Research Article

Clinico-investigative assessment and comparison of cardiovascular risk factors in young and elderly patients of acute coronary syndrome

Prithwiraj Bhattacharjee[1], Soumyabrata Munshi[2]*, Gargi Das[2], Seikh Sahidul Islam[1]

[1]Department of Cardiology, Institute of Cardiovascular Sciences, Institute of Post-Graduate Medical Education and Research, Calcutta, West Bengal, India
[2]Department of Biochemistry, Institute of Post-Graduate Medical Education and Research, Calcutta, West Bengal, India

*Correspondence:
Dr. Soumyabrata Munshi, M.D.
E-mail: drsoumyabrata@gmail.com

ABSTRACT

Background: Coronary artery disease in Indians occurs at an earlier age than most other populations. Risk profile and angiographic severity of young acute coronary syndrome (ACS) patients differ from those in the elderly.
Methods: This cross-sectional study included 46 young (≤45 years) and 45 elderly (>45 years) ACS patients. Clinical features, risk factor profiles and coronary angiograms of these patients were studied and compared.
Results: Compared with the elderly, more young patients had chest pain and ST-elevated myocardial infarction. Smoking, atherogenic dyslipidemia and abdominal obesity were most frequent in young, while hypertension, high low-density lipoprotein (LDL) cholesterol and abdominal obesity were most prevalent in elderly. High serum homocysteine was the most prevalent novel risk factor in either group. Serum Lp(a) was significantly higher in the young group compared to elderly ($p = 0.03$). Angiographically, multivessel coronary disease and high Gensini score were more common in elderly. Young group had a low positive correlation between serum triglyceride level and Gensini score ($r_s = 0.33, p = 0.03$). In the elderly, fasting blood glucose and serum triglyceride levels had low positive correlation with Gensini score ($r_s = 0.36$, $p = 0.01$ and $r_s = 0.32, p = 0.04$ respectively).
Conclusions: Cardiovascular risk factors differ in young and elderly ACS patients. Lifestyle changes and behavioral modifications should be emphasized to prevent the development of ACS in the young Indians.

Keywords: Acute coronary syndrome, Cardiovascular risk factors, Young Indians

INTRODUCTION

Acute coronary syndrome (ACS) is a devastating life-threatening condition causing high morbidity and mortality and hence requires prompt therapeutic interventions. It is a generalized term that includes a wide spectrum of clinical signs and symptoms suggestive of acute myocardial ischemia and is clinically an initial working diagnosis.[1-4] The clinical conditions that constitute ACS range from unstable angina (UA) and non-ST-segment elevation myocardial infarction (NSTEMI) to ST-segment elevation myocardial infarction (STEMI).[3,4] The underlying pathology is the rupture or erosion of coronary arterial plaque complicated by thrombosis, embolization and obstruction to myocardial perfusion.[4] Although they have same pathophysiologic origin and clinical presentation, UA and NSTEMI differ in severity.[3] In NSTEMI, severely damaged myocardium causes release of biomarkers like cardiac-specific troponins (T or I) and/or muscle and brain fraction of creatine kinase (Creatine phosphokinase-MB [CPK-MB]) into the circulation, while in cases of UA no such phenomena occur and cardiac markers are not found in the blood.[3] Electrocardiogram (ECG) changes help both in diagnosis of ACS as well as in risk stratification of the patients. Pathologically, ST-segment depression, transient ST-segment elevation, T-wave inversion, or a combination

of these is/are present in UA and these features may be present in 30-50% of patients of ACS.[3]

The manifestation and underlying risk factors may differ according to the age of the patients.[5] Half of the cardiovascular disease-related deaths in India occurs below 50 years of age, and about 25% of acute myocardial infarction (MI) in India occurs below 40 years of age in men.[6] In Western countries smoking, family history, dyslipidemia and obesity have been found as the prevalent risk factors in young ACS patients.[7] Studies have shown increasing prevalence of coronary artery disease (CAD) in Indians, especially in younger population.[8] There is a paucity of data regarding the prevalence of risk factors in young Indian ACS patients. Moreover, the novel cardiovascular risk factors (CVRFs) like homocysteine (Hcy), lipoprotein(a) (Lp[a]), high-sensitivity C-reactive protein (hsCRP) and *Chlamydia pneumoniae* infection are less well studied in Indian ACS patients. The present study aims to evaluate and compare the clinical features and types of ACS, risk factor profile and the severity of CAD among young and elderly ACS patients; and also looks into any possible correlation between the risk factors and the severity of CAD in either age-group in a tertiary care hospital setting.

METHODS

Study population

The study was performed in the Departments of Cardiology and Biochemistry, Institute of Post-Graduate Medical Education and Research (IPGMER), India. Those patients who were admitted to the Department of Cardiology with the diagnosis of ACS and underwent assessment of CVRFs along with coronary angiogram within 48 h of admission were included in the study. Informed consents from the patients or their close relatives were obtained. Those patients with chronic kidney disease, chronic liver disease, malignancy, chronic infectious disease, and/or on therapy with drugs documented to significantly modify serum glucose and lipid levels were excluded from the study population. A total of 91 ACS patients ($n = 91$) included in the study were divided into two groups: young (≤45 years, $n = 46$) and elderly (>45 years, $n = 45$).

