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FREQUENCY OF TRADITIONAL RISK FACTORS AND EVALUATION OF LIPID PROFILE IN PATENTS WITH ACUTE CORONARY SYNDROME

Bahauddin Khan,[1] Shah Sawar,[2] Mahmood Ul Hassan,[3] Amir Taj Khan,[4] Fouzia Rahman,[5] Naila Noor[6]

[1-4]Department of Cardiology, Hayatabad Medical complex, Peshawar-Pakistan
[5]Department of Radiology, Khyber Teaching Hospital, Peshawar-Pakistan
[6]Department of Gynecology Hayatabad Medical complex, Peshawar-Pakistan

Address for Correspondence:

Bahauddin Khan

Department of Cardiology, Hayatabad Medical complex, Peshawar-Pakistan

Emails: bahauddin.khan@yahoo.com

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Contribution

BK and SS designed the study and did statistical analysis. MUH and ATK did data collection and manuscript writing. FR and NN did review and final approval all. Authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To determine the frequency of traditional risk factors with evaluation of lipid profile in patients with acute coronary syndrome.

Methodology: This was a descriptive cross sectional study with non-randomized consecutive sampling. The study was conducted from 1st June to 30th November, 2018 in Coronary Care Unit, Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan in which all patients with age >18 years with diagnosis of acute coronary syndrome were recruited. Detail history of hypertension, diabetes mellitus, smoking, and family history for coronary artery disease was taken. Dyslipidemia was evaluated by measuring blood lipid profile. SPSS version 20 was used for analysis. Significance was set at $P \leq 0.05$.

Results: We analyzed 384 patients with acute coronary syndrome out of which 60.7% were male. There was no significant difference in age of male (25-91 years) and female (26-90 years) patients. ST segment elevation acute coronary syndrome was 74.5% and non ST segment elevation acute coronary syndrome was 25.5%. Frequency of dyslipidemia, hypertension, diabetes mellitus, smoking, and family history of coronary artery disease was 86.7%, 52.3%, 34.1%, 26% and 9.6%, respectively. The most frequent lipid abnormality was in HDL cholesterol, followed by triglycerides, total cholesterol and LDL cholesterol.

Conclusion: Dyslipidemia was the most common risk factor followed by hypertension, diabetes mellitus and smoking. The most common abnormalities in lipid profile were low level of HDL cholesterol, followed by triglycerides, total cholesterol and LDL cholesterol.

Key Words: Acute Coronary Syndrome, Risk Factors, Dyslipidemia, Hypertension, Diabetes Mellitus, Smoking

INTRODUCTION

Cardiovascular disease (CVD) is the most common cause of death and roughly accounts for seven million death worldwide.[1] CVD includes both coronary heart disease (CHD) and coronary artery disease (CAD) that can lead to acute coronary syndrome (ACS).[2] ACS is an acute presentation of CVD that includes ST segment elevation acute coronary syndrome (STE-ACS), non-ST segment elevation acute coronary syndrome (NSTE-ACS) and unstable Angina (UA).[3] About 129 million years are lost due to ill-health, disability or early death resulting from CAD.[1] It is a significant disease burden and accounts for great economic losses.[1,4,5] The South Asian countries have highest proportion of CVD in the world.[6] Due to health transition, CVD has now emerged as the leading cause death in developing world.[1,7] Indeed, it has now been recognized that south Asian population has highest susceptibilities to CAD in the world.[6,8] It is therefore not surprising that CAD is now the leading cause of death in the Indo-Pakistan subcontinent.[9] The mortality due to CVD in south Asian countries is expected to increase from estimated 25 percent in 1990 to more than 40 percent in 2020.[7] The development of CVD in south Asian population is attributed to high prevalence of risk factors for CVD.[6] With social and economic development, the lifestyle of populations changed that resulted in increased prevalence of risk factors for CVD.[1,7] The poor and rich, the educated and less educated are equally struck by these factors.[7] The protective factors, like daily exercise and fruit consumption, are relatively less common in south Asian than rest of the world.[6] Hyperlipidemia is one of the major known risk factor for CAD which is associated with high morbidity and mortality in patients with ACS.[10] Early initiation of treatment for hyperlipidemia is recommended by multiple trials that has improved outcomes in patients with ACS.[11]

Risk factors for CAD can be divided into traditional risk factors that include dyslipidemia, hypertension, diabetes mellitus, smoking and family history of CAD and modifiable risk factors. The aims of this study were to study the traditional risk factors and evaluate blood lipid profile in patients with ACS that will give us knowledge about the baseline levels of lipid profile and their relation with different clinical and demographic characteristics of patients.

