

Sex Related Difference in Nstemi/UA- A Study from Major Centre in North-Eastern India

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Abstract:

Background: Data on sex related difference in clinical presentation of NSTEMI/UA are sparse in our country. Sex related in NSTEMI/UA difference has never been studied in North-Eastern India

Aim: The present study was undertaken to study the sex related difference in clinical characteristic, treatment and outcome in NSTEMI/UA

Methods: We prospectively collected data of 194 NSTEMI/UA patients from February 2011 to August 2012 in Gauhati Medical College, a tertiary care center in North-Eastern India. We evaluated data on sex related difference in clinical characteristic, treatment, and outcome in NSTEMI/UA patients.

Results. Of the 194 patient with NSTEMI/UA, 121(62.37%) presented with NSTEMI (positive cardiac biomarkers) & 73(37.6%) presented with Unstable Angina(UA). Females in NSTEMI/UA were older (54.4 years in males compared to 60 years in females, $P<0.001$), have greater atypical presentation (44.69% in females & 28% in males , $P=0.01$), higher mean time to presentation and higher incidence of diabetes ,hypertension and high BMI among females whereas males had higher incidence of smoking. . Females are less likely to undergo revascularization with 12% of males and 3.1% of females underwent revascularization during index hospitalization ($P =0.29$), 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 ,though statistically not significant (8.5% in female & 4% in male, p value-0.23).

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

I. Introduction

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 accounts for over 1.5 million hospitalizations and around 30% of all death in United States and many millions worldwide. (1). The situation in developing countries and in our country, India, is more dismal. Between 1990 and 2020, Coronary Artery Diseases(CAD) are expected to increase by 120% for women and 137% for men in developing countries, compared with 30–60% in developed countries(2) .CAD affects Indians at a younger age than counterparts in developed countries, as well as many other developing countries (3,4,5). 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 (5).CAD 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. (5). 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(6).

Sex related difference in ACS has been reported in various studies from western countries.(7,8,9,10). In a large study from US involving 35,875 patients (CRUSADE) ,women were more likely to be older and have higher incidence of diabetes and hypertension and less likely to be smokers (7).Women in the US with unstable angina are generally older, more likely to have a history of hypertension, and less likely to present with typical anginal symptoms than men (8). Women with unstable angina are also less likely to receive recommended pharmacologic care or receive cardiac catheterization, coronary angioplasty, or bypass surgery compared to men (9)

There are limited studies on sex related difference in ACS from our country. The national registry CREATE in India have not explored sex related differences in presentation, management, and outcomes in ACS

(5). The DEMAT registry, a multicentre registry from 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 (11).

In NSTEMI/UA, sex related difference in clinical presentation; treatment and outcome are less well known than STEMI. There are limited studies on sex related difference in NSTEMI/UA, especially from our country. Sex related difference NSTEMI/UA has never been reported from North Eastern India Therefore the present study entitled “*Sex related difference in NSTEMI/UA- A study from major centre in North-Eastern India*” was undertaken in Cardiology Department of this hospital with the aims of studying the sex related difference in clinical characteristics, treatment and outcome of NSTEMI/UA.

II. Methods

The study entitled “*Sex related difference in NSTEMI/UA-A study from major centre in North-Eastern India*” has been conducted in Department Of Cardiology, Gauhati Medical College, Guwahati from February 2011 to August 2012.

All patients presenting with NSTEMI/UA were included in the study. Detailed history, physical examination & necessary investigation were done in all patients.

Inclusion Criteria for Study.

1. Patients must be greater than 18 years of age
 2. 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: (10)

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

Cases of ischemic symptoms without ST segment elevation were categorized as NSTEMI if their cardiac biomarkers are positive and were included in the study.

Unstable angina is defined as angina pectoris (or equivalent type of ischemic discomfort) with at least one of three features:

- (1) Occurring at rest (or minimal exertion) and usually lasting >20 minutes (if not interrupted by nitroglycerin administration);
- (2) Being severe and described as frank pain, and of new onset (i.e., within 1 month; and
- (3) Occurring with a crescendo pattern (i.e., more severe, prolonged, or frequent than previously).