Diagnosis of ACS

The presenting clinical status was evaluated, and the working diagnosis of ACS was established in every patient in the study population. The patients were evaluated for their presenting symptoms (chest pain and its nature, breathing difficulty, vertigo, pallor, tremor, sweating) and signs (blood pressure, pulses, and auscultatory findings). Rapid and thorough physical examinations were done to exclude any non-cardiac causes of chest pain and non-ischemic cardiac disorders and potential extra-cardiac causes. Resting 12-lead ECG was obtained within the first 10 min of patients' arrival to the medical facility. The working diagnosis of NSTE-ACS was done by a rule-out diagnosis based on the lack of persistent ST elevation on ECG.[4] Cardiac biomarkers (Troponin T and CPK-MB) were measured in patients' blood to establish the diagnosis, stratify the risk, and to

distinguish between NSTEMI and UA. Echocardiography was done primarily to determine the mechanical function of the heart and the ejection fraction. Coronary angiography was performed to observe the vessel involvement.

Assessment of CVRFs

The CVRFs assessed in this study were divided as traditional and emerging. CVRFs other than advancing age and gender are shown in Table 1. They were studied with the help of biochemical and anthropometric assays, general examination and proper history-taking using approved well-designed proforma.

Biochemical assays

After obtaining informed consent, 10 mL of fasting venous blood samples were collected aseptically from the patients. Blood for glucose estimation was collected in fluoride-containing vials. The sera were used within 1 h for estimation of the blood parameters. For the estimation of Lp(a) and Hcy, the sera were stored at −80°C and analyzed within 20 days. All assays were done using commercial kits obtained from Randox Laboratories Ltd. (India) unless mentioned otherwise. Blood glucose concentration was estimated by the glucose oxidase-peroxidase (GOD-POD) method as per manufacturer's protocol. Serum total cholesterol levels were estimated based on cholesterol oxidase/ p-aminophenazone (CHOD-PAP) colorimetric method using reagent kit. High-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were estimated by direct clearance method following kit literature. Serum triglyceride was measured by glycerol-3-phosphate oxidase/ PAP (GPO-PAP) method. Serum hsCRP was estimated by immunoturbidimetric method, where the turbidity produced by the insoluble immune complexes of the protein with its antibody is proportional to the hsCRP concentration in the sample and is measured spectrophotometrically. All measurements were made using clinical automated analyzer (Randox, Daytona) with proper internal quality control. Serum Lp(a) levels were estimated by immunoturbidimetry (Daiichi, Japan) as per the manufacturer's protocol.[9] Serum Hcy level was measured using sandwich enzyme-linked immunosorbent assay (ELISA) using human Hcy commercial kit as per the manufacturer's protocol (Cusabio Biotech, Newark, DE, USA).

Estimation of serum C. pneumoniae immunoglobulin G (IgG) antibody

Serum *C. pneumoniae* IgG antibody was estimated by ELISA using a commercial kit (NovaTec Immunodiagnostica Gmbh, Germany). Briefly, patients' sera, controls (negative and positive), cut-off and blank were added to the respective microtiter wells coated with *C. pneumoniae* antigens, followed by addition of horseradish peroxidase (HRP)-labeled anti-human IgG conjugate. The immune complex formed by the bound conjugate was visualized by addition of tetramethylbenzidine that produced a blue product, the absorbance of which when taken at 450 nm using an ELISA microplate reader gave the amount of

Table 1: Cardiovascular risk factors: Definition and prevalence.

Risk factors	Definition used in the study	Entire group (%)	Young ACS group (≤45 years) (%)	Elderly ACS group (>45 years) (%)	p values
Traditional risk-factors					
Generalised obesity	BMI≥25 kg/m²	34/91 (37.36)	16/46 (34.78)	18/45 (40.00)	0.60
Abdominal obesity	Waist circumference ≥80 cm (females) and ≥90 cm (males)	44/91 (48.35)	18/46 (39.13)	26/45 (57.78)	0.41
Hypertension	Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg	46/91 (50.55)	15/46 (32.61)	31/45 (68.89)	<0.001***
Diabetes mellitus	Fasting plasma glucose ≥126 mg/dL	31/91 (34.06)	12/46 (26.08)	19/45 (42.22)	0.10
Hypercholesterolemia	Fasting serum cholesterol ≥200 mg/dL	33/91 (36.26)	12/46 (26.08)	21/45 (46.67)	0.04*
Low HDL-C	Fasting serum HDL-C<50 mg/dL (females) and <40 mg/dL (males)	31/91 (34.06)	20/46 (43.48)	11/45 (24.44)	0.05
High LDL-C	LDL-C≥100 mg/dL	48/91 (52.75)	20/46 (43.48)	28/45 (62.22)	0.07
Hypertriglyceridemia	Fasting serum triglyceride level ≥150 mg/dL	44/91 (48.35)	19/46 (41.30)	25/45 (55.55)	0.17
Substance abuse	Intake history of recreational and over-the-counter drugs and substances	15/91 (16.48)	8/46 (17.39)	7/45 (15.55)	0.81
Smoking	History of smoking	55/91 (60.44)	34/46 (73.91)	21/45 (46.67)	0.007**
Family history	Coronary artery disease at age <55 years (father) or <65 years (mother)	4/91 (4.39)	3/46 (6.52)	1/45 (2.22)	0.31
Emerging risk factors					
High serum lipoprotein (a) (>30mg/dL)	≥30 mg/dL	29/91 (31.87)	19/46 (41.30)	10/45 (22.22)	0.05
High serum homocysteine (>15 μmol/L)	≥15 μmol/L	66/91 (72.53)	33/46 (71.74)	33/45 (73.33)	0.86
High hsCRP (>3mg/dL)	≥3 mg/L	49/91 (53.85)	23/46 (50.00)	26/45 (57.78)	0.45
Positive *C. pneumoniae* IgG antibody (>11 units) in serum	>11 units	19/91 (20.88)	9/46 (19.56)	10/45 (22.22)	0.75