METHODOLOGY

This was a descriptive cross sectional study with non-random consecutive sampling. The sample size was calculated through WHO Sample size calculator using 50% estimated proportion of risk factors with 95% confidence intervals and 5% error of margin. We conducted this study from 1st June to 30th November, 2018 in Coronary Care Unit, Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan. All patients with age >18 years with diagnosis of ACS were recruited. ACS was defined according to definition of recent guidelines of American College of Cardiology/American Heart Association.[12,13] We divided patients into STE-ACS and NTE-ACS as UA and Non ST segment Elevation Myocardial Infarction (NSTEMI) differ in severity only. Hypertension was defined as a mean systolic pressure ≥ 140 mm Hg or a mean diastolic pressure ≥90 mm Hg in upper arms through properly calibrated mercury sphygmomanometer on three separate occasions measured during admission 6 hours apart, OR current use of medication for hypertension for minimum of one month prescribed by registered medical practitioner. Diabetes mellitus was be defined as fasting blood sugar ≥ 126 mg/dl measured in hospital laboratory by Modular EVO P-800 by Roche OR current use of antidiabetic medication for minimum of one month prescribed by registered medical practitioner. The serum levels of total cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglycerides were determined within the first 24 hours of admission. Five milliliters venous blood was taken from each participant. Dyslipidemia was defined as total cholesterol ≥200mg/dl or triglycerides ≥150 mg/dl or HDL-C ≤40mg/dl or LDL-C ≥100 mg/ dl (measured in hospital laboratory by Modular EVO P-800 by Roche). Family history was taken positive if there is history of CAD in first degree relative before 55 years in male and 65 years in female. Current smoker was defined as someone who has smoked at least 100 cigarettes over his or her life time and now smoke every day or some days or some weeks in the last 6 months. Ex-smoker was defined as someone who has quit smoking cigarettes for at least 6 months while nonsmoker was defined as someone who has never smoked actively in his/her entire life. We divided patients into two categories i.e. past/current smoker and non-smoker. Data was collected after approval of the manuscript from Institutional Ethical Board. Informed written consent was taken from each participant before conducting the study. Patients unwilling to participate in the study were excluded. Patients with known thyroid disease, chronic inflammatory disease, on chronic anti-inflammatory or anti-neoplastic medication, acute febrile infection in past 14 days, chronic liver and kidney disease, and patients with any neoplastic disorder were also excluded. Patients who Left Against Medical Advice (LAMA) and Discharged On Will (DOW) before the arrival of lipid profile report were also excluded.

Statistical analysis was performed by dividing male and female into separate groups. Statistical Package for Social Science version 20 (SPSS, Inc., Chicago, IL, USA) statistical software was used for analysis. Continuous variables were displayed as mean ± standard deviation (SD) while categorical variables were displayed using frequencies, percentages, tables; and bar charts. Groups were compared usingchi-square or Fisher's exact test.Independent student t test was used for comparing means. The results were reported using two-tailed significance. Significance was set at $p \leq 0.05$.

RESULTS

During the study period, 398 patients with acute coronary syndrome were admitted. Fourteen patients met the exclusion criteria (6 patients had thyroid disease, 1 patient had carcinoma esophagus, 3 patients had severe liver disease, 1 patient had leukemia, 2 patients had chronic kidney disease, and 1 patient had recent dengue hemorrhagic fever).

We analyzed 384 patients with acute coronary syndrome. Demographic and clinical characteristics of patients as shown in table 1. Out of 384 patients, 60.7% were male and 39.3% were female. The mean age of male was 58.4 ± 13 years while mean age of female was 59.1 ± 11 years. However, there was no significant difference between age, t(355) = -0.55, p>. 05. STE-ACS was 74.5% and NSTE-ACS was 25.5%. Compare to female (66.2%), male (79.8%) patients were more likely to have STE-ACS, $\chi^2(1) = 8.9$, p<. 05; odds ratio [OR](Male/Female)= 2.0, (95% confidence interval [CI] 1.3-3.2). Similarly, female patients (33.8%) were more likely to be admitted with NSTE-ACS compare to male patients (20.2%), $\chi^2(1) = 8.9$, p<.05; OR = 2.0, (95% CI 1.7-3.2). Patients

with positive history of ACS were 27.9%, in which 16.9% male and 10.9% female had positive history of ACS.However, there was no statistical difference between male and female patients regarding past history of ACS. Eighteen point five percent of patients were using statin therapy at the time of admission (male vs female: 17.2% vs 20.5% respectively; p >.05).

