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Research Article

RISK FACTORS AND ANGIOGRAPHIC PROFILE IN YOUNG PATIENTS WITH NAIVE ACUTE CORONARY SYNDROME

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A B S T R A C T

Introduction: Despite cardiovascular diseases having grown to epidemic proportions, there are few studies from India pertaining to acute coronary syndrome (ACS), more so from the region of Purvanchal which is less developed. There is also increasing prevalence of coronary artery disease in young patients. Our study is first of its kind in this region of young patients presenting for the first time with ACS.

Aim: The present study was done with the aim of evaluation of clinical and angiographic characteristics of young ACS patients of Purvanchal and compare with that of the elderly.

Methods: This was a prospective cohort study of 180 patients admitted with acute coronary syndrome. Patients were excluded if they had prior cardiac pathology like valvular heart disease, cardiomyopathy, pericardial disease, cor pulmonale, ischaemic heart disease or cardiac revascularisation. Patients who did not undergo angiography were excluded. Patients were divided into two groups of young ACS (age 18-40 years) and older ACS patients (age > 40 years). Clinical characteristics analyzed in each group were age, gender, presence or absence of diabetes mellitus, hypertension, dyslipidaemia, smoking, obesity, family history, duration of chest pain, and treatment received. Angiographic profile were also studied in both groups.

Results: Males were predominant with mean age 57.8 years and 35.6 years respectively in the two groups. Young patients had greater prevalence of smoking whereas hypertension was more prevalent in the elderly group. Family history of CAD, Diabetes and obesity were not significantly different in the two groups. Average serum levels of LDL-C and TG were significantly higher in the young ACS patients as compared to the older ACS patients. Younger patients more commonly presented with STEMI and predominantly had SVD. Significant number of patients in the young ACS group had insignificant stenosis. Multivessel disease was more common in older age patients. Distribution of coronary lesions was not significantly different in the two groups.

Conclusions: Young patients have a different risk factor profile in comparison to older patients. Risk factor identification and control, early presentation and treatment are crucial.

INTRODUCTION

Coronary artery disease (CAD) is a major cause of mortality and morbidity worldwide. With epidemiologic, demographic and health transition, India is facing problems with both communicable as well as non communicable diseases. In the most productive age group of 25-69, cardiovascular disease is the leading cause of death responsible for 25% of all deaths in males as well as females across the country[1].

Reports have shown that risk of CAD among Asian Indians is 3–4 times higher than white Americans, 6 times higher than Chinese, and 20 times higher than Japanese counterparts[2,3].

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A conservative estimate indicates that there could be 30 million CAD patients in India. If the current trend continues, the burden of CAD in India will surpass other regions of the world by the year 2020[4]. In addition to higher rate, it is also reported that Indian individuals may develop CAD at a very early age[5]. According to an estimate, more than half of death related to cardiovascular disease occurs in patients below the age of 50 years and one-fourth of acute myocardial infarction cases are being reported in patients under the age of 40 years[5]. Until now maximum data are from western countries regarding coronary artery diseases. The health status of Purvanchal area of Uttar Pradesh is different from other states of India as this area is more backward with less health awareness and more poverty. It is important to study the patient characteristics, risk factors and presentation of patients presenting with acute coronary syndrome to provide data unique to this region that will help to improve primary, secondary as well as tertiary preventive efforts and to address problems unique to Indian

population. We therefore evaluated the risk factors and angiographic profile in young patients with acute coronary syndrome admitted to our centre. We further compared them with the elderly population.

MATERIAL AND METHODS

Design: Prospective, randomised, observational, non-interventional, descriptive, cohort study.

Setting: An academic tertiary care centre hospital with interventional cardiac care unit.

Duration: Study was conducted from march 2012 to april 2014.

Inclusion criteria

- All patients fulfilling diagnostic criteria for acute coronary syndrome and exclusion criteria.
- Age ≥ 18 years.
- Genders -both sexes

Diagnostic criteria of acute coronary syndrome

- It includes ST elevation myocardial infarction (STEMI), non ST elevation myocardial infarction (NSTEMI] or unstable angina.
- Cases of chest pain/ discomfort with elevation of ST segment in electrocardiogrphic (ECG) leads/ presumed new onset left bundle branch block in ECG were categorized as STEMI.
- Cases of angina at rest without ST segment elevation were categorized as NSTEMI if their cardiac Troponin T (Trop T) levels exceeded 0.1 nanogram/ml and as UA if their Trop T levels were lower.
- Angina that occurred at rest and was prolonged, usually lasting ≥ 10 min consistent with pain or discomfort of myocardial ischemic origin.

