

# Frequency of Conventional Risk Factors in Patients with Acute Coronary Syndrome in Males and Females

Butt Z.,<sup>1</sup> Shahbaz U.,<sup>2</sup> Hashmi A.T.,<sup>3</sup> Naseem T.,<sup>4</sup> Khan M.Z.,<sup>5</sup> Bukhari M.H.<sup>6</sup>

*Address for Correspondence:* Zeeshan Butt, Pathology Department, King Edward Medical University, Lahore

---

**Background:** The frequency of conventional risk factors for acute coronary syndrome differs in women compared to men, both in the general population and in patients with acute coronary syndrome.

**Objective:** To find out the frequency of conventional risk factors in patients with acute coronary syndrome in males and females that exists in Pakistani patient population.

**Design:** Cross-sectional survey.

**Material and Methods:** A total of one hundred patients with acute coronary syndrome who presented in the Cardiology Department, Mayo Hospital Lahore were interviewed between May, 2008 and March 2009. Patients were enquired about the presence of hypertension and diabetes mellitus. Information was also obtained regarding smoking and history of ischemic heart disease in their first degree relatives. Lipid profile was recorded from the investigation chart of every patient.

**Results:** 91% of subjects had at least one risk factor out of four conventional factors. When comparing men and women, more women were hypertensive and diabetic ( $p = 0.003$  and  $0.009$  respectively). None of the females had ever smoked as compared to 34% of males ( $P = <0.001$ ).

**Conclusion:** Women with acute coronary syndrome, when compared to men, have more prevalence of diabetes and hypertension, and less prevalence of smoking. Further research is needed to better understand the gender differences in various aspects of ischemic heart disease that exist in our population.

**Key Words:** Acute coronary syndrome, gender differences, risk factors.

---

## Introduction

Acute coronary syndrome (ACS) comprises unstable angina, ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction. ACS is the major manifestation of ischemic heart disease (IHD) which in turn is a major part of cardiovascular diseases.<sup>1</sup> In women, cardiovascular diseases are under-estimated although they are the leading cause of death in females.<sup>2</sup> More women than men die due to cardiovascular causes each year. In the year 2004, 32% of women died of cardiovascular diseases worldwide as compared to 27% of men.<sup>3</sup> In Pakistan IHD is the 2nd leading cause of death at all ages contributing to 11% of all deaths.<sup>4</sup> However, IHD is the commonest cause of death worldwide in both genders.<sup>3</sup>

Ischemic heart disease in women is not the same as it is in men. Important gender differences exist in almost every aspect of this disease complex. IHD develops 10-20 years later in women compared to men. Incidence of IHD in men is several times of that in age-adjusted pre-menopausal women.<sup>5</sup> Various explanations have been given for this observation but accepted one is that serum levels of high density lipoprotein cholesterol (HDLc) are higher in pre-menopausal women due to the protective effect of oestradiol. HDL is protective against CHD and as its level falls after menopause due to oestradiol deficiency, the incidence of IHD in women rises.<sup>6</sup> Although women are less likely to develop IHD than men, they are more likely to die of it.<sup>7</sup> In a recent study, women with ACS were found to have worse

outcomes at six month interval compared with men.<sup>8</sup> Moreover, gender differences regarding IHD also exist in clinical presentation, therapeutic response and rates of complication.<sup>2</sup>

Hypertension, diabetes mellitus, smoking, and hypercholesterolemia are called the conventional or major risk factors for IHD. They are called conventional because majority of patients with IHD have one or more of these risk factors.<sup>9</sup> A recent cohort study found that development of more than 80% of myocardial infarction in the general population is attributable to these conventional factors and physical inactivity.<sup>10</sup> Their prevalence differs in women compared to men, both in general population and in patients with IHD. In this study we have examined the gender differences in the frequency of conventional risk factors in patients with ACS. There is little work done so far regarding sex differences in Pakistan and our study will contribute to a better understanding of gender differences that exist in our patients with acute coronary syndromes.

## Material and Methods

### Design, Setting and Participants

Our study was a cross-sectional survey of 100 patients with acute coronary syndrome who presented in the Cardiology Department, Mayo Hospital, Lahore from May, 2008 to March 2009. Only those patients were eligible for this study who had had their diagnoses confirmed through clinical evaluation, echocardiography, and cardiac enzymes investi-

gations. Patients without recent lipid profile report were excluded from the study.

