Epidemiological and clinical profile, management and outcomes of young patients (≤40 years) with acute coronary syndrome: A single tertiary care center study

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1. Introduction

Cardiovascular disease (CVD) is the most common cause of mortality worldwide and in India.1 Approximately 25% of all the deaths in India are attributable to CVD.2 Indians are affected by CAD a decade earlier as compared to the western populations.2–4 In 2016, there were an estimated 62.5 million years of life lost prematurely due to CVD in India.1

Due to the epidemiological transition, the prevalence of coronary artery disease (CAD) is rising in young adults.5 The age cut-off of 40 years was used to define “young” patients with CAD.5 The clinical and risk factor profile and the coronary artery involvement pattern differs between young CAD patients and those who are elderly.7,8 Young CAD patients have a good prognosis with a predominance of SVD, and the most common risk factors include smoking, family history of CAD, and hypercholesterolemia.9 Coronary atherosclerosis is the most common cause (80%) for CAD in the young.7 Less common reasons for CAD among young adults include coronary vasospasm, medium vessel vasculitis, hypercoagulable states, substance abuse, and embolism, among many other causes.7 Although CAD in young has a relatively good prognosis, it carries substantial morbidity, psychological impact, financial burden, and more significant loss of Disability-adjusted life years (DALYs) as the
young productive age group is being affected. The prevalence of young CAD ranges from 5% to 7% in various registries. There have been limited data on the epidemiological and clinical profile and angiographic profile of young adults with ACS in India. Therefore, we sought to evaluate the demographic profile, clinical presentation, echocardiographic and angiographic characteristics, in-hospital outcomes, and 30-day mortality of young adults (<40 years) with ACS.

2. Materials and methods

2.1. Study design

Our study was a single tertiary care center prospective cross-sectional study of young patients (age <40 years) with ACS presenting to the cardiac critical care unit (CCU).

2.2. Material and methods

The study was conducted from January 2018 to June 2019. The study enrolled subjects with acute coronary syndrome and aged <40 years. Acute myocardial infarction was defined as per the fourth universal definition of myocardial infarction. NSTE-ACS was defined as per the 2014 American heart association (AHA) NSTE-ACS guidelines. ECG diagnosis of STE-ACS was made in a patient with new ST-segment elevation at the J point in two contiguous leads of ≥0.1 mV in all leads other than leads V2–V3. For leads V2–V3, the criteria taken was ≥0.2 mV in men ≥40 years, >0.25 mV in men <40 years, or >0.15 mV in women. Two dimensional (2D) echocardiography (Vivid Q, GE Healthcare, New York, USA) was done to assess the left ventricular (LV) systolic function and any mechanical complications. Ejection fraction (EF) was measured using the modified Simpson method. Normal LV function was defined as LVEF of 50–70%, Mild LV dysfunction was defined as LVEF of 40–49%, Moderate LV dysfunction was defined as LVEF of 30–39%, and Severe LV dysfunction was defined as LVEF less than 30%. Cardiogenic shock was defined as systolic blood pressure (SBP) measurements of <90 mm Hg for ≥30 min or the use of drugs or mechanical support to maintain an SBP ≥90 mm Hg.

Hypertension was defined based on the 2018 AHA/ACC guidelines for hypertension. Diabetes was described as a fasting blood glucose level of >126 mg/dl or HbA1C of >6.5 or a patient already being treated for diabetes mellitus. Smoking was defined as the regular tobacco smoking in any form at present or in the last year. A family history of premature CAD was defined as the documented CAD in a first-degree relative (male <55 years, female <65 years). Modified Kuppuswamy’s scale was used for the assessment of socioeconomic status. In-hospital risk assessment was done for ACS groups using thrombolysis in myocardial infarction (TIMI) risk score. Dyslipidemia was defined by the presence of any one of the following: LDL >130 mg/dl, Total cholesterol >200 mg/dl and HDL <40 mg/dl in men and <50 mg/dl in women. Obesity was defined as BMI ≥25 kg/m². Physical inactivity was defined as non-achievement of physical activity guidelines. Alcohol dependence was determined based on ICD–10 diagnostic guidelines for the dependence syndrome. The MINOCA was defined based on the ESC working group position paper on myocardial infarction with nonobstructive coronary arteries.

Two physicians analyzed the angiographic profiles. >70% stenosis of the left anterior descending artery (LAD), right coronary artery (RCA), or left circumflex artery (LCX), and >50% stenosis of the left main coronary artery (LMCA) was considered obstructive. Patients were monitored until discharge from the hospital to assess outcomes.

2.3. Data collection

Data related to demographics, socioeconomic status, rural/urban background, risk factors, and time to first medical contact/appropriate medical treatment, ACS types, and angiographic profiles, hemodynamics including cardiogenic shock, treatments, and in-hospital and 30 day mortality rates were recorded.

2.4. Ethical consideration

Institute’s ethics committee approved our study protocol, and informed consent was obtained from every patient or appropriate legally authorized relative. The study conforms to the ethical guidelines of the Declaration of Helsinki.