The most common risk factor was dyslipidemia (86.7%) (Table 2). Hypertension was the next most common risk factor i.e. 52.3%, which was more common in female (66.9%) compared to male (42.9%) patients; $\chi^2(1) = 21.1$, p<.001; OR(F/M) = 2.7 (95% CI 1.7-4.1). Similarly, diabetes mellitus was more common in female (47.7%) than male patients (25.3%); $\chi^2(1) = 20.4$, p<.001; OR(F/M) = 2.7 (95% CI 1.7-4.1). Family history was positive for CAD in 9.6% of patients with no statistical difference between male and female patients.Of26% of smokers, only one (0.7%) female patient was smoker while 42.5% male had positive past/current smoking history; $\chi^2(1) = 83.2$, p<.001; OR(M/F) = 111 (95% CI 15.2-805)

In 95.6% of study population, at least one risk factor was found.(Table 3). Over all, female patients were more likely to have more risk factor than male (p>.05). (Figure 1).

Table 1: Demographic and Clinical Characteristics of Patients

Characteristic	All n=384	Male n=233	Female n=151	P value
Mean age ± Standard deviation	58.6 ± 12.3	58.4 ± 13	59.1 ± 11	0.59
STE-ACS (%)	74.5	79.8	66.2	0.003
NSTE-ACS (%)	25.5	20.2	33.8	0.003
Previous ACS (%)	27.9	27.9	27.8	0.99
Previous Statin Therapy (%)	18.5	17.2	20.5	0.41

STE-ACS = ST segment Elevation Acute Coronary Syndrome, NSTE-ACS = Non ST segment Elevation Acute Coronary Syndrome
ACS = Acute Coronary Syndrome

Table 2: Frequency of Traditional Risk Factors

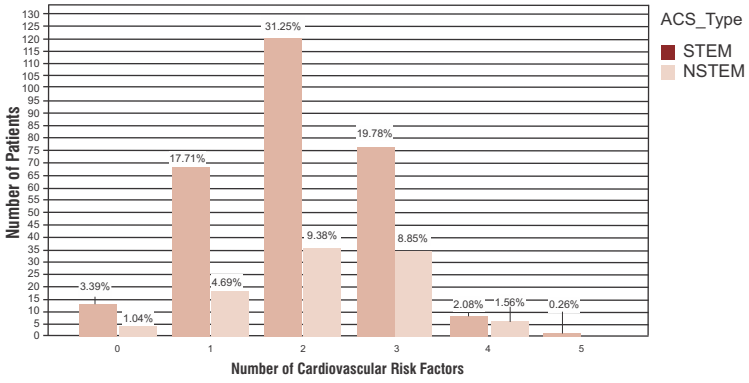
Risk factor	All (n=384)	Male (n=233)	Female (n= 151)	P value
Hypertension (%)	52.3	42.9	66.9	<.001
Diabetes Mellitus (%)	34.1	25.3	47.7	<.001
Smoking (%)	26	42.5	0.7	<.001
Family history of CAD (%)	9.6	10.7	7.9	0.37
Dyslipidemia (%)	86.7	88.8	83.4	0.13

CAD = Coronary Artery Disease

Table 3: Frequency of Number of Traditional Risk Factors

Number of risk factors (%)	All (n=384)	Male (n=233)	Female (n= 151)	P value
0	4.4	5.2	3.3	0.39
1	22.4	21.5	23.8	0.58
2	40.6	42.1	38.4	0.48
3	28.6	26.6	31.8	0.27
4	3.6	4.3	2.6	0.4
5	0.3	0.4	0	0.42

Figure 1: Number of Cardiovascular Risk Factor in Different STE-ACS and NSTE-ACS



The frequency of risk factor in different group of ACS according to sex is shown in Table 4. In STE-ACS, female patients compared to male patients were more likely to have hypertension (66% vs 39.2%, p<.001), diabetes mellitus (44% vs 26.3%, p<.05), while smoking (1% vs 43%, p<.001), dyslipidemia (80% vs 89.8%, p<.05), and positive family history for CAD (4% vs 10.8, p=.05) were less common in female than in male patients, respectively.