**Data Collection and Variables**

A short structured questionnaire was prepared and patients were interviewed in the ward after taking verbal consent. In addition to collecting basic demographic details, patients were asked about the presence of chronic hypertension and diabetes mellitus. Information was also obtained regarding smoking history and history of ischemic heart disease in first degree relatives. Ever smoking was defined as smoking at least 100 cigarettes during lifetime.<sup>11</sup>

The serum levels [in mg/dl] of total cholesterol, triacylglycerol (TAG), high density lipoprotein cholesterol (HDLc), and low density lipoprotein cholesterol (LDLc) were recorded from the investigation chart of every patient. Hypercholesterolemia was defined as serum total cholesterol of  $\geq 200$  mg/dl, and hyperlipidemia as serum TAG levels of  $\geq 150$  mg/dl based on guidelines of American Heart Association.<sup>12</sup>

**Ethical Issues**

Because the study was non-invasive and did not touch the sensitive barriers of religion and social norms, so a formal ethical approval was not taken. But the possible ethical concerns were fully discussed with the senior faculty members of the Department of Pathology, King Edward Medical University, Lahore.

**Statistical Analysis**

Both descriptive and inferential statistical analyses were done in Statistical Package for Social Sciences (SPSS) version 16.0. The presence of the four conventional risk factors, hypertension, diabetes, smoking, and hyperlipidemia, was coded as ‘1’ and ‘0’ if otherwise. A new variable was computed by adding the values a person had for the four conventional risk factors. It corresponded to the number of risk factors a patient had out of four conventional factors. The variable was further dichotomized as  $< 2$ , and  $\geq 2$ . Proportions were calculated for categorical variables, and mean  $\pm$  2S D for continuous variables. To compare men and women regarding categorical variables, chi-square test was done and p values were calculated.  $P < 0.05$  was considered significant.

Before comparing men and women for difference in continuous variables, a histogram for every continuous variable, separate for both genders, was created. These histograms were critically analyzed to verify the assumption of normal distribution. Age was normally distributed, so t-test for two independent samples was carried out to know the significance of difference between mean ages of men and women.

Serum levels of total cholesterol, TAG, LDLc, and HDLc had skewed distribution, so t-test was not appropriate for them. To compare men and women regarding these variables Mann-Whitney U test was done and p value calculated. Like chi-square test,  $p < 0.05$  was considered significant for both t-test and Mann-Whitney U test.

**Table 1:** Characteristics of men and women regarding age, diagnosis, and risk factors.

Variables	All	Men	Women	p-value*
	N = 100 %	N = 67 n (%)	N=33 n (%)	
Age $\geq 45$ years	83	54 (80.6)	29 (87.9)	0.413
Diagnosis				
MI	85	59 (88.1)	26 (78.8)	0.244
USA	15	8 (11.9)	7 (21.2)	
Hypertension	54	29 (43.3)	25 (75.8)	0.003
Diabetes Mellitus	41	21 (31.3)	20 (60.6)	0.009
Smoking <sup>†</sup>	34	34 (50.7)	0	0.000
Family History	34	25 (37.3)	9 (27.3)	0.374
Hypercholesterolemia <sup>‡</sup>	28	20 (29.9)	8 (24.2)	0.640
Hyperlipidemia <sup>§</sup>	86	56 (83.6)	30 (90.9)	0.377
Risk Factors $\geq 2$	55	35 (52.2)	20 (60.6)	0.523

\* All p-values are calculated by  $\chi^2$  test at 1 degree of freedom

<sup>†</sup>Smoking is defined as smoking at least 100 cigarettes during ones lifetime

<sup>‡</sup>Hypercholesterolemia is defined as total serum cholesterol levels of  $\geq 200$  mg/dl

<sup>§</sup>Hyperlipidemia is defined as serum triacylglycerol levels of  $\geq 150$  mg/dl

MI=Myocardial Infarction (includes both ST-segment elevation and non-ST-segment elevation myocardial infarction), USA=Unstable Angina

**Results**

Out of 100 patients 67 were male and 33 were female. No subject had missing value for any of the variables analyzed and described here. Myocardial infarction was the diagnosis in 85% of subjects and unstable angina in 15%. More females than males had unstable angina but the difference was not statistically significant (Table 1).

Mean age in men was  $53.18 \pm$  and mean age in women was  $53.73 \pm$ . Mean ages of men and women did not differ significantly (t-statistic = 0.245,  $p = 0.807$ ) Majority of subjects, both male and female,

were  $\geq 45$  years of age.

