Internal Medicine Section

Gender Based Differences in Risk Factor Profile and Coronary Angiography of Patients Presenting with Acute Myocardial Infarction in North Indian Population

SUPRIYA BAJAJ[1], VIJAY MAHAJAN[2], SUMIT GROVER[3], AMIT MAHAJAN[4], NIPUN MAHAJAN[5]

ABSTRACT

Introduction: Coronary Artery Disease (CAD) among women presents atypically with atypical chest pain, neck pain, nausea, fatigue and dyspnoea. Co-existing co-morbidities such as Diabetes Mellitus (DM) and hypertension along with difference in risk factor prevalence makes it necessary to have a gender specific approach.

Aim: To study gender specific differences in diagnosing and treating Acute Myocardial Infarction (AMI) in North Indian population.

Materials and Methods: Fifty consecutive men and women presenting with AMI were studied. A detailed history including symptoms, history of DM, hypertension, smoking and dyslipidaemia was obtained. ECG, evaluation of cardiac enzymes (CPK-MB, Troponin I), RBS, lipid profile, two dimensional transthoracic echocardiography and coronary angiography were performed. The data was statistically analysed.

Results: Among 100 patients (50 males and females each), we found a later age at presentation (62 y vs 56.5 y) and higher prevalence of diabetes (52% vs 24%, p=0.004) and hypertension (46% vs 28%) among females but more dyslipidaemia (34% vs 26%), smoking (44% vs 0%, p=0.0) and higher BMI (25.58 vs 23.74, p=0.019) among males. More females presented with atypical symptoms (16% vs 6%) and were detected to have insignificant CAD (14% vs 2%) than males.

Conclusion: North Indian women with presentation at a later age, with atypical symptoms, more incidences of risk factors such as diabetes and hypertension along with lesser dyslipidaemia and BMI than males need a higher index of suspicion while evaluating them for CAD. Misdiagnosis is more likely because of atypical presentation. A milder disease on angiography and a lower incidence of multiple vessel disease is a common finding. We recommend more and larger Indian studies to acquire more data so that this growing prevalence of CAD in women can be curbed.

Keywords: Atypical, Coronary artery disease symptoms, Diabetes, Dyslipidaemia, Hypertension, Sex differences

INTRODUCTION

Coronary Artery Disease (CAD) for long has been called "men's disease"; however these days an increasing trend of CAD is observed in women [1,2]. There are major differences in the prevalence of various risk factors such as diabetes mellitus, hypertension, family history of CAD, dyslipidaemia, obesity and cigarette smoking probably because of advanced age of women at presentation and greater co-existence of co-morbidities such as diabetes and hypertension as compared to men. The presenting symptoms also differ as women are more likely to present with atypical chest pain, neck pain, nausea, fatigue and dyspnoea making the diagnosis more difficult subjecting women to suboptimal and less aggressive care [3-5].

This often leads to a higher mortality after the first episode of myocardial infarction and a greater incidence of complications among women necessitating a gender specific approach to primary and secondary prevention [4-7].

AIM

Through this study, we try to evaluate the differences in clinical presentation, risk factor profile and angiographic disease pattern among women and men presenting with acute myocardial infarction in North Indian population.

MATERIALS AND METHODS

A cross-sectional observational study was conducted in Tagore Hospital and Heart Care Center, Jalandhar, Punjab for a duration of one year period from July 2012 to June 2013. The study included 50 consecutive men and 50 consecutive women presenting with Acute Myocardial Infarction (AMI) in the emergency department. The study was approved by institutional human ethical committee. AMI was diagnosed on the basis of symptoms, ECG changes and elevated serum biochemical markers of myocardial necrosis. Patients with previous history of myocardial infarction, thrombolysis, percutaneous angioplasty or coronary artery bypass grafting or with structural, valvular or congenital heart disease were excluded. A detailed history was obtained from the patients after obtaining informed written consent including the symptoms, their duration, history of DM, hypertension, smoking, dyslipidaemia and family history of CAD. Diabetes, hypertension, dyslipidaemia, obesity and significant stenosis on angiography were defined using most recent criteria. Hypertension was defined as systolic BP >139 mmHg or diastolic BP >89 mmHg or history of treatment for hypertension. Diabetes was defined as fasting blood glucose >126mg/dl or 2 hour post load blood glucose >200mg/dl or history of treatment of diabetes. Dyslipidaemia was defined as LDL cholesterol ≥100mg/dl, HDL cholesterol ≤40 mg/dl, TGL levels ≥150 mg/dl. History of smoking was considered if consumption of tobacco in form of cigarettes or beedis was present since past 6 months or more. BMI was obtained by dividing the weight in kilograms by the square of height in meters. And the cut off for overweight was taken as BMI >23kg/m^2; and obese as BMI >25kgm^2 according to current Asian standards. On angiography, significant disease was defined as stenosis of more than 50% in the involved coronary artery.