Patients with above features without elevation in cardiac markers were categorized as Unstable Angina)(11).

3. Written consent must be given

Exclusion Criteria for Study.

1. Patients who were initially treated elsewhere and referred to the study centre only for additional management;
2. Patients with proven non-cardiac chest pain and
3. Patients who were discharged before completion of the treatment for any reasons

The baseline clinical characteristics which were analyzed 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)& Body mass Index(BMI).

Mode of presentation, time of occurrence of the NSTEMI/UA, clinical course in the hospital, time to reach hospital, treatments in hospital, the mean duration of hospital stay and complications related to the NSTEMI/UA and its treatment were analyzed.. 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

The in hospital outcome were analysed. Those patients giving consent for angiography were taken up for angiography. Angiographic findings were noted. They were categorized as

- 1.Normal Coronaries
- 2.Insignificant Disease(less than 50% diameter stenosis as per visual estimation)
- 3.Single Vessel Disease
- 4.Double Vessel Disease
- 5.Triple Vessel Disease
- 6.Left Main Disease.

A comparison of clinical parameters ,treatment received in hospital & outcome and angiographic profile between males and females.

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

III. Statistical Methods.

All baseline parameter, treatment, outcome & angiographic profile were compared between male & female.

Statistical analysis was performed using the online statistical calculator ,www.graphpad.com.

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.

IV. Results.

A total of 194 consecutive cases of NSTEMI/UA admitted to cardiology department of Gauhati Medical College Hospital from February 2011 to August 2012 were included in the present study. Of the 194 patient with NSTEMI/UA, 121(62.37%) presented with NSTEMI (positive cardiac biomarkers) & 73(37.6%) presented with Unstable Angina (UA). Males and females were almost equal with 100(51.5%) being males and 94 (48.5%) being females (p value-0.61)

The mean age of presentation was 57. 2 years (57.3 years for UA & 57 years for NSTEMI,P-0.9). Females in NSTEMI/UA were older than males (54.4 years in males compared to 60 years in females, P<0.001) . Of the 194 patients, 7(3.60%) were below 40 years, 98(50.51%) were between 40-60 years, 78(40.2%) were between 60-75 & 11(5.67%) were greater than or equal to 75 years. (Ref .Table 1)

In NSTEMI/UA, of the 194 patients 65.9% patients had predominant symptom as chest discomfort & 36.09 % had atypical presentation. The most common presentation other than central or left sided chest discomfort was dyspnea which as observed in 14.43% of patients. Overall atypical presentation was more common in females with 44.69% of females presenting with atypical presentation compared to 28% in males (P-0.01).

In NSTEMI/UA, mean time to presentation was 12.86 hours. 57.5% (54/94) of females patients presented to hospital after 12 hours from symptom onset compared to 42%(42/100) of male patients.(P-0.04).The mean time to presentation to hospital was 13.4 hours in females compared to 12.1 hours in males(P-0.33). (Ref .Table 1)

In NSTEMI/UA, out of 194 patients, 82(42.2%) were smokers(past or present), 98(50.5%)were hypertensive's , 82(42.2%) were diabetic & 62(31.9%) had BMI \geq 25. There was higher incidence of diabetes ,hypertension and high BMI among females whereas males had higher incidence of smoking. (Ref .Table 1)

On observing the treatment pattern in NSTEMI/UA, we noted that females are less likely to undergo revascularization with 12% of males and 3.1% of females underwent revascularization during index hospitalization (P-0.29). 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. (Ref .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 ,though statistically not significant . In NSTEMI/UA patients, 30 day mortality was found to be 6.18%. (8.5% in female & 4% in male, p value-0.23) . The most common cause of death was pump failure which was observed in 66.66% of all death. Females had higher incidence of pump failure as mode of death in NSTEM/UA. (Ref .Table 1)