91% of subjects had at least one risk factor out of four conventional factors. 60% of women had  $\geq 2$  risk factors as compared to 52% of men. Overall, the most common risk factor was hyperlipidemia; but out of four conventional factors, hypertension was the most common one. When comparing men and women, more women were hypertensive and diabetic ( $p = 0.003$  and  $0.009$  respectively). None of females had ever smoked as compared to 34% of males (Table 1).

Results of the Mann-Whitney U test for continuous variables that had skewed distribution are presented in table 2. Men and women did not differ significantly regarding total serum cholesterol, TAG, LDLc, and HDLc.

**Discussion**

We found that majority of patients (91%) with acute coronary syndrome had at least one conventional risk factor. The proportion of ACS patients with at least one risk factor is variable in previous studies. In 2003, Khot et. al. analyzed data of patients enrolled in 14 randomized clinical trials of coronary heart disease. Out of 122458 patients, majority had ACS. They found that at least one of four conventional factors was present in 84.6% of women 80.6% of men<sup>9</sup>. Similar high proportions were observed in Hammoudeh et. al.<sup>13</sup> and Greenland et. al.<sup>14</sup>. In our study more women than men had coexistence of risk factors but it was not statistically significant. Many studies have shown that women, compared to men, had higher combined prevalence of cardiovascular risk factors.<sup>8,9</sup> Another important observation was that serum TAG was elevated in 86% of patients while serum cholesterol was elevated in only 26% of patients.

We found that hypertension and diabetes were more prevalent in women with ACS than in men. This observation has been consistently found in literature both for younger and older patients.<sup>15,16,9</sup>

In our study more male patients had ever smoked than females. This finding has been observed in many previous studies.<sup>15,16,9</sup> Although our results about smoking prevalence in women were in the expected direction but we cannot confidently say that no female in our study had ever smoked. This may be explained by fear of disclosure of their smoking habits and hesitation. We found no difference between men and women regarding hyperlipidemia. This finding is in contrast with previous studies which demonstrated that hyperlipidemia was more prevalent in women with ACS than in men.<sup>17,9</sup>

High prevalence of hypertension and diabetes in women and smoking in men can be explained in two ways. First, as these are major risk factors for ischemic heart disease,

**Table 2. Characteristics of men and women regarding lipid profile**

Variable	Men	Women	Mann-Whitney U Statistic	P value
	N = 67 Mean Rank	N = 33 Mean Rank		
Total cholesterol	47.1	55.76	932	0.203
TAG	47.63	56.33	913	0.158
LDLc	49.16	53.23	1015	0.509
HDLc	52.07	47.30	1000	0.437

TAG = Triacylglycerol, LDLc = Low Density Lipoprotein Cholesterol, HDLc = High Density Lipoprotein Cholesterol

so their gender –related distribution in general population will be reflected in their gender-related prevalence in patients who develop IHD. Recently Jafar et. al<sup>11</sup> have presented cross-sectional analysis of a sample of subjects recruited in a randomized trial of strategies to control hypertension. The sample consisted of 3143 adults aged  $\geq 40$  years residing in Karachi, the largest city of Pakistan. They found that diabetes, hypertension and hyperlipidemia were significantly more prevalent in women than in men, while smoking was more prevalent in men.

National Health Survey of Pakistan (1990-1994) made an excellent contribution in understanding the health status of Pakistani people. Additional results from this survey have been published recently. According to these results, 28.6% of men aged  $\geq 15$  years in the general population were smokers compared to 3.4% of women<sup>18</sup>.

Second, men and women are at different risk of developing IHD if they have these conventional risk factors.<sup>19</sup> Howard et al showed that overall prevalence of myocardial infarction was higher in men than in women but diabetic women had significantly higher prevalence of MI than diabetic men.<sup>20</sup> Moreover, diabetic women with ACS had worse outcome compared with diabetic men<sup>7</sup>. Given the gender-related prevalence of a risk factor is different in population at risk (general population), this difference will be augmented in IHD patients if that factor poses different risk for women compared to men.

Our study had some limitations. First, the sample size was small but even with this sample size we were able to demonstrate the same gender differences in prevalence of conventional risk factors in Pakistani patients that were observed in western countries using very large sample sizes. This shows that these gender differences are significant enough that they can be demonstrated using a small sample.

Second, except for hypercholesterolemia, the decision of whether or not a patient had hypertension, diabetes, and history of ever smoking was based on self-report of the patient. Although it is not the best method but it is reliable. We

assumed that using self-reporting for measuring these variables would not generate results much different from those obtained using more sophisticated techniques e.g. physical examination and laboratory studies.