*p<0.05 (significant), **p<0.01 (highly significant), ***p<0.001 (extremely significant). ACS: Acute coronary syndrome, BMI: Body mass index, HDL-C: High density lipoprotein-cholesterol, LDL-C: Low density lipoprotein-cholesterol, hsCRP: High-sensitivity C-reactive protein, *C. pneumoniae: Chlamydia pneumoniae*

C. pneumoniae - specific IgG antibodies in the sample. Samples were considered positive when readings were higher than 10% over the cut-off. The results were expressed in NovaTec Unit (NTU) as: (Absorbance × 10)/cut-off.

Anthropometric measurements

The height (in m), weight (in kg) and waist circumference (in cm) of the patients were measured using standard techniques and noted systematically.[8,10] Body mass index was estimated using the expression: (weight [kg])/(height [m]).[2]

Gensini score

Gensini score is used to quantify the severity of CAD.[11,12] Reduction in the lumen diameter, and the roentgenographic appearance of concentric lesions and eccentric plaques were evaluated. The reductions of 25%, 50%, 75%, 90%, 99%, and

100% occlusion were given the Gensini scores of 1, 2, 4, 8, 16 and 32 respectively.[11] Each principal vascular segment was assigned a multiplying factor in accordance with the functional significance of the myocardial area supplied by that segment: the left main coronary artery ×5; the proximal segment of left anterior descending (LAD) coronary artery ×2.5; the proximal segment of the circumflex artery ×2.5; the mid-segment of the LAD ×1.5; the right coronary artery, the distal segment of the LAD, the postero-lateral artery and the obtuse marginal artery ×1, and others ×0.5.

Statistical analyses

The data were systematically entered in Microsoft Excel spread-sheet. The values were expressed as mean ± standard error of mean, or as percentages. Comparisons between the groups were done using Student's independent *t*-test and Chi-square test using Statistica version 12 (Statsoft Inc, Tulsa, Oklahoma, USA). $p < 0.05$ was considered as statistically significant. Correlation of Gensini scores with the serum parameters of the CVRFs, and that of serum LDL and total cholesterol were done by Spearman's rank correlation tests. Size of Spearman's correlation coefficient (r_s) was interpreted as described previously.[13] Briefly, r_s between 0.9 and 1.0 was considered very high (very strong), 0.7-0.9 was high (strong), 0.5-0.7 was moderate, 0.3-0.5 was low, and 0.0-0.3 was considered as negligible correlation.

RESULTS

Demographic characteristics and clinical features of the ACS patients

Mean age of the entire ACS population studied was 48.97 ± 14.54 years. The mean age of the young ACS patients was 36.65 ± 6.48 years as compared to that of the elderly group which was 61.58 ± 8.27 years ($p < 0.001$) (Table 2). The total number of male ACS patients was 80 (87.91%), while the female patients were 11 (12.09%) in number (Table 2). In the young group of ACS patients, 44/46 (95.65%) were males while in the elderly group it was 36/45 (80%) (Table 2).

Of the presenting symptoms, chest pain was the most common (Table 2). It was present in 69/91 (75.82%) of the total number of ACS cases studied and comprised of 39/46 (84.78%) in the younger group and 30/45 (66.67%) in the elderly group. The number of patients presenting with chest pain was significantly higher in the younger group than in the elderly ($p = 0.04$). Dyspnea and other features were also present in a proportion of the patients but did not comprise of significant differences between the young and the elderly ACS groups (Table 2). STEMI was the most common ECG feature present in the ACS patients and accounted for 73/91 (80.22%) of the total cases, 41/46 (89.13%) of the younger patients and 32/45 (71.11%) of the elderly patients (Table 2). The prevalence of STEMI was significantly higher in the younger ACS group compared to the elderly one ($p = 0.03$). NSTEMI/UA was present in 18/91 (19.78%) of the total ACS patients studied

(Table 2). The prevalence of NSTEMI/UA was significantly more in the elderly group (13/45 = 28.89%) compared to the younger one (5/46 = 10.87%; $p = 0.03$) (Table 2).