3. Statistical analysis

All the study subjects’ data were entered in a Microsoft Excel spreadsheet (Microsoft Excel 2016™, Microsoft Corporation, USA). The data were analyzed using SPSS software (SPSS Inc., version 23.0TM; IBM Corporation, Chicago, USA). Data was collected in a preset proforma. The Kolmogorov–Smirnov test was used to assess continuous variables; the results were median and interquartile range or mean with standard deviations (SD). The significance of differences between the means of normally distributed data was evaluated using the Student’s t-test, and that of non-normally distributed data were assessed using the Mann–Whitney U test. Categorical variables were shown as percentages and numbers. Comparison of categorical variables between the study groups was performed by the chi-square test with the Yates’ correction for continuity, or the Fisher’s exact test if the minimum expected count in the cell was <5. All probability values were calculated using two-sided tests, and a P-value of <0.05 was considered statistically significant.

4. Results

One hundred eighty-two young patients aged <40 years with the ACS were included in our study. Table 1 describes the sociodemographic factors and risk factors among the study population. Most of the study population aged between 30 and 40 years. The

Table 1
Sociodemographic factors and risk factors for CAD in young ACS patients.

| Variables                       | n (%)                          |
|---------------------------------|-------------------------------|
| Mean Age (Years)                | 35.5 ± 4.7                     |
| Total number of patients        | 182                           |
| Sex (%)                         |                               |
| Males                           | 175 (96.2%)                    |
| Females                         | 7 (3.8%)                       |
| Socioeconomic Status*           |                               |
| Upper                           | 97 (53.3%)                     |
| Lower                           | 85 (46.7%)                     |
| Area of residence               |                               |
| Rural                           | 90 (49.5%)                     |
| Urban                           | 92 (50.5%)                     |
| Risk Factors                    |                               |
| Hypertension                    | 54 (29.7%)                     |
| Diabetes Mellitus               | 29 (15.0%)                     |
| Smoking                         | 102 (56%)                      |
| Family history of CAD           | 33 (18.2%)                     |
| Physical inactivity             | 21 (11.5%)                     |
| Alcohol dependence             | 94 (51.8%)                     |

Abbreviations: ACS: Acute coronary syndrome, CAD: Coronary artery disease. * Classification based on modified Kuppuswamy scale.
youngest patient aged 18 years. The most common risk factor was smoking. Diabetes and hypertension were not uncommon among the study population. Lipid profile was available in only 56 patients of the study population, out of which 27.2% had dyslipidemia. Tables 2 and 3 describe the clinical profile and coronary angiographic and revascularization patterns of the study population. The most common presenting symptom was angina. STE-ACS was more common as compared to NSTE-ACS. Few patients had the ischemic shock and left ventricular failure at presentation. Median TIMI Score among the study population was 2(1−6), while those with cardiogenic shock were 8(3−10) (p<0.001). Among STE-ACS, AWMI was the most common type. All ACS patients were managed with dual antiplatelets, statins, heparin (low molecular weight heparin, unfractionated heparin). Roughly 1/4th had non-obstructive CAD, and 3/4th had obstructive CAD among patients who underwent coronary angiography.

SVD was the most common angiographic pattern, and LAD was the most common vessel involved. Of the 149 patients with STE-ACS, 51.7% underwent thrombolysis. More than half underwent revascularization, and PCI was the most common mode of revascularization. Only 3% of the cohort underwent primary PCI. All patients of ACS were discharged successfully from the hospital. There was no in-hospital mortality. Four patients were readmitted over a three-month follow-up with acute decompensated heart failure (ADHF), and all the four patients had severe left ventricular systolic dysfunction. Of the four patients with ADHF, one patient died due to refractory cardiac shock.

Table 4 describes the factors associated with a delayed presentation to the hospital. Of the 182 patients with ACS, only 4.4% presented to the nearest hospital on time (<30 mins). None of the patients presented to PCI capable hospitals within 30 min. Only 6.6% came to PCI capable hospitals within 120 min. Patient attitude and surrounding factors were the main factors that contributed to the delayed presentation to the hospital. The median time to first medical contact among study participants was 300(10−43200) minutes. The median time for transport to PCI capable hospital and the median time to a balloon was 1440(60−86400) and 2880(75−86400) minutes.

The median duration of stay in hospital was significantly higher in patients with a cardiogenic shock when compared to patients without cardiogenic shock [4(1−11) v/s 2(1−25) days, p<0.001]. Patients with cardiogenic shock presented earlier [270(120−7200) v/s 1500(60−86400) minutes, p = 0.009] to PCI capable hospital and underwent revascularization earlier [1440(240−7200) v/s 3420(75−86400) minutes, p<0.001] as compared to those without cardiogenic shock as shown in supplementary table 1. Various characteristics of patients with and without cardiogenic shock, STE-ACS, and NSTE-ACS are provided in supplementary tables 1 and 2.