ECG criteria of STEMI

- New or presumed new ST-segment elevation, new LBBB (Left bundle branch block), or isolated inferobasal (posterior) MI.
- ST-segment elevation at the J point in 2 contiguous leads with the cutpoints ≥ 0.1 mv in all leads other than V2/ V3, where ≥ 0.2 mV in men age ≥ 40 yrs, ≥ 0.25 mV in men age <40 yrs, or ≥ 0.15 mV in women.
- ST-segment depression ≥ 0.1 mV in at least 2 contiguous leads of V1 through V3 with upright T waves.
- ST-segment elevation ≥ 0.05 mV in leads V7 through V9 or ≥ 0.1 mV in men age < 40 y (inferobasal [posterior] infarction).
- ST-segment elevation ≥ 0.05 mV (≥ 0.1 mV in men age <30 y) in leads V3R, V4R (right ventricular infarction).
- ST-segment elevation ≥ 0.1 mV in lead aVR with concomitant ST-segment depression ≥ 0.05 my in at least 2 contiguous leads.

Exclusion criteria

- Any history or records of or suggestive of previous angina, angina equivalent or myocardial infarction or coronary revascularisation (more than 2 weeks old).
- Patients with prior cardiac pathology like valvular heart disease, cardiomyopathy, pericardial disease or cor pulrnonale.
- Patients who did not undergo angiography.

Study Details

Patients were included in the study cohort when fulfilling the inclusion and exclusion criteria. Detailed history was taken. Structured questionnaires were administered and physical examinations were undertaken. The baseline clinical characteristics analyzed in each group were the age, gender, hypertension, diabetes melltus, dyslipidemia, smoking status, personal and family history of cardiovascular history, duration of chest pain before hospitalization, time of occurrence of the ACS, symptoms, killip class and treatment received. Body mass index was calculated any time before discharge. Echocardiography was clone at the time of admission with bed side echocardiogram machine (sonosite).

- The details of the area of myocardium infarcted, the killip class, complications and whether thrombolytic therapy was received or not were analyzed.
- Angiographic findings were noted. Persons doing and reporting angiography were not aware of the process and thus blinded to the study. Coronary artery with more than 50% of occlusion was taken as significant.
- Patients were further divide into 2 groups based on their age. Patients 18-40 years were considered young and those > 40 years were considered as elderly.

Ethical considerations - As the study was observational and descriptive and involved no intervention, the ICU and patient data were collected with the usual guarantees of confidentiality.

Statistical analysis

Statistical analysis was done using patient related variables as well as process of care variables. Patient related variables included age, gender, diagnosis at the time of hospital admission, signs and symptoms, associated risk factors, killip class while process of care variable included investigation parameters like lipid profile, electrocardiogram, echocardiography and angiography.

The above mentioned factors were evaluated in both groups. Patient characteristics and process of care variables were compared gender wise, in diabetics and number of coronary vessel involvement.

The data was studied and statistically treated. The univariate analysis was clone using chi-square/fischer test. Results between two groups were compared using unpaired t test. Test of significance was set <0.05.

Terminologies

Diabetes- History of diabetes diagnosed and/or treated by a healthcare provider.

Documentation of Hemoglobin Alc ≥ 6.5%; or
Fasting plasma glucose ≥ 126 mg/dl or 2-h Plasma glucose ≥200 mg/dL during an oral glucose tolerance test; or
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl.

Hypertension- History of hypertension diagnosed and treated with medication, diet, and/or exercise or prior documentation

of blood pressure ≥ 140 mm Hg systolic and/or 90 mm Hg diastolic for patients without diabetes or chronic kidney disease, or prior documentation of blood pressure ≥ 130 mm Hg systolic or 80 mm Hg diastolic on at least 2 occasions for patients with diabetes or chronic kidney disease or currently undergoing pharmacological therapy for treatment of hypertension.

Dyslipidemia- Total cholesterol >200 mg/dL or LDL ≥ 130 mg/dL or HDL <40 mg/dL in men and <50 mg/dL in women or currently receiving antilipidemic treatment.