Traditional CVRFs

In the total population studied and in the younger group, smoking was the most prevalent traditional risk factor (55/91 = 60.44% and 34/46 = 73.91% respectively), while in the elderly group it was hypertension (31/45 = 68.89%) (Table 1). The next most prevalent CVRF in the entire ACS group was high LDL-C (48/91 = 52.75%), followed by hypertension (46/91 = 50.55%), hypertiglyceridemia and abdominal obesity (44/91 = 48.35% each of the latter two) (Table 1). However, in the younger group, the subsequent most prevalent CVRFs were high LDL-C and low HDL-C (both being present in 20/46 = 43.48%), followed by hypertriglyceridemia (19/46 = 41.30%) and abdominal obesity (18/46 = 39.13%) (Table 1). In the elderly group also, high LDL-C was the second most prevalent CVRF (28/45 = 62.22%), followed by abdominal obesity (26/45 = 57.78%) (Table 1). The least prevalent CVRF in our study was family history of CAD in all the groups (Table 1). In the elderly ACS patients, prevalence of hypertension (31/45 = 68.89% vs. 15/46 = 32.61% in young ACS group; $p < 0.001$) and hypercholesterolemia (21/45 = 46.67% vs. 12/46 = 26.08% in young ACS group; $p = 0.04$) were significantly higher (Table 1). However, smoking was significantly less prevalent in the elderly group than in the younger ACS patients ($p = 0.007$) (Table 1). Figure 1 shows the values of the traditional CVRFs in the young and the elderly ACS patients studied. Serum level of total cholesterol, HDL-C and LDL-C were significantly more in the elderly ACS patients compared to the younger ACS patients ($p < 0.001$, $p = 0.01$ and $p = 0.03$ respectively) (Figure 1).

Emerging CVRFs

Of the emerging CVRFs, high serum Hcy level was prevalent in all the groups of ACS patients studied: 66/91 (72.53%) in the entire ACS population, 33/46 (71.74%) in the younger ACS group and 33/45 (73.33%) in the elderly ACS patients (Table 1). High hsCRP was present in 49/91 (53.85%) of the total ACS patients, 23/46 (50.00%) of the younger patients and in 26/45 (57.78%) of the elderly group of ACS patients (Table 1). High serum Lp(a) was present in 29/91 (31.87%) of the entire ACS population, 19/46 (41.30%) of the younger group and in 10/45 (22.22%) of the elderly ACS patients (Table 1). Positive *C. pneumoniae* IgG antibody in serum was present in 19/91 (20.88%) of the entire ACS patients, in 9/46 (19.56%) of the younger patients and in 10/45 (22.22%) of the elderly ACS group (Table 1). There was no significant difference between the elderly and the young groups of ACS patients in terms of prevalence of these emerging CVRFs (Table 1). However, the serum level of Lp(a) was significantly lower in the elderly group compared to the younger patients ($p = 0.03$) (Figure 2). Figure 2 shows the values of the emerging CVRFs in the young and the elderly ACS patients studied.

Table 2: Demographic distribution and presenting features of the young and the elderly ACS groups.

Characteristics and presenting features	Entire group (%)	Young ACS group (≤45 years) (%)	Elderly ACS group (>45 years) (%)	p value
Total number	91	46	45	
Age (years)	48.97±14.54	36.65±6.48	61.58±8.27	<0.001***
Gender (M/F)	80/11 (M: 87.91)	44/2 (M: 95.65)	36/9 (M: 80)	0.02*
Presenting chief complaints				
Chest pain	69/91 (75.82)	39/46 (84.78)	30/45 (66.67)	0.04*
Dyspnea	20/91 (21.98)	7/46 (15.22)	13/45 (28.89)	0.11
Pre-syncope	2/91 (2.19)	0/46 (0.00)	2/45 (4.44)	0.14
ECG findings at presentation				
AWMI	47/91 (51.65)	25/46 (54.35)	22/45 (48.89)	0.60
IWMI	26/91 (28.57)	16/46 (34.78)	10/45 (22.22)	0.18
STEMI (AW+IW)	73/91 (80.22)	41/46 (89.13)	32/45 (71.11)	0.03*
NSTEMI/UA	18/91 (19.78)	5/46 (10.87)	13/45 (28.89)	0.03*

*$p<0.05$ (significant), ***$p<0.001$ (extremely significant). Denominator indicates total number of subjects in the particular group unless mentioned otherwise. M: Male, F: Female, ACS: Acute coronary syndrome, ECG: Electrocardiogram, AWMI: Anterior wall myocardial infarction, IWMI: Inferior wall myocardial infarction, STEMI: ST-segment elevated myocardial infarction, AW: Anterior wall, IW: Inferior wall, NSTEMI: Non-ST-segment elevated myocardial infarction, UA: Unstable angina
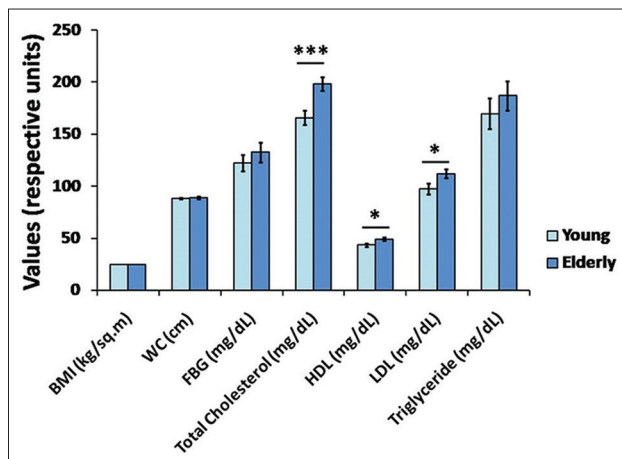
Figure 1: Traditional cardiovascular risk factors in the young and the elderly Acute coronary syndrome (ACS) patients. The bar diagram compares the values of the traditional risk factors (as mentioned in Table 1) in the young (light blue bars) and the elderly (dark blue bars) ACS patients. Values represented as mean ± standard error of mean. Comparison between the groups has been done with Student's independent *t*-test. *$p < 0.05$, ***$p < 0.001$. BMI: Body mass index; WC: Waist circumference; FBG: Fasting blood glucose; HDL: High density lipoprotein-cholesterol; LDL: low density lipoprotein-cholesterol.

