs. 9%; $p < 0.001$) [14].

Study Limitation

There are certain limitations of our study. First, this is a single center study and gender related difference in STEMI can be different in other parts of state. Secondly our sample size was relatively small and there were relatively few events to compare differences in outcomes. Thus, we may not have had sufficient power to detect important gender differences in short-term outcomes.

Conclusion

There is definite impact of gender on clinical presentation, treatment and outcome of ST Elevation MI in this part of country. Females have a higher mean age of presentation, higher incidence of atypical presentation, diabetes, hypertension, dyslipidemia and high BMI. The increased mortality in female is partially accounted by higher risk factor, but in addition there is a gender discrimination as they are brought to hospital later than males and family members are less keen to provide them with costly treatment like thrombolysis and revascularization.

Consent and Ethical Approval

The authors certify that informed consent has been obtained from each patient and the study protocol conforms to the ethical guidelines as approved by the institution's human ethics committee.

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