RESULTS

In the present study 180 patients with acute coronary syndrome were analyzed. Patients were divided into two categories according to age. Of them 88 were <40 years and considered as young and 92 were above 40 years of age. Males and females were 75% and 25% respectively in older group. In younger group patients 82% were male and 18% were female. The mean ages of the younger and elder groups were 57.8 years and 35.6 years respectively.

Table 1 shows the risk factor distribution between the two groups. There were no significant differences with respect to diabetes, obesity, and family history between the two groups. However younger ACS patients had significantly higher prevalence of smoking. In contrast hypertension was more prevalent in the older group. Serum LDL and triglycerides were significantly elevated in the young ACS patient group when compared to the older patients. Significantly more patients presented within 6 hours in the young ACS group.

Table 1 Clinical profile of ACS patients undergoing coronary angiography

Parameter	< 40 years (n=85)	>40 years (n=95)	P value
Obesity	22 (25.8%)	17 (17.9%)	0.825
Hypertension	10 (11.7%)	21 (22.1%)	0.003
Diabetes Mellitus	19 (22.3%)	23 (24.2%)	0.640
Smoking	38 (44.7%)	16 (16.8%)	0.023
Family history	7 (8.2%)	11 (11.5%)	0.925
Biochemical parameters			
Total cholesterol	186.7±39.3	182.5±38.4	0.926
Serum LDL-C	130.6±41.8	115.7±35.0	0.024
Serum HDL-C	37.8±6.7	39.7±9.2	0.856
Serum TG	178.7±65.2	150.5±52.9	0.010
Presentation within 6 hr of pain	42(49.4%)	26(27.3%)	0.005

Patients with STEMI were higher in both the groups as compared to NSTEMI (Table 2). The difference between STEMI and NSTEMI was significantly more in the younger age group with 87% patients presenting as STEMI (p=0.02).

Table 2 Comparison of clinical presentation of the study group (N=180)

Clinical presentation	Age <40 years (n=85)	Age >40 years (n=95)
STEMI	74 (87%)	60 (63.1%)
NSTEMI/UA	11 (13%)	35 (36.9%)

Table 3 shows the distribution of coronary vessel involvement with age. Younger patients had predominantly single vessel disease with a trend towards multivessel involvement in older age patients. There was a significant association of age with number of vessels involved (p 0.023). 16.5% young patients had insignificant stenosis on coronary angiogram.

Table 3 Comparative analysis of coronary angiographic profile between the two groups

Disease severity/Number of vessels on coronary angiogram	Age <40 years (n=85)	Age > 40 years (n=95)
Insignificant stenosis	14 (16.5%)	0
Single vessel disease	50 (58.9%)	40 (42.1%)
Double vessel disease	11(12.9%)	28(29.5%)
Triple vessel disease	10(11.7%)	27(28.4%)

LAD was the most frequent involved culprit vessel in both the groups. The distribution of coronary lesions did not vary significantly with age (p=ns) (Table 4)

Table 4 Distribution of coronary artery disease in single and double vessel disease

Single vessel disease	Total	LAD	RCA	LCX
Age < 40 years	50	30	12	8
Age > 40 years	40	24	10	6
Double vessel disease				
Age < 40 years	11	10	8	4
Age > 40 years	28	30	15	11

DISCUSSION

This is one of the first reported study on ACS in young from the Purvanchal area of Uttar Pradesh. Majority of the patients were male in both the groups. In the young patient group 82% were male. Earlier studies have reported that ACS occurs more in young male than females, CAD being less frequent in premenopausal females due to the protective effect of estrogen[6,7]. In one study it was noted that young patients with myocardial infarction are predominantly males at 94.5%[8]. However in recent studies it was reported that young women who are current smoker and are obese are more likely to suffer from ACS[9,10].

Among the conventional risk factors the prevalence of smoking was significantly more in subjects < 40 years age. In our study smoking was seen in 44.7% young patients. This is lower as compared to other Indian studies because of more incidence of tobacco chewing in this part of Uttar Pradesh. In one study from south India smoking was seen in 46% of young patients whilst 26% were tobacco chewers[11]. The literature reports smoking by upto 82% of young adults suffering from ACS[12]. Case control studies indicate that smoking is an independent risk factor for the development of ischaemic heart disease in young patients[13]. Since it is a preventable risk factor, healthy lifestyle should be encouraged among young individuals.