Patients were subjected to a general and systemic examination and laboratory tests including ECG, random blood sugar (at the time of admission), cardiac enzymes (CPK-MB, Troponin I), lipid

profile and two-dimensional transthoracic echocardiography. Coronary angiography was performed on all the patients. The data was statistically analysed using Chi-Square test and ANOVA test.

RESULTS

Out of the 100 patients studied, on comparing the age at presentation, we found that average age of presentation in male patients was 56.5 years compared to 62 years among females, indicating a later age of presentation in females. On comparing the prevalence of risk factors between both sexes we found a higher prevalence of diabetes, hypertension and family history of CAD among females as compared to males with a significant difference in the prevalence of diabetes (p=0.004) [Table/Fig-1]. Among males smoking was a major risk factor contributing to coronary artery disease (p=0.00). When taken according to Asian standards, we found that mean body mass index (BMI) among males was 25.58 kg/m^2, SD 3.937as compared to 23.74 kg/m^2, SD 3.767 among females. (p=0.019) [Table/Fig-1].

Comparing the lipid profiles, we found that mean HDL levels were lower in females (47.3 mg/dl, SD 11.431) as compared to males (52.98 mg/dl, SD 43.223) while, mean LDL and mean serum triglyceride (TGL) was higher among male patients than females [Table/Fig-2]. The difference is, however, not significant. Both men and women showed similar higher TGL values. However, the difference in terms of lipid profiles in the two groups was non-significant.

Chest pain was the most frequently reported symptom at presentation in both men and women. As compared to 6% of male patients, 16% of females presented with atypical symptoms such as epigastric pain, neck pain, arm pain, dyspnoea, indigestion and vomiting. On coronary angiography, single vessel disease was the most common lesion found (58% in males vs. 56% in females), while multiple vessel disease was found in 40% males as compared to 30% females [Table/Fig-3]. Normal coronaries/insignificant CAD were found in 14% females as compared to 2% males, with a p-value of 0.059, suggesting an insignificant difference. More females having multiple vessel disease were found to have co-morbid conditions like diabetes as compared to males (66% vs 30%).

Risk Factors	Male (N=50)	Female (N=50)	p-value
HTN	28%	46%	p=0.062
DM	24%	52%	p=0.004
Family History of CAD	20%	30%	p=0.248
Smoking	44%	0%	p=0.000
BMI	Mean 25.58kg/m^2, SD 3.937	Mean 23.74kgm^2, SD 3.767	p =0.019

[Table/Fig-1]: Differences in the risk factors among males and females.

Type of lipid	Male (N=50)	Female (N=50)	p-value
HDL	Mean 52.98 mg/dl, SD 43.223	Mean 47.32 mg/dl, SD 11.431	p =0.373
LDL	Mean 117.22 mg/dl, SD 38.102	Mean 108.04 mg/dl, SD 35.378	p =0.215
TGL	Mean 144.66 mg/dl. SD 62.548	Mean 130.16 mg/dl, SD 41.214	p =0.174

[Table/Fig-2]: Lipid profile among male and female patients.

Angiographic Study	Male (N=50)	Female (N=50)	p-value
Single Vessel Disease	29/50	28/50	p=0.840
Multiple Vessel Disease	20/50	15/50	p=0.295
Insignificant/Normal Coronaries	1/50	7/50	p=0.059

[Table/Fig-3]: Coronary angiographic profile of males and female patients.

Hence, it was found that most significant risk factor among males was smoking whereas among females it was diabetes.

Clinically females presented at a later age and with atypical symptoms.

DISCUSSION

Our study showed that women with AMI were on an average 5.5-year-older than men. This observation is consistent with previous studies [8-11]. This difference in the age of presentation varies in various studies between 5-10 years. The later age in women could be because of exposure to endogenous oestrogens before menopause. Since, oestrogens regulate metabolic factors like lipids, mediators of coagulation and inflammatory cytokines as well as the α and β receptors in the vessel wall leading to vasodilatation during the fertile period of life, this delays the manifestation of atherosclerotic disease in women [12]. Furthermore, signs of subclinical atherosclerosis, as visualised by intima-media thickness measurements, can already be found in women before menopause, especially when several CHD risk factors are present [13].