Imaging studies

Normal coronary arteries were present in 5/46 (10.86%) of the younger patients, 1/45 (2.22%) of the elderly patients, and 6/91 (6.59%) of the total number of ACS patients (Table 3). Number of single vessel disease (SVD) was significantly more in the younger group (23/46 = 50%) than in the elderly (11/45 = 24.44%; $p = 0.01$). Number of double vessel disease (DVD) was significantly more in the elderly group (19/45 = 42.22%) compared to the younger group (10/46 = 21.74%; $p = 0.03$). Number of triple vessel disease (TVD) was not significantly different between the groups with 8/46 (17.39%) in the younger and 14/45 (31.11%) in the elderly ACS group ($p = 0.12$). However, the total number of combined DVD and TVD in the elderly group (33/45 = 73.33%) was significantly higher than in the younger group (18/46 = 39.13%; $p = 0.001$). On the other hand, prevalence of total cases with normal coronaries and SVD was significantly more in the younger group (28/46 = 60.87%) compared to the elderly (12/45 = 26.67%; $p = 0.001$) (Table 3).

Severity of the disease

The Gensini score was significantly higher in the elderly (40.13 ± 22.46) compared to the younger ACS group (26.93 ± 24.14; $p = 0.008$) (Table 3). In the elderly ACS patients, a low yet significant positive correlation with Gensini score was found with the serum levels of fasting blood glucose ($r_s = 0.36$, $p = 0.01$) and triglyceride ($r_s = 0.32$, $p = 0.04$) (Figure 3). In the younger ACS patients, a similar low yet significant positive correlation with Gensini score was found only with the serum levels of triglyceride ($r_s = 0.33$, $p = 0.03$) (Figure 3). The ejection fraction was not statistically different between the younger (48.63 ± 8.55) and the elderly (49.06 ± 9.22) patients (Table 3).

DISCUSSION

Significantly higher percentage of cardiovascular deaths occurs in younger people in the developing world than in developed countries.[14] Our study compared the differences of established and emerging risk factors between the young

Table 3: Distribution of imaging characteristics of young and elderly ACS patients.

Imaging characteristics	Entire group (%)	Young ACS group (≤45 years) (%)	Elderly ACS group (>45 years) (%)	p values
Normal coronary arteries	6/91 (6.59)	5/46 (10.86)	1/45 (2.22)	0.09
SVD	34/91 (37.36)	23/46 (50)	11/45 (24.44)	0.01*
DVD	29/91 (31.87)	10/46 (21.74)	19/45 (42.22)	0.03*
TVD	22/91 (24.17)	8/46 (17.39)	14/45 (31.11)	0.12
Normal coronaries+SVD	40/91 (43.95)	28/46 (60.87)	12/45 (26.67)	0.001**
DVD+TVD	51/91 (56.04)	18/46 (39.13)	33/45 (73.33)	0.001**
Gensini score	33.46±24.12	26.93±24.14	40.13 (22.46)	0.008**
Ejection fraction	48.85±8.84	48.63±8.55	49.06±9.22	0.81

*$p<0.05$ (significant), **$p<0.01$ (highly significant), ***$p<0.001$ (extremely significant). ACS: Acute coronary syndrome, SVD: Single-vessel disease, DVD: Double-vessel disease, TVD: Triple-vessel disease
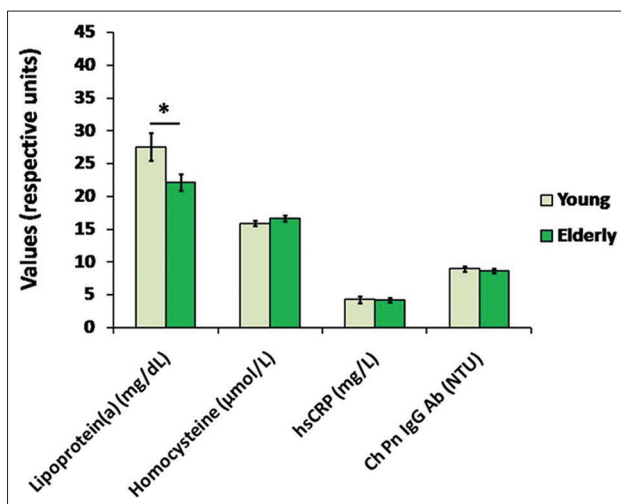
Figure 2: Emerging cardiovascular risk factors in the young and the elderly acute coronary syndrome (ACS) patients. The bar diagram compares the values of the emerging risk factors (as mentioned in Table 1) in the young (light green bars) and the elderly (dark green bars) ACS patients. Values represented as mean ± standard error of mean. Comparison between the groups has been done with Student's independent *t*-test. *$p < 0.05$. hsCRP: High-sensitivity C-reactive protein; Ch Pn IgG Ab: *Chlamydia pneumoniae* immunoglobulin G antibody.

and elderly ACS patients, as well as the differences in the clinico-angiographic profile between these two groups. Some important observations made in this study are as follows: Firstly, young ACS patients are mostly males (95.65%) who more commonly present with typical anginal pain when compared to elderly ($p = 0.04$). STEMI is the most common form of ACS in this age group, whereas NSTEMI and UA are significantly higher in elderly population ($p = 0.03$). Secondly, smoking is the most prevalent established CVRF in the younger patients as well as in the total study population, whereas hypertension is the most prevalent established CVRF in the elderly group. Thirdly, among the emerging CVRFs, serum Lp(a) level was found to be significantly higher in the younger group

($p = 0.03$). Fourthly, younger patients have lesser number of coronary artery involvements and less severe disease compared to elderly. Finally, high serum triglyceride level may be associated with increased disease severity (higher Gensini score) in younger patients.