In NSTEMI/UA, Coronary angiography was obtained in 42.26% of patients during index hospitalization. Normal coronaries was found in 21.95 % ,insignificant CAD was observed in 8.53% ,SVD in 35.36%, DVD in 14.63%, TVD in 16.6% & left main disease in 3.65%. There was a trend towards higher incidence of normal coronaries in females with NSTEMI/UA. (Ref .Table 2)

V. Discussion

In this study, we have studied the sex related difference in clinical presentation ,treatment and outcome of NSTEMI/UA in Gauhati Medical College ,which is a tertiary care Hospital of Assam. This is the first reported study on sex related difference in NSTEMI/UA from North –Eastern India.

Our results show that on presentation, women were more likely to be older and to have a history of hypertension and diabetes than men, though they were less likely to be smokers. Women were also less likely to undergo revascularization, though medical treatment did not differ. Women were also more likely to develop heart failure either at presentation or at 30 days and also had a higher 30 day mortality ,though statistically not significant.

In our study, in NSTEMI/UA, males and females were almost equal with 100(51.5%) being males and 94 (48.5%) being females (p value-0.61) . This is in contrary to various western and Indian studies, where males outnumbered females (7, 8, 10, 11, 14, and 15)

In our study, the mean age of presentation was 57. 2 years which is a decade earlier than western studies (16-18) and is comparable with mean age of cases from Indian studies (5, 14, and 19). In our study,

females were older than males (54.4 years in males compared to 60 years in females, $P < 0.001$). Similar observation has been made in various western and Indian studies(7,8,10,11,14,15).

In our study, the mean time to presentation to hospital was significantly higher in females. The mean time to presentation to hospital was 13.4 hours in females compared to 12.1 hours in males ($P = 0.33$). Similar observation has also been made with various western & Indian studies(7,11,14). In an Indian study, by Misiriya et al, mean duration of symptom before hospitalization was 3.6 hrs in male and 6.1 hrs in female(14)

In our study, atypical presentation was more common in females with 44.68% of females presenting with atypical presentation compared to 28% in males ($P = 0.01$). Similar observation has also been made with various western & Indian studies.(7,8,14)

In our study, there was higher incidence of diabetes, hypertension and high BMI among females whereas males had higher incidence of smoking. There was also a trend towards higher incidence of dyslipidemia and history of previous MI in females, though statistically not significant. In a large study from US involving 35,875 patients (CRUSADE), women were more likely to have higher incidence of diabetes and hypertension and less likely to be smokers(7), but in contrary to our study they are less likely to have dyslipidemia. Similar to our study, an Indian study by Misiriya et al, has also observed higher incidence of diabetes, hypertension and dyslipidemia in females(14).

On observing the treatment pattern in our study, we noted that females are less likely to undergo revascularization with 12% of males and 3.1% of females undergoing revascularization during index hospitalization($P = 0.29$). Other studies has also observed that females are less likely to undergo revascularization(7,9)

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 centre, 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.

On analyzing 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, though statistically not significant. Higher incidence of heart failure in females has also been noted in few other studies(7,14). CRUSADE data from US also observed higher incidence of heart failure and death in females. The DEMAT registry, a multicentre registry from our country, however failed to observe sex related difference in 30 day outcome after adjustment for confounding factors(11). Contrary to DEMAT registry, an Indian study by Misiriya et al, observed higher mortality in females(14)

On analyzing the coronary angiographic patterns, between male and females we observed that females have higher incidence of normal coronaries, whereas males have higher incidence of single vessel disease. Similar observation has been made in western studies including GUSTO IIB, where they have observed that females tend to have milder disease with higher incidence of normal coronaries in females (20).