In patients with NSTE-ACS, except for smoking (0% vs 40.4%, p<.001), hypertension (68.6% vs 57.4%, p>.05), diabetes mellitus (54.9% vs 21.3, p<.05), positive family history for CAD (15.7% vs 10.6%, p>.05) and dyslipidemia (90.2% vs 85.1%, p>.05) were more common in female compare to male patients, respectively.

Table 4: Frequency of the Risk Factors in Different Acute Coronary Syndrome Groups According to Sex

	STE-ACS				NSTE-ACS			
Risk factor (%)	**All n= 286**	**Male n= 186**	**Female n=100**	**P value**	**All n =98**	**Male n= 47**	**Female n=51**	**P value**
Hypertension	48.6	39.2	66	<.001	63.3	57.45	68.62	0.25
Diabetes Mellitus	32.5	26.3	44	0.002	38.8	21.3	54.9	0.001
Smoking	28.3	43	1	<0.001	19.4	40.4	0	<0.001
Family history of CAD	8.4	10.8	4	0.05	13.3	10.6	15.7	0.46
Dyslipidemia	86.4	89.8	80	0.02	87.8	85.1	90.2	0.13

STE-ACS = ST segment Elevation Acute Coronary Syndrome, NSTE-ACS = Non ST segment Elevation Acute Coronary Syndrome
CAD = Coronary Artery Disease

The blood lipid profile is shown in Table 5. The mean level for triglycerides, HDL cholesterol, total cholesterol and LDL cholesterol was 150.74 mg/dL, 33.41 mg/dL, 161.34 mg/dL and 95.95 mg/dL, respectively. About 86.7 % of patients had at least on abnormal level lipid. Low HDL cholesterol (83.3%) was most frequent lipid abnormality (male 86.7% versus female 78.1%; p<.05). triglycerides was high in 42.4%, total cholesterol 15.6% and LDL cholesterol in 10.4% of patients. The mean level of triglycerides was higher in female (156 mg/dL) than male (146 mg/dL); t(382) = -1.9, p>.05. Similarly, the mean level of total cholesterol (female 168mg/dL versus male 156 mg/dL; t(382) = -3.1, p<.05) and LDL cholesterol (female 100 mg/dL versus male 93 mg/dL; t(382) = -2.7, p<.05) was higher in female compared to male patients. The mean level of HDL cholesterol was lower in female (78.1 mg/dL) than male (86.7 mg/dL); t(382) = -2.5, p<.05).

Table 5: Blood Lipid Profile of Patients with Acute Coronary Syndrome

Risk factor		**All (n=384)**	**Male (n=233)**	**Female (n= 151)**	**P value**
Dyslipidemia (%)		86.7	88.8	83.4	0.13
Triglycerides (mg/dL)	Mean±SD	150.74±51.65	146.82±51	156.78±52.24	0.07
	<150 mg/dL (%)	57.6	61.8	51	0.04
	=150 mg/dL (%)	42.4	38.2	49	
HLD-C (mg/dL)	Mean±SD	33.41±7.33	32.67±7.37	34.56±7.14	0.01
	>40 mg/dL (%)	16.7	13.3	21.9	0.02
	=40 mg/dL (%)	83.3	86.7	78.1	
Total cholesterol (mg/dL)	Mean±SD	161.34±34.33	156.97±33.59	168.1±34.49	0.002
	<200 mg/dL (%)	84.4	87.6	79.5	0.03
	=200 mg/dL (%)	15.6	12.4	20.5	
LDL-C (mg/dL)	Mean±SD	95.95±24.57	93.22±24	100.2±24.87	0.007
	<130 mg/dL (%)	89.6	91.4	86.8	0.14
	=130 mg/dL (%)	10.4	8.6	13.2	

SD = Standard Deviation, HDL-C = High Density Lipoprotein cholesterol
LDL-C = Low Density Lipoprotein cholesterol

DISCUSSION

In this study, we included all patients admitted with ACS and then we divided ACS into two categories i.e. STE-ACS and NSTE-ACS. STE-ACS was more common in our study population compared to NSTE-ACS. Patients with NSTE-ACS are more likely to have hypertension, diabetes mellitus, dyslipidemia, and positive family history for CAD, while patients with STE-ACS are more likely to be smoker.