The fact that ACS occurs more in males than females has been reported previously in the literature.[4,15-18] Coronary artery disease is much less frequent in premenopausal women; however the protection from CAD is much less evident after menopause.[19,20] However, diabetes negates the protection of premenopausal women from CAD.[20] In a recent study, researchers have found that young women who are current smoker and obese are more likely to suffer from ACS.[21] Intensity of chest pain has been reported to be similar between men and women.[22] In our study, only two patients in the young ACS group were female, and both of them had abdominal obesity and diabetes.

Cardinal symptom of ACS is anginal chest pain usually described as a tightness or heaviness or burning sensation over the chest with typical radiation. However, "anginal equivalent" symptoms such as dyspnea, nausea, vomiting, diaphoresis and fatigue may occur. In a study by Puricel *et al.*, 85% of young patients presented with typical chest pain.[17] Present study corroborates this finding. We have also found that STEMI is significantly more common ($p = 0.03$) in younger patients (Table 2). Similar finding has been observed by another group where majority (70%) of the young patients with ACS presented with STEMI.[7] Several studies have shown that STEMI is the most common form of ACS in young. In a Thai ACS Registry study 67% young ACS patients had STEMI.[23] On the other hand, NSTEMI and UA have been reported to be more common in the elderly.[24,25] Our present study corroborates these findings.

Several studies have found smoking as the most prevalent risk factor among young ACS patients.[23,26] In this study also we found smoking to be the most prevalent established CVRF in young patients. Atherogenic dyslipidemia, characterized by high serum triglyceride and low serum HDL-C level is shown to be common in Indians.[27,28] This

is characterized by formation of small dense LDL particles which are more atherogenic. Abnormal pattern of fat disposition characterized by increased waist circumference is prevalent in Indians and a risk factor for insulin resistance and increased CV risk. In this study, atherogenic dyslipidemia (high triglyceride and low HDL-C) was found to be the second most prevalent established CVRF (41%), followed by abdominal obesity.

Hypertension remains the most ubiquitous risk factor for CAD worldwide. We found hypertension to be the most prevalent established risk factor in the elderly group. However it was much less frequent in the younger group. Other similar studies have also shown high prevalence of hypertension in elderly patients.[5]

In the present study, prevalence of SVD is significantly higher in younger ACS patients (Table 3) with majority having involvement of the LAD artery territory (data not shown). Findings having similar trends in a similar population have been reported previously in literature.[29] We have also found here that no-vessel involvement or single-vessel involvement is more common in the young while multi-vessel disease is more common in the elderly (Table 3).

Gensini scores indicating severity of the involvement of the coronary arteries have been found to be more in the elderly than the younger ACS patients in this study. Previous researches have shown correlation of Gensini score with hsCRP, glucated hemoglobin A1c (HbA1c), and carotid intima medial thickness.[30-32] Our study has however found a low positive correlation of the Gensini score with the triglycerides levels (TGLs) in the younger ACS patients (Figure 2), which means high serum TGL levels in young group is associated with more severe CAD. This is very interesting as several studies have shown that high TGL

level in Indian patients has been associated with higher risk of CAD.[33]

Although atypical risk factors have been implicated to cause premature CAD in young individuals, till date no study has conclusively demonstrated their role. Although some studies have shown plasma Hcy level to be an independent risk factor for CAD in young, treatment of hyperhomocysteinemia did not lead to reduced CV risk.[34,35] Another novel risk factor to generate interest is hsCRP. It has been used as a prognostic marker in ACS. Lp(a) is a genetic risk factor and prevalent in Indians compared with the Whites in Great Britain.[36] We found significantly higher level of Lp(a) in the younger group compared with the elderly suggesting a genetic propensity. Hyperhomocysteinemia was found to be equally prevalent in either study groups. Elderly patients had a higher prevalence of high hsCRP level compared with the younger patients, though the difference was not statistically significant.

Infection and atherosclerosis have been a matter of debate for a long time and final word has not been spoken. One study has shown significantly higher level of *C. pneumoniae* IgG antibody in patients of ACS compared with the control group.[37] In the present study, 19.46% of young and 22.22% of elderly ACS patients have higher serum level of *C. pneumoniae* IgG antibody.

