ORIGINAL ARTICLE
DIABETIC PATIENTS AND THEIR PRESENTATION IN ACUTE CORONARY SYNDROME WITH OUTCOMES: DOES GENDER PLAY ROLE?

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Objectives: To determine the frequency of different acute coronary syndrome (ACS) presentations and their outcomes in diabetic patients and gender based difference.

Methodology: This cross sectional study was conducted in Cardiology Department of Khyber Teaching Hospital, Peshawar from 1st January to 31st July 2018. Diabetic patients admitted via emergency department presenting with acute coronary syndrome were included .The patients were followed during their hospital stay for complications like left ventricular failure, recurrent angina and mortality. All the variables were addressed according to gender difference. Chi-square test was used for final analysis. P< 0.05 was considered statistically significant.

Results: A total of 388 diabetic patients were included. Of them males were 217 with mean age of 60.64 ± 9.24 years. About 65.46% patients presented to us with acute myocardial infarction. Thrombolytic therapy was done in 78.74% patients. About 86 males and 61 females developed symptoms of heart failure post MI ($p < 0.001$). In hospital mortality was found to be significant according to gender, $p = 0.03$. About 48.27% and 44.44% male patients presented with NSTEMI and USA respectively with no significant difference compared to females ($p = 0.21$). However results were significant for stable angina [35.29% females vs. 64.70% males, $p < 0.001$].

Conclusion: Diabetic patients present with coronary artery disease and its complications with heart failure and death more common among males as compared to females, needing special consideration for diagnosis and treatment.

Keywords: diabetes mellitus, coronary artery disease, heart failure

INTRODUCTION

Cardiovascular mortality has been decreased in most of the developed countries, but still CVD remains an important cause of morbidity and mortality.[1-4] This might be due to rapidly increasing important risk factors like type 2 diabetes and impaired glucose tolerance as a whole.[5,6] In next 30 years it has been estimated that the number of diabetic patients in the world will be at least doubled.[7] Cardiovascular diseases (CVD) are mostly involved in mortality of type 2 diabetic patients accounting for about 75%.[8] According to some epidemiological studies, diabetic patients have four folds increased risk of CVD mortality.[9]

Studies have shown a significant gender based difference in the prevalence and prognosis of coronary artery disease and acute myocardial infarction (AMI).[10] Risk factors like systemic hypertension and diabetes mellitus are found to be more common in women.[11] Studies reported decreased or similar mortality rates post AM1 in women as compared to male counterparts but still higher mortality has been reported in women.[12] This might be due to age of more than 60 for women in the patient group.[13] Combined presence of diabetes mellitus, obesity and coronary artery disease may have resulted in poor prognosis in females.[14]

Females tend to have a lower risk of developing coronary heart disease (CHD) than men even after menopause, but in the presence of certain diseases, relative survival differences between men and women either disappear or reverse. Including myocardial infarction (MI) and diabetes.[15]

According to some studies, the risk of developing CVD is almost double in men while it becomes four times higher for diabetic females.[15,16] The fact might being the delayed onset of CVD in diabetic females as compared to non- diabetic ones, equalizing the CVD risk similar to diabetic men.[16] Young diabetic women are also found to be at higher risk.[2] Moreover treatment for co-morbidities such as heart failure post MI is often delayed in women as compared to men specially in diabetic group.[3,4]

Diabetes influence on excess long-term mortality in women has been studied, but its impact on short-term mortality is less clear.[15] In the Rancho Bernado study, the relative risk of death due to ischemic heart disease

was found to be doubled for diabetic men while it was three times higher in diabetic women compared to non-diabetic control subjects after adjusting for confounding factors like hypercholesterolemia and smoking. Similar results were found in Framingham study on follow up for fatal cardiovascular diseases risk factors.[4]

The 28 days case fatality was found to be twice as high in diabetic patients as in non-diabetic patients in patients of AMI according to Finnish study.[5] Only a few studies have focused on the gender difference in the impact of diabetes on AMI but data on short term effect of diabetes on cardiovascular diseases is scarce.[6]

This study was conducted to find out frequency of different acute coronary syndrome presentations and in hospital outcomes in diabetic patients on basis of gender difference.