In our study, we also found that risk factors like Diabetes and Hypertension are more prevalent among women presenting with CAD than men. 52% of our female patients were diabetic as compared to just 24% of male patients. Two Indian studies conducted by Gupta and Anand respectively [14,15] have reported higher incidence of diabetes and hypertension in men as compared to women. However, our data shows higher prevalence of diabetes and hypertension in women which is in concordance with the data reviewed from the West and China [16,17]. This disparity may be explained by higher prevalence of diabetes and hypertension in females in the studied population of Punjab. Women with diabetes are at greater risk for cardiovascular complications than their male counterparts [12]. In a meta-analysis of 37 prospective cohort studies, the risk of fatal CHD is 50% higher in women with diabetes compared with male diabetics [18]. This happens because of more involvement of inflammatory factors, small coronary size and less aggressive treatment of diabetes in women [12].

46% of our female patients were found to be hypertensive as compared to 28% of males which is similar to the studies from West where hypertension on an average was 25% more common in females [19,20]. The declining oestrogen levels increased plasma rennin activity due to up-regulated rennin-angiotensin system, increased salt sensitivity with sympathetic activity with menopause are few factors which lead to a steep rise in blood pressure in peri-menopausal and post menopausal women [21]. Moderate or borderline hypertension (<140/90 mmHg) causes more endothelial dysfunction and cardiovascular complications in women than in men [22].

On comparing the BMI, more males were found to be obese with a BMI of 25.58 kg/m^2 as compared to females (BMI 23.74 kg/m^2), whereas Butala NM et al., found a higher BMI in females than males [19]. Dyslipidaemia was more common among male patients as compared to female patients. This, too, is in concordance with most of the previous studies [20,23].

Smoking was the most common risk factor in the male patients presenting with acute myocardial infarction in our hospital and was totally absent in the female patients. This is because of the cultural and social factors in Punjab where very few women smoke. This is consistent with studies conducted in different populations across other states and countries [14,15,17] where smoking is less common among female patients, though, in our study it was totally absent. Hence smoking is a very significant risk factor in men presenting with CAD.

Regarding atypical presentation, we share similar findings with other studies where women presented more frequently with neck pain, back pain and indigestion as compared to men [5,7,19].

On angiography, we found that single vessel disease was equally prevalent among men and women (58% vs.56%), while multiple vessel disease was more common in men as compared to women (40% vs. 30%). Females were also found to have insignificant coronary artery disease or normal coronaries. This is in concordance with study conducted by Mega JL et al., and Rosengren A *et al.,* [24,25].

LIMITATION

The main limitation of our study was the small sample size. The small sample size prevented us from obtaining sufficient data among men and women to study the significant differences between the two genders. The second limitation is age matching between the two groups, which would substantiate the difference in risk factor profile even more significantly. These findings need to be replicated in larger populations with age matched controls and removal of confounding factors to understand the exact etiopathogenesis and factors influencing the varied presentations in two populations.

CONCLUSION

North Indian women present with CAD on an average 5.5 years later than men. Incidence of diabetes in Indian women presenting with CAD is significantly more than in men while smoking and obesity are the significant risk factor among men. Incidence of hypertension is more in women and that of dyslipidaemia is more in men, however, the differences are not statistically significant. Women have significantly milder disease on angiography with lower incidence of multiple vessel disease in-spite of higher incidence of diabetes and hypertension than men. Women more commonly present with atypical symptoms and are more likely to be misdiagnosed; hence, a higher index of suspicion is required while evaluating women with CAD. Larger Indian studies are required to acquire more data so that this growing prevalence of CAD in women can be curbed.

REFERENCES

[1] Mosca L, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, Lloyd-Jones DM, *et al*. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update: A guideline from the american heart association. *Circulation*. 2011;123:1243–62.

[2] Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T. Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2006;113:e85-151.

[3] Bedinghos J, Leshan L, Deihr S. Coronary artery disease prevention: what's different for women? *Am Fam Physician*. 2001;63:1393-401.

[4] Jneid H, Thacker HL. Coronary artery disease in women: Different, often undertreated. *Cleve Clin J Med*. 2001;68:441-48.

[5] Milner KA, Funk M, Richards S, Wilmes RM, Vaccarino V, Krumholz HM. Gender differences in symptom presentation associated with coronary heart disease. *Am J Cardiol*. 1999;84:396-99.

[6] Park JS, Kim YJ, Shin DG, Jeong MH, Ahn YK, Chung WS. Gender differences in clinical features and in-hospital outcomes in ST-segment elevation acute myocardial infarction: from the Korean Acu Myocardial Infarction Registry (KAMIR) study. *Clin Cardiol*. 2010;33:E1-6.

[7] Wenger NK. Clinical characteristics of coronary heart disease in women: emphasis on gender differences. *Cardiovasc Res*. 2002;53:558-67.

[8] Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, *et al*. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364(9438):937-52.