5. Discussion

Our study included 182 patients ≤40 years of age presenting with ACS. CAD in young patients is relatively uncommon. Young patients usually present with the acute coronary syndrome as a manifestation of CAD. The definitions for young CAD in various studies vary. Compared to other communities, south Asians, particularly Indians, are at higher risk of developing CAD at a young age (5−10% v/s 1−2%). The prevalence of CAD is increasing among the young population. However, the details on risk factors and outcomes among young CAD populations, especially ≤40 years of age, is very much limited. Earlier studies have reported a CAD incidence of 3% in ≤40 years of age. In recent data from the
The most common diagnosis was AWMI (58%) followed by IWMI (23%) and NSTE-ACS (18%), which was similar to prior studies in young ACS patients.28–31

Patients with STE-ACS were younger (p<0.001) and had a higher proportion of severe LV systolic dysfunction (p<0.001) as compared to patients with NSTE-ACS. The history of prior CAD was higher in patients with NSTE-ACS as compared to STE-ACS (P = 0.0012).

Angiographic patterns are different in young MI patients as compared to older MI patients. About 1/4th of the population who underwent coronary angiogram had nonobstructive CAD in our study, which was concordant to prior studies.6,28–31 Seventeen patients (10.2%) were diagnosed as MINOCA, which included seven patients with spontaneous coronary artery dissection, and ten patients with nonobstructive CAD. Twenty-five patients with nonobstructive CAD had STE-ACS and underwent thrombolysis.

Coronary plaque disruption is common among MINOCA patients. The term plaque disruption encompasses plaque rupture and plaque erosion. Plaque disruption can trigger thrombus formation that leads to acute MI via distal embolization, superimposed coronary spasm, and in some cases, complete transient thrombosis with spontaneous thrombolysis.24 Plaque disruption can only be established with intracoronary imaging, preferably with the higher-resolution optical coherence tomography (OCT) imaging or, to a lesser extent, with intravascular ultrasound (IVUS).24 Plaque disruption is located in a vessel segment that appears angiographically normal in nearly half of the cases with rupture or ulceration.24

Most studies in young ACS patients revealed a predominance of SVD, as seen in the present study.2,28–31 DVD (12%), TVD (8%), and LM disease (2.4%) were infrequent in the present study re-emphasizing that extensive CAD is rare in a young population with ACS.

No in-hospital deaths were noted, and all patients were discharged in a hemodynamically stable condition. More than 45% were managed medically. These findings show that young adults with ACS have a good prognosis. A comparison of various ACS registries of young patients with age less than or equal to 40 years, including more than 100 patients, is shown in Table 5.28–31,34,40,41

6. Limitations

The study is a cross-sectional one without a control group; therefore, each factor’s risk and statistical significance could not be analyzed. Risk predictors like lipid profile data were not available in all patients. Intravascular imaging could have accurately demonstrated the underlying cause for CAD (atherosclerotic versus nonatherosclerotic) in these young patients, especially in patients with MINOCA and patients with non-obstructive coronaries.
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7. Conclusion

The conventional risk factors are highly prevalent even among young patients with CAD. Despite all the recent advances, delayed presentation in acute coronary syndrome, especially among young patients, is unfortunately widespread. Anterior wall MI is more common, most of the patients have a single-vessel disease, and in-hospital mortality is low in this young population.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijh.2021.01.015.

Table 5

| Study | Age cut-off (Years) | Male (%) | STE-ACS vs NSTE-ACS (%) | Thrombo–lysis (%) | CAG/PCI (%) | Normal coronaries (%) | Cardiogenic shock (%) | In-hospital mortality (%) |
|-------|---------------------|----------|-------------------------|------------------|-------------|-----------------------|-----------------------|--------------------------|
| Bharradwaj et al.11 (n = 124), 2011 | 40 | 99% | 95% vs 6% | 32% | 100% vs NA | 10.5% | 2.41% | 1.6% |
| Prajapati et al.11 (n = 100), 2015 | 40 | 96% | 85% vs 15% | NA | 100% vs NA | 22% | NA | NA |
| Deora et al.15 (n = 820), 2016 | 30 | 93% | 75% vs 26% | NA | 100% vs NA | 33% | NA | NA |
| AMIYA study14 (n = 1116), 2017 | 30 | 95% | 100% STE-ACS | 61% | 100% vs 56% | 7.3% | – | 2.4% |
| Deshmukh et al.11 (n = 41), 2019 | 30 | 95% | 100% STE-ACS | 61% | 100% vs 56% | 7.3% | – | 2.4% |
| Gupta et al.11 (n = 102), 2020 | 35 | 97% | 91% vs 88% | 32.3% | 95% vs 37% | 3.1% | 1% | 2.9% |
| Present study (n = 182) | 40 | 96% | 82% vs 18% | 42.3% | 92% vs 54% | 6% | 6.6% | – |

Abbreviations: ACS: acute coronary syndrome, CCU: Cardiac critical care unit, PCI: Percutaneous coronary intervention, STE-ACS: ST-elevation ACS, NSTE-ACS: Non-ST elevation ACS, CAG: coronary angiography; NA – Not available.

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