METHODOLOGY

This cross sectional study was conducted in Cardiology Department of Khyber Teaching Hospital Peshawar from 1st January to 31st July 2018. Data was collected using consecutive non probability sampling technique after the approval from the Ethical committee of Khyber Medical College Peshawar dated 15/08/2017. Diabetic patients were admitted via emergency department after the inclusion criteria was scrutinized. Informed consent was obtained from all the patients. The presenting disease including ST elevation myocardial infarction (STEMI), Non ST elevation myocardial infarction (NSTEMI), unstable angina (USA) and stable angina along with patients' demographic (name, age, gender, and admission number) details were recorded on a Performa. All the patients were followed during their hospital stay for complications. The outcomes included complications including left ventricular failure, recurrent angina and mortality were recorded. Appropriate investigations including Echocardiography and Electrocardiography were performed. Troponin levels were also noted where needed. Study was conducted after ethical approval of the hospital.

Patients with atypical chest pain, borderline Troponin levels and with multiple co morbidities or multisystem involvement were excluded.

Data analysis was done using software SPSS 16.0. Mean and standard deviation were used for numerical variables like age and duration of hospital stay while categorical variables like gender and presence of diabetes mellitus (DM), in-hospital complications (Left ventricular failure, recurrent angina and mortality) were presented as frequency and percentages. Chi-square test was used for final analysis. A $p < 0.05$ was considered statistically significant for gender based differences in presentation.

RESULTS

A total of 388 diabetic patients were included in the study. Of them males were 217 (55.9%) with mean age of 60.64 ± 9.24 years (Table 1). During period of study 251 (65.46%) patients presented to us with acute myocardial infarction (AMI). Of them anterior MI was found in 132 (34.02%) patients while lateral and inferior MI were found in 32 (08.24%) and 87 (22.42%) patients respectively (Table 2). Thrombolytic therapy with streptokinase was done in 200 (78.74%) patients with AMI. In about 30 (15%) males and 37 (18.55%) females, thrombolysis was not successful (p=0.32).

Table 1: Demographic Variables of Study population (n=388)

Variables	Frequency (n)	Percentage (%)
Age (years)	60.64+-9.24	
Male	217	55.9%
Female	171	44.1%
Thrombolysis	200	78.74%

Table 2: Frequency of coronary artery disease (CAD) diagnosed at presentation in study population (n=388)

CAD	Frequency (n)	Percentage (%)
Anterior MI	132	34.02%
Inferior MI	87	22.42%
Lateral MI	32	08.24%
Total	**251**	**64.46%**
NSTEMI	58	14.94%
USA	45	11.59%
Stable Angina	34	08.76%
Total	**137**	**35.3%**

For complications related to coronary artery disease, left ventricular dysfunction developed in 147 (37.88%) presenting with CAD. About 86 (58.50%) males and 61 (41.49%) females developed symptoms of heart failure post MI (p<0.001) (Table 3).

Table 3: In Hospital Outcomes in Study Population

Gender	Male n(%)	Female n(%)	P-value
Heart failure (n=147)	91(41.93%)	66 (38.59%)	0.01
Re angina (n=95)	30(31.57%)	65(68.42%)	0.04
Death (n=43)	29(67.49%)	14(32.55%)	0.03
Streptokinase failure (n=200)	30(15.0%)	37(18.55%)	0.32

Recurrent angina during hospital stay was found in 95 (24.48%) patients with 65(68.42%) females and 30

(31.57%) males with p = 0.04. In hospital mortality was found to be 11.08% with 29 (67.44%) males and 14 (32.55%) females having p value of 0.03 as shown in Table 3.

Apart from AMI, 28 (48.27%) and 20 (44.44%) male patients presented with NSTEMI and unstable angina (USA) respectively. While in females, NSTEMI and USA were diagnosed in 30 (51.72%) whereas in males 25 (55.55%) patients respectively with p=0.21 showing no gender difference in these outcomes on the basis of gender. For stable angina a significant difference on the basis of gender was found [12 (35.29%) females and 22 (64.70%) males with p<0.001] as shown in Table 4.