[9] Enas EA, Senthilkumar A, Juturu V, Gupta R. Coronary artery disease in women. *Indian Heart J*. 2001;53:282-92.

[10] Hochman JS, Tamis JE, Thompson TD, Weaver WD, White HD, Van de Werf F, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators. *N Engl J Med*. 1999;341:226-32.

[11] Anand SS, Islam S, Rosengren A, Franzosi MG, Steyn K, Yusufali AH, et al. Risk factors for myocardial infarction in women and men: insights from the INTERHEART study. *Eur Heart J*. 2008;29:932-40.

[12] Maas AHEM, Appelman YEA. Gender differences in coronary heart disease. *Netherlands Heart Journal*. 2010;18(12):598-602.

[13] Sutton-Tyrell K, Lassila HC, Meilahn E, Bunker C, Matthews KA, Kuller LH. Carotid atherosclerosis in premenopausal and postmenopausal women and its association with risk factors measured after menopause. *Stroke*. 1998;29:1116-21.

[14] Gupta R, Sharma KK, Gupta A, Agrawal A, Mohan I, Gupta VP, et al. Persistent high prevalence of cardiovascular risk factors in the urban middle class in India: Jaipur Heart Watch-5. *J Assoc Physicians India*. 2012;60:11-6.

[15] Anand K, Shah B, Yadav K, Singh R, Mathur P, Paul E, et al. Are the urban poor vulnerable to non-communicable diseas? A survey of risk factors for non-communicable diseases in urban slums of Faridabad. *Natl Med J India*. 2007; 20:115-20.

[16] Cheng CI, Yeh KH, Chang HW, Yu TH, Chen YH, Chai HT, *et al*. Comparison of baseline characteristics, clinical features, angiographic results, and early outcomes in men vs women with acute myocardial infarction undergoing primary coronary intervention. *Chest*. 2004;126:47-53.

[17] Hendricks AS, Goodman B, Stein JH, Carnes M. Gender differences in acute myocardial infarction: the University of Wisconsin experience. *WMJ*. 1999;98:30-36.

[18] Huxley R, Barzi F, Woodward M. Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies. *BMJ*. 2006;332:73-78.

[19] Butala NM, Desai MM, Linnander EL, Wong YR, Mikhail DG, Ott LS, et al. Gender Differences in Presentation, Management, and In-Hospital Outcomes for Patients with AMI in a Lower-Middle Income Country: Evidence from Egypt. *PLoS ONE*. 2011; 6(10): e25904. doi:10.1371/journal.pone.0025904.

[20] Yasar AS, Turhan H, Basar N, Metin F, Erbay AR, Ilkay E, et al. Comparison of major coronary risk factors in female and male patients with premature coronary artery disease. *Acta Cardiol*. 2008;63:19-25.

[21] Dubey RK, Oparil S, Imthurn B, Jackson EK. Sex hormones and hypertension. *Cardiovasc Res*. 2002;53:688-708.

[22] Vasan RS, Larson MG, Leip EP, Evans JC, O'Donnell CJ, Kannel WB, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. *N Engl J Med*. 2001;345:1291-97.

[23] Enas EA, Senthilkumar A. Coronary artery disease in Asian Indians: an update and review [online] *Internet J Cardiol*. 2001:1. Accessed 15 Feb 2005. URL: http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijc/vol1n2/cadi.xml.

[24] Rosengren A, Wallentin L, K Gitt A, Behar S, Battler A, Hasdai D. Sex, age, and clinical presentation of acute coronary syndromes. *Eur Heart J*. 2004;25:663-70.

[25] Mega JL, Hochman JS, Scirica BM, Murphy SA, Sloan S, McCabe CH, et al. Clinical features and outcomes of women with unstable ischemic heart disease: observations from metabolic efficiency with ranolazine for less ischemia in non-ST-elevation acute coronary syndromes-thrombolysis in myocardial infarction 36 (MERLIN-TIMI 36). *Circulation*. 2010;121(16):1809-17.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Medicine, Tagore Hospital and Heart Care Center, Jalandhar, Punjab, India.
2. Director and Head of Department, Department of Medicine, Tagore Hospital and Heart Care Center, Jalandhar, Punjab, India.
3. Assistant Professor, Department of Pathology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India.
4. Consultant, Department of Medicine, Tagore Hospital and Heart Care Center, Jalandhar, Punjab, India.
5. Consultant, Department of Cardiology, Tagore Hospital and Heart Care Center, Jalandhar, Punjab , India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Supriya Bajaj,
C/o Dr. Sumit Grover, Assistant Professor, Department of Pathology, Dayanand Medical College and Hospital,
Ludhiana, Punjab-141001, India.
E-mail: supriyabajaj1913@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.