We collected information regarding the presence and absence of five traditional risk factors namely, hypertension, diabetes mellitus, past/current smoking, dyslipidemia and family history for CAD. Although, identifying risk factors at time of admission in patients with ACS doesn't improve short term mortality; however, patients with unknown status of their risk factors are less likely to receive guideline directed medical therapy.[14,15]

We found that the frequency of risk factor was very high in our study population and 95.6% of patients had one or more risk factor for

CAD. This is in accordance with other published national and international studies on risk factors in ACS patients.[16-18]

In our study, the most frequent risk factor was dyslipidemia, followed by hypertension, diabetes mellitus, smoking and family history of CAD. The same sequence of findings was found in other national study, except in another study where family history was more common than smoking.[17,18] In an international study, diabetes mellitus was more common than dyslipidemia.[19] Another national studies in patients with ACS found dyslipidemia and smoking as the most common risk factors.[20,21] In National Health Survey of Pakistan (NHSP) 1990–1994, the prevalence of smoking in general population aged ≥15 years was 15.2%, in which male smokers were 28.6% compared to female 3.4%.[22] The results of our study is roughly similar to NHSP 1990-1994. We had only one female patient (0.7%) in STE-ACS group as smoker, while none of the female patient in NSTE-ACS was smoker. Similar finding was also noted in another study. So, our entire group of smokers (26%) was mainly represented by male patients. In fact, male gender, age, illiteracy and ethnicity have been identified as independent predictors of smoking in NHSP 1990-1994.[22]

The lower frequency of smoking may be explained by the two facts. First, we used strict criteria of including patients smoking only "cigarettes". If other methods of traditional ways of smoking that contains tobacco like chilam, huqqa, shisha, naswar, etc had been included then the proportion of smoker patients may have been raised. Second, it is note worthy, that only one female patient was found to be smoking cigarettes. Female patients of this region where this study was conducted use other methods that contain tobacco, most commonly naswar, but less commonly smoke cigarettes. Furthermore, fear of disclosure in front of relatives may have led to decreased number of female smoker in this study.[18] Moreover, the relationship of smoking with male is highly significant but due to large range of confidence interval of odds ratio, this relationship would have become more reliable if we would have got enough female smokers for comparison.

In-hospital morality in patients with ACS is inversely related to the number of risk factor for CAD.[23] The number of risk factor in each patient in our study is roughly similar to other studies.[17,18] Females with ACS are older and have more cardiovascular risk factors as compared to males. Similarly, female patients are less likely to receive guideline directed medical therapy as compared to male patients.[24,25] In our study, hypertension and diabetes mellitus were more common in female patients. Likewise, female patients were older than male in our study but the mean age was not significantly different between the two groups. This is in accordance with other national published data.[17,18]

We used non-fasting lipid profile during the first 24 hours of ACS. The optimum time of measuring lipid profile after ACS is within 24 hours.[26] Within 24 hours after ACS, lipid profile shows little changes.[27]

Dichotomizing patients into either dyslipidemic or not, yielded male patients to have greater proportion of dyslipidemia compare to female patients. However, dichotomizing a continuous variable has several disadvantages.[28] Looking at the mean levels of different lipid levels and their significance level, except HDL cholesterol, female patients had more significant abnormalities in lipid profile compared to male patients. The most frequent lipid abnormality was low level of HDL cholesterol and 86.7% of patients had at least one abnormal level in lipid profile. These findings are also found in other national studies.[17,18] We also saw that 18.5% of patients were on statin therapy (Male 17.2 versus 20.5%). Despite that, female patients had more lipid abnormalities compared to male patients. Mere use of statin therapy isn't the treatment goal but optimizing statin therapy to achieve recommended lipid level without side effects gives therapeutic and prognostic benefits.[27]

CONCLUSION

Dyslipidemia was the most common risk factor followed by hypertension, diabetes mellitus and smoking. We saw that these risk factors were more common in female than male, except smoking. We also saw that overall female patients are more likely to harbor multiple risk factors compare to male patients. The most common abnormalities in lipid profile was low level of HDL cholesterol, followed by triglycerides, total cholesterol and LDL cholesterol.

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