In contrast older group included more hypertensives. There were no significant differences with respect to diabetes, obesity, and family history between the two groups. The prevalence of diabetes and hypertension is lower as compared to other Indian studies. In the CREATE registry Diabetes mellitus and Hypertension were seen in 30.4% and 37.7% of young patients respectively[14]. The incidence of diabetes mellitus was not very high in the young population. One study that compared ACS in patients aged under 40 years with those over 40 years demonstrated the incidence of diabetes to be greater in older patients[15]. This might be explained by the pathophysiology of hyperglycemia in the atherosclerotic process which is time-dependent. Moreover, the pathophysiology of ACS in the young person does not seem to share the same classic risk factors fully. Family history of premature CAD was seen in only 8.2% young patients which

is in contrast to 40.2% in one study on young American population with ACS[16]. This may suggest the importance of lifestyle and environmental factors involved in our population. Serum LDL-C and serum triglycerides levels were significantly higher in the former group than in the latter group. This could be explained by the lifestyle of young patients. Patwary MSR *et al*[17] has shown that young patient in their study 53.33 % were dyslipidaemic. However in one Indian study the prevalence of dyslipidemia (TC>200mg/dl, LDL-C > 130mg/dl) was only 8.5% in young ACS patients[11]. 49.4% patients in the young ACS group presented within 6 hours of symptom onset. Early presentation was even lower (27.3%) for older group patients. The median time taken by patients is much higher than reported in other registries[18]. One study however reported the mean duration of symptoms before hospitalisation in STEMI patients of 11.37 hours[19]. In one study 62.75% young patients presented within 6hour of chest pain[11]. Lack of ambulance with long distance from health care facility in peripheral locations, economic reasons, a lack of awareness of the importance of the symptoms, delay by local practitioner and non availability of medication were the reasons for delayed presentation.

We recorded more cases of STEMI than non-STEMI or unstable angina in both groups. Bhattacharjee *et al*. in a recent study found that STEMI is significantly more common in younger patients[20]. In a Thai ACS Registry study, 67% young ACS patients had STEMI[21]. Similar finding has been observed by another group where majority (70%) of the young patients with ACS presented with STEMI[22]. On the other hand, NSTEMI and UA have been reported to be more common in the elderly[23,24]. However our older group has more prevalence of STEMI which was simllarily reported by some Indian studies[25,26,27,28].

In our study angiographically normal coronaries or mildly obstructive coronary arteries (insignificant stenosis) was seen in 16.5% patients in the young group. This group included recanalised infarct related artery with < 50% lesion with TIMI III flow in the echocardiographically and ECG correlated target vessel. This subgroup of insignificant stenosis shows that thrombotic state could be one of the major factor for ACS. One study showed that angiographically normal coronaries were seen in 1% of patients[29]. The actual prevalence of angiographically normal coronary arteries with myocardial infarction has been difficult to determine because some reports have included patients with upto 50% coronary stenosis as well as those free of luminal narrowing. In our study 58.9% had single vessel disease, 12.9% had double vessel disease and 11.7% had triple vessel disease in the young group. The prevalence of multivessel disease was significantly more in the older group patients as compared to the younger patients. Other studies have also showed that younger patients have lesser number of coronary artery involvement s and less severe disease[30,31,32]. The less extensive CAD observed in younger patients might suggest that premature CAD is associated with rapid disease progression rather than with a gradually evolving process.

LAD was the most commonly involved vessel in both the groups. Many studies have shown LAD to be the vessel most commonly involved followed by RCA and LCX in young patients[33,34]. In comparison with old age ACS patients, our study indicates that the distribution of coronary lesions is not age dependent.

Study Limitations

This study was single centre study where patients were randomly selected. Due to single centre nature the practice patterns at such centres might not necessarily represent practice at all hospitals in the country. However the study is unique in the sense that no patient with prior coronary disease was included in this study. Second, one-month follow-up data were not available. We did not calculate 30 day mortality to assess survival difference. In many patients lipid profile was done after 48 hours which might have caused lower level of HDL and LDL cholesterol in this study.

SUMMARY AND CONCLUSION

Young patients have some differences in the risk factor profile and coronary artery involvement in comparison to elderly. Risk factor identification and control, early presentation and treatment are important.

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