### Conclusion

Majority of patients with acute coronary syndrome have at least one of four conventional risk factors. Women have higher combined prevalence of cardiovascular risk factors although it was not statistically significant. Women with acute coronary syndrome, as compared to men, have more prevalence of diabetes and hypertension, and less prevalence of smoking. Further research is needed to better understand the gender differences in various aspects of ischemic heart disease that exist in our population.

### References

- Braunwald E, Fauci AS, Kasper DL, et al.: Harrison's Principles of Internal Medicine. 15 ed. New York, McGraw-Hill, 2001: pp 1386-8.
- Stramba-Badiale M, Fox KM, Priori SG, et al.: Cardiovascular diseases in women: a statement from the policy conference of the European Society of Cardiology. *Eur Heart J* 2006 Apr; 27 (8): 994-1005.
- Gao YT, Shu XO, Dai Q, et al.: Association of menstrual and reproductive factors with breast cancer risk: results from the Shanghai Breast Cancer Study. *Int J Cancer* 2000 Jul 15; 87 (2): 295-300.
- Andrieu N, Prevost T, Rohan TE, et al.: Variation in the interaction between familial and reproductive factors on the risk of breast cancer according to age, menopausal status, and degree of familiarity. *Int J Epidemiol* 2000 Apr; 29 (2): 214-23.
- Barrett-Connor E: Sex differences in coronary heart disease. Why are women so superior? The 1995 Ancel Keys Lecture. *Circulation* 1997 Jan 7; 95 (1): 252-64.
- Rossouw JE: Hormones, genetic factors, and gender differences in cardiovascular disease. *Cardiovasc Res* 2002 Feb 15; 53 (3): 550-7.
- Pilote L, Dasgupta K, Guru V, et al.: A comprehensive view of sex-specific issues related to cardiovascular disease. *CMAJ* 2007 Mar 13; 176 (6): S1-44.
- Dey S, Flather MD, Devlin G, et al.: Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the Global Registry of Acute Coronary Events. *Heart* 2009 Jan; 95 (1): 20-6.
- Khot UN, Khot MB, Bajzer CT, et al.: Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 2003 Aug 20; 290 (7): 898-904.
- Heidemann C, Hoffmann K, Klipstein-Grobusch K, et al.: Potentially modifiable classic risk factors and their impact on incident myocardial infarction: results from the EPIC-Potsdam study. *Eur J Cardiovasc Prev Rehabil* 2007 Feb; 14 (1): 65-71.
- Jafar TH, Qadri Z, Chaturvedi N: Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. *Heart* 2008 Apr; 94 (4): 408-13.
- Cholesterol Levels: AHA Recommendation. [online]: American Heart Association; 2009 [cited 2009 May 8]; Available from: [www.americanheart.org](http://www.americanheart.org).
- Hammoudeh AJ, Al-Tarawneh H, Elharassis A, et al.: Prevalence of conventional risk factors in Jordanians with coronary heart disease: the Jordan Hyperlipidemia and Related Targets Study (JoHARTS). *Int J Cardiol* 2006 Jun 16; 110 (2): 179-83.
- Greenland P, Knoll MD, Stamler J, et al.: Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. *JAMA* 2003 Aug 20; 290 (7): 891-7.
- Kurtulmus N, Bos S, Arslan S, et al.: Differences in risk factors for acute coronary syndromes between men and women. *Acta Cardiol* 2007 Jun; 62 (3): 251-5.
- Yasar AS, Turhan H, Basar N, et al.: Comparison of major coronary risk factors in female and male patients with premature coronary artery disease. *Acta Cardiol* 2008 Feb; 63 (1): 19-25.
- Castanho VS, Oliveira LS, Pinheiro HP, et al.: Sex differences in risk factors for coronary heart disease: a study in a Brazilian population. *BMC Public Health* 2001; 1: 3.
- Ahmad K, Jafary F, Jehan I, et al.: Prevalence and predictors of smoking in Pakistan: results of the National Health Survey of Pakistan. *Eur J Cardiovasc Prev Rehabil* 2005 Jun; 12 (3): 203-8.
- Theresa M. Witzemann, Mary-Lou Pardue: Exploring the Biological Contributions to Human Health: Does Sex Matter? Washington, National Academies Press 2001.pp.
- Howard BV, Lee ET, Fabsitz RR, et al.: Diabetes and coronary heart disease in American Indians: The Strong Heart Study. *Diabetes* 1996 Jul; 45 Suppl 3: S6-13.