VI. Study Limitation

There are certain limitation of our study. First, this is a single centre study and sex related difference in NSTEMI/UA 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. Moreover coronary angiography was obtained in only 42.26% patients(who gave consent). So sex related difference in angiographic pattern could have been different, had we got all patients for coronary angiography

VII. Conclusion

This study represents the first reported study on sex related difference in NSTEMI/UA from North-Eastern India and has observed that females have a higher mean age of presentation, higher incidence of atypical presentation, diabetes, hypertension & high BMI. Females also present later than males, though statistically not significant and also less likely to receive revascularization than males. This reflects gender discrimination to provide evidence based treatment to females, largely by their family members in this part of country. The 30 day mortality was also higher in females though statistically not significant.

Further studies with larger sample sizes in varied clinical settings are required to understand possible differences in clinical characteristic, treatment and outcomes of women vs. men with NSTEMI/UA, specially from our country.

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Table 1(clinical characteristic ,treatment and outcome in NSTEMI/UA)

VARIABLE	TOTAL	MALE	FEMALE	P VALUE	
N	194	100	94	0.61	
CLINICAL CHARACTERISTIC					
MEAN AGE	57.2 yrs	54.4yrs	60 yrs	<.001	
SMOKER	82(42.2%)	78(78%)	4(4.2%)	<0.001	
HYPERTENSION	98(50.5%)	40(40%)	58(61.7%)	0.002	
DIABETES	78(42.2%)	32(32%)	46(48.9%)	0.02	
BMI>25	62(31.9%)	22(22%)	40(42.5%)	0.003	
H/O OF PREVIOUS MI	34	14(14%)	20(21.2%)	0.19	
DYSLIPIDEMIA	55	23(23%)	32(34%)	0.11	
MEANTIMETOPRESENTATION	12.86hrs	12.1hrs	13.4hrs	0.33	
ATYPICAL PRESENTATION	70(36.09%)	28(28%)	42(44.68%)	0.01	
TREATMENT IN HOSPITAL					
ASPIRIN	193(99.4%)	100(100%)	93(98.9%)	0.48	
CLOPIDOGREL	193(99.4%)	100(100%)	93(98.9%)	0.48	
STATINS	193(99.4%)	100(100%)	93(98.9%)	0.98	
ACEI/ARB	182(93.8%)	93(93%)	89(94.6%)	0.76	
Beta blockers	177(91.23%)	93(93%)	84(89.3%)	0.44	
LMWH	191(98.4%)	99(99%)	92(97.8%)	0.61	
PCI	15(7.7%)	12(12%)	3(3.19%)	0.29	
OUTCOME AT 30 DAYS					
HEART FAILURE/ CARDIOGENIC SHOCK	22(11.3%)	8(8%)	14(14.89%)	0.17	
REINFARCTION	4(2.06%)	2(2%)	2(2.12%)	1.00	
CARDIAC ARREST(resuscitated)	5(2.57%)	3(3%)	2(2.12%)	1.00	
STROKE	0%	0%	0%	-	
DEATH	12(6.18%)	4(4%)	8(8.51%)	0.23	
Cause of death	Pump failure	8(66.6%)	2(50%)	6(75%)	0.54
	Asystole	0%	0%	0%	-
	VF	2(16.6%)	1(25%)	1(12.5%)	1.00
	Multifactorial	2(16.6%)	1(25%)	1(12.5%)	1.00

TABLE 2: Coronary angiography in NSTEMI/UA

ACS	TOTAL	STEMI	NSTEMI/UA	P VALUE
N(%)	82(42.26%)	48(48%)	34(36.1%)	0.11
NORMAL	18(21.95%)	6(12.5%)	12(35.2%)	0.28
INSIGNIFICANT CAD	7(8.53%)	5(10.41%)	2(5.88%)	0.69
SVD	29(35.36%)	20(41.66%)	9(26.4%)	0.24
DVD	12(14.63%)	7(14.58%)	5(14.7%)	1.00
TVD	13(16.6%)	8(16.6%)	5(14.7%)	1.00
Left Main	3(3.65%)	2(4.1%)	1(2.9%)	1.00