Table 4: Coronary Artery Disease other than Myocardial infarction in study population (n=388)

CAD	Gender (n=136)		P-value
	Male n (%)	Female n (%)	
NSTEMI	28 (48.27%)	30 (51.72%)	0.21
USA	20 (44.44%)	25 (55.55%)	0.21
Stable Angina	22 (64.70%)	12 (35.29%)	0.001

NSTEMI= Non ST Elevation Myocardial Infarction, USA= Unstable Angina

DISCUSSION

Diabetes plays an important role in cardiovascular death as shown by some studies. It was found that men with history of MI were at increased risk of CHD as compared to woman with underlying diabetes mellitus. Some of the studies compared the burden of the different types of AMI in patients with diabetes history.[9] In our study mortality was found in only 43 patients and all of them were diagnosed with STEMI, which is second by studies like Health Professionals Follow-up study, the ARC study, and the MRF Interventiontrial.[5,6] In the Hoorn study, it was found that women with the history of diabetes at baseline had raised risk of CVD adverse outcomes.[3,7] Similarly in our study a significant number of female population presented with CHD having prior history of diabetes mellitus.

One of the study from Scottish population compared incidence of diabetes mellitus and MI.[6] In follow-up it was found that the risk of CVD mortality the time was more in diabetic males with prior history of MI.[6,17] Frequency of CVD was more in males in our study as well. One of the study showed that the effect of diabetes on MI and cardiovascular disease risk depends upon duration of diabetes and its magnitude. It was also found that the extra natural advantage of estrogen in females is also jeopardized due to presence of diabetes, as we found in our study that rate of MI

and CAD in females was comparable with males in case of diabetics.[16]

UKPDS (UK prospective diabetes study) demonstrated that more aggressive treatment of diabetes particularly in women reduces CVD risk.[9] Although in our study we didn't analyzed glycemic control and different medications used by patients at time of presentation. One of the study showed that women with diabetes had more frequent post MI heart failure as compared to males.[14] However in our study heart failure was found more pronounced in males as compared to females while Re current angina was more significant in females. This difference might be due to increased number of male patients admitted to our unit as compared to females.

It is proved that Left ventricular function (EF) calculated at of discharge from CCU, can be considered as an important prognostic factor following AMI.[14] Females of any age had a higher left ventricular EF (ejection fraction) as compared to males. Similar findings were addressed in our study also. Ventricular arrhythmias observed during hospital stay were also observed as poor prognostic factor however this was not found on our study.[14]

In DIGAMI 2 (Diabetes and Insulin Glucose Infusion in Acute Myocardial Infarction) trial diabetic patients with myocardial infarction, it was found that female patients had an increased rate of cardiovascular mortality as well as morbidity on follow-up. Although follow up was not made in our study which can be added as limitation.

In diabetic patients a notorious relationship exists between myocardial infarction and diabetes status along with its comorbidities which can predict the future cardiovascular events in women as well as men. Therefore according to UKPDS study, effective glucose control needs to be initiated as soon as possible. This assumption was further supported by ACCORD (Action to control cardiovascular risk in Diabetes) and ADVANCE (Action in diabetes and vascular diseases) trials. It has been observed in most of the MI related trials, the percentage of women having complications related to MI is lower than that of men, which reduces the statistical power to some extent.[3,4] This same thing might be responsible for reduced event rate in females as compared to males in our study as well.

Limitations: This was a single center based study and most of the population presented to us was illiterate not knowing about their past history properly. Moreover certain parameters like medications and

strict glycemic control was not taken in to account which might have effected results of study more precisely. Follow up is also needed to make strong assumptions about diabetes and its gender based effects.

CONCLUSION

As proven previously diabetes mellitus is an important risk factor for CAD which adversely affects prognosis of patients presenting with acute coronary syndrome. Therefore strict control of diabetes, if possible primary prevention is needed to lower its rates. Gender based differences in study outcomes implies that more aggressive treatment and follow ups should be done according to gender and to look for certain complications which are more relevant to one gender as compared to other.

AUTHORS' CONTRIBUTION:

UA: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AA, AA: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

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