Limitations of the study

Being a hospital-based cross-sectional study it is difficult to generalize and project its findings on the population. This study did not have a control group and also the number of patients included in the study was small. Larger study with an appropriate age- and sex-matched control group is needed to further confirm the findings of this study. Our study has also failed to find any significant correlation between the Gensini scores and the emerging risk factors studied.
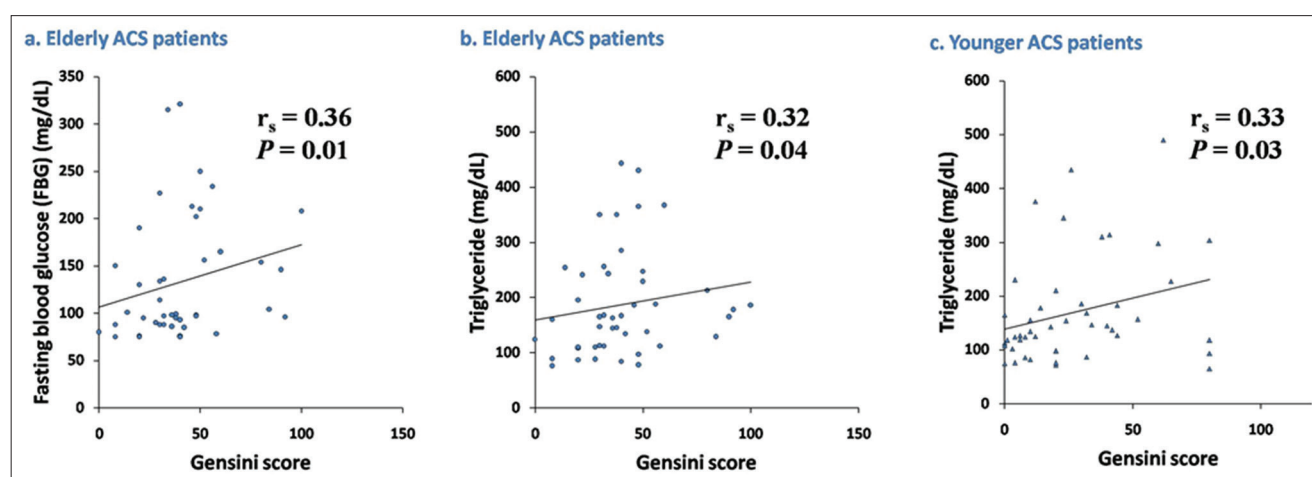
Figure 3: Significant correlation between the severity of the disease and the cardiovascular risk factors in acute coronary syndrome (ACS) patients. XY scatter plots showing low yet significant correlation between Gensini scores and serum levels of (a) Fasting blood glucose in the elderly ACS patients, (b) triglyceride in the elderly ACS patients, and (c) triglyceride in the young ACS patients. Correlation coefficient (r_s) represents the degree and nature of correlation between the Gensini score and the serum parameters in the elderly and the younger ACS groups as mentioned in the materials and methods (statistical analysis). A value of $p < 0.05$ was considered as statistically significant.

CONCLUSIONS

In spite of some of its inherent limitations, this study is a strong step forward in trying to underscore the significance of the roles of various CVRFs in ACS. Young smoker males with dyslipidemia are more commonly affected with ACS and present with typical chest pain, STEMI and single vessel CAD. Elderly patients however present with more severe CAD although they may have more atypical symptoms of the disease. Early risk stratification, identification of the disease and its management may prevent fatal outcomes in a large number of cases. Smoking cessation and lifestyle modification in the younger population are strongly advocated to lower the ACS risk. Further research is needed in a larger population to elucidate the roles of these risk factors and help to undertake specific measures to prevent the development of such disease in the population.

REFERENCES

1. Kolansky DM. Acute coronary syndromes: morbidity, mortality, and pharmacoeconomic burden. Am J Manag Care. 2009;15 2 Suppl: S36-41.
2. Nagesh CM, Roy A. Role of biomarkers in risk stratification of acute coronary syndrome. Indian J Med Res. 2010;132:627-33.
3. Kumar A, Cannon CP. Acute coronary syndromes: diagnosis and management, part I. Mayo Clin Proc 2009;84:917-38.
4. Hamm CW, Heeschen C, Falk E, Fox Keith AA. Acute coronary syndromes: pathophysiology, diagnosis and risk stratification. In: Camm AJ, Lüscher TF, Serruys PW, editors. The ESC Textbook of Cardiovascular Medicine. 1st Edition. Oxford: Blackwell; 2006: 333-60.
5. Rosengren A, Wallentin L, Simoons M, Gitt AK, Behar S, Battler A, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. Eur Heart J. 2006;27(7):789-95.
6. Enas E, Senthilkumar A. Coronary artery disease in Asian Indians: an update and review. Internet J Cardiol 2001;1(2). Available at https://www.ispub.com/IJC/1/2/4493.
7. Schoenenberger AW, Radovanovic D, Stauffer JC, Windecker S, Urban P, Niedermaier G, et al. Acute coronary syndromes in young patients: presentation, treatment and outcome. Int J Cardiol. 2011;148(3):300-4.
8. Mohan V, Deepa R, Rani SS, Premalatha G, Chennai Urban Population Study (CUPS No.5). Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India: the Chennai Urban Population Study (CUPS No. 5). J Am Coll Cardiol. 2001;38(3):682-7.
9. Ray L, Khemka VK, Behera P, Bandyopadhyay K, Pal S, Pal K, et al. Serum homocysteine, dehydroepiandrosterone sulphate and lipoprotein (a) in alzheimer's disease and vascular dementia. Aging Dis. 2013;4(2):57-64.
10. Ghosh A, Bhagat M, Das M, Bala SK, Goswami R, Pal S. Prevalence of cardiovascular disease risk factors in people of Asian Indian origin: age and sex variation. J Cardiovasc Dis Res. 2010;1(2):81-5.
11. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 1983;51(3):606.
12. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Veglia F, Briganti A, et al. Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: the COBRA trial. Eur Heart J. 2006;27(22):2632-9.
13. Mukaka MM. Statistics corner: a guide to appropriate use of correlation coefficient in medical research. Malawi Med J. 2012;24(3):69-71.
14. Institute of Medicine (US). Committee on Preventing the Global Epidemic of Cardiovascular Disease: meeting the Challenges in Developing Countries. Washington, DC: Institute of Medicine; 2010.
15. Mohanan PP, Mathew R, Harikrishnan S, Krishnan MN, Zachariah G, Joseph J, et al. Presentation, management, and outcomes of 25 748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. Eur Heart J. 2013;34(2):121-9.
16. Sarr M, Ba DM, Ndiaye MB, Bodian M, Jobe M, Kane A, et al. Acute coronary syndrome in young Sub-Saharan Africans: a prospective study of 21 cases. BMC Cardiovasc Disord. 2013;13:118.
17. Puricel S, Lehner C, Oberhänsli M, Rutz T, Togni M, Stadelmann M, et al. Acute coronary syndrome in patients younger than 30 years – Aetiologies, baseline characteristics and long-term clinical outcome. Swiss Med Wkly. 2013;143:w13816.
18. El-Menyar A, Ahmed E, Albinali H, Al-Thani H, Gehani A, Singh R, et al. Mortality trends in women and men presenting with acute coronary syndrome:

insights from a 20-year registry. PLoS One. 2013;8(7):e70066.

19. Sutton-Tyrrell 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(6):1116-21.

20. Maas AH, Appelman YE. Gender differences in coronary heart disease. Neth Heart J. 2010;18(12):598-602.

21. Diamond J, Davis M, Krishnan S, Jackson E. Young women with acute coronary syndrome events: are all women the same? J Am Coll Cardiol. 2012;59(13s1):E439.

22. DeVon HA, Ryan CJ, Ochs AL, Shapiro M. Symptoms across the continuum of acute coronary syndromes: differences between women and men. Am J Crit Care. 2008;17(1):14-24.

23. Tungsubutra W, Tresukosol D, Buddhari W, Boonsom W, Sanguanwang S, Srichaiveth B, et al. Acute coronary syndrome in young adults: the Thai ACS Registry. J Med Assoc Thai. 2007;90 Suppl 1:81-90.

24. Ahmed E, El-Menyar A, Singh R, Al Binali1 HA, Al Suwaidi J. Effect of age on clinical presentation and outcome of patients hospitalized with acute coronary syndrome: a 20-year registry in a Middle Eastern country. Open Cardiovasc Med J. 2012;6:60-67.

25. Avezum A, Makdisse M, Spencer F, Gore JM, Fox KA, Montalescot G, et al. Impact of age on management and outcome of acute coronary syndrome: observations from the global registry of acute coronary events (GRACE). Am Heart J. 2005;149(1):67-73.

26. Haque AFM, Siddiqui AR, Rahman SMM, Iqbal SA, Fatema NN, Khan Z. Acute coronary syndrome in the young – Risk factors and angiographic pattern. Cardiovasc J. 2010;2:175-8.

27. Misra A, Luthra K, Vikram NK. Dyslipidemia in Asian Indians: determinants and significance. J Assoc Physicians India. 2004;52:137-42.

28. Manjunath CN, Rawal JR, Irani PM, Madhu K. Atherogenic dyslipidemia. Indian J Endocrinol Metab. 2013;17(6):969-76.

29. Biswas PK, Dasbiswas A, Roy S, Roy D, Biswas A, Chatterjee SS, et al. Risk factors and angiographic profile of coronary artery disease in young. J Indian Med Assoc. 1995;93(3):90-2, 94.

30. Masood A, Jafar SS, Akram Z. Serum high sensitivity C-reactive protein levels and the severity of coronary atherosclerosis assessed by angiographic gensini score. J Pak Med Assoc. 2011;61(4):325-7.

31. Ertem AG, Bagbanci H, Kiliç H, Yeter E, Akdemir R. Relationship between HbA1c levels and coronary artery severity in nondiabetic acute coronary syndrome patients. Turk Kardiyol Dern Ars. 2013;41(5):389-95.

32. Adams MR, Nakagomi A, Keech A, Robinson J, McCredie R, Bailey BP, et al. Carotid intima-media thickness is only weakly correlated with the extent and severity of coronary artery disease. Circulation. 1995;92(8):2127-34.

33. Rissam HS, Kishore S, Trehan N. Coronary artery disease in young Indians-the missing link. J Indian Acad Clin Med. 2001;2(3):128-32.

34. Abraham JM, Cho L. The homocysteine hypothesis: still relevant to the prevention and treatment of cardiovascular disease? Cleve Clin J Med. 2010;77(12):911-8.

35. Puri A, Gupta OK, Dwivedi RN, Bharadwaj RP, Narain VS, Singh S. Homocysteine and lipid levels in young patients with coronary artery disease. J Assoc Physicians India. 2003;51:681-5.

36. Bhatnagar D, Anand IS, Durrington PN, Patel DJ, Wander GS, Mackness MI, et al. Coronary risk factors in people from the Indian subcontinent living in west London and their siblings in India. Lancet. 1995;345(8947):405-9.

37. Maia IL, Nicolau JC, Machado MN, Maia LN, Takakura IT, Rocha PR, et al. Prevalence of *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* in different forms of coronary disease. Arq Bras Cardiol. 2009;92(6):405-11, 422.