Original Article

Clinical and Angiographic Profile of CAD in Young Smokers

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Abstract

Introduction: The aim was to study the clinical, social, biochemical, and angiographic profile of premature coronary artery disease (PCAD) in young smokers. **Subjects and Methods:** The PCAD registry has 3450 patients till date, of which 1985 (57.53%) patients fulfilled the entry criteria: tobacco smokers. The entire clinical data, biochemical parameters, and angiographic profiles of these patients were documented. The data were analyzed by statistical software R version 3.5.0. **Results:** The study enrolled 1985 patients after satisfying the entry criteria. The mean age of this study group was 33.97 years, with 100% male population. A total of 140 (7.05%) patients had diabetes mellitus, 246 (12.39%) had hypertension, and 269 (13.55%) patients had a strong family history of PCAD. Majority of them (1415 [71.28%]) had abdominal obesity; polycythemia was seen in 738 (37.17%) patients. One thousand three hundred and three (65.06%) patients had low high-density lipoprotein (HDL) cholesterol, 293 (14.76%) patients had elevated low-density lipoprotein (LDL) cholesterol, and 656 patients (33.04%) had elevated triglycerides. The most common index presentation of coronary artery disease (CAD) in these patients was ST elevation myocardial infarction (STEMI) seen in 1583 (79.74%) patients. One thousand six hundred and eighty-nine (85.08%) patients underwent coronary angiography, of which 999 patients (59.16%) had recanalized/normal/nonobstructive coronary arteries. Six hundred and ninety-five patients (41.14%) had significant CAD, of which 77 patients (4.55%) particularly had high thrombus containing lesions. Ultimately, 1441 (71.08%) were treated only with optimal medical therapy. Five hundred and thirty-six patients (27.01%) underwent revascularization in the form of angioplasty (515 patients) and coronary artery bypass surgery (21 patients). **Conclusions:** Common presentation of PCAD in young smokers was acute coronary syndromes predominantly as STEMI. Polycythemia and other conventional risk factors such as low HDL cholesterol levels, elevated LDL cholesterol levels, and abdominal obesity are also seen commonly in this subgroup.

Keywords: Premature coronary artery disease, prospective observational study, smoker

Introduction

Premature coronary artery disease (PCAD) by definition occurs at a younger age (before the age of 55 years in men and 65 years in women).[1] In its severe form, PCAD occurs below the age of 40 years.[2] Cardiovascular disease (CVD) is the leading cause (28%) of death in India.[3] The risk of coronary artery disease (CAD) in Asian Indians is 4 times Caucasians, 6 times Chinese, and 20 times Japanese.[4] Indians are prone to CAD at a much younger age.[5] Approximately 50% of first heart attacks occur before 55 years and 25% occur before 40 years of age.[6]

Smoking is the most important risk factor associated with the severity of CAD and is significantly linked with increased

Received: 01-08-2020 **Revised:** 08-09-2020 **Accepted:** 05-10-2020
Published Online: 27-11-2020

Access this article online

Quick Response Code:

Website: http://www.ijcva.com

DOI: 10.4103/IJCA.IJCA_42_20

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How to cite this article: Shetty LH, Sheetal KC, Chandrashekar VG, Patil RS, Vijaykumar JR, Patil V, *et al*. Clinical and angiographic profile of CAD in young smokers. Int J Cardiovasc Acad 2020;6:164-8.

risk of coronary plaque vulnerability, myocardial infarction, and cardiovascular death.[7,8] In the Framingham Study, the risk of myocardial infarction also increased with the daily number of cigarettes smoked. An increase of 10 cigarettes per day increased the risk of CVD by 18% in men and 31% in women of all ages.[9]

The prevalence of smoking in younger individuals with CAD (<45 years of age) ranged from 60% to 90% as compared to 24% to 56% in subjects aged 45 years and over.[10,11] In addition, smoking served as the most important modifiable risk factor for young adult patients with acute coronary syndrome (ACS).[12]

Smokers tend to present a social and behavioral profile favoring coronary heart disease.[13,14] Smoking is negatively correlated with body weight, physical activity, and high-density lipoprotein (HDL) cholesterol and positively with alcohol abuse, psychological stress, total serum cholesterol, and hematocrit levels.[15,16]

Studies of platelet aggregability, platelet turnover, and platelet activation have in general suggested that smokers compared to nonsmokers tend to have stickier platelets, a shorter platelet life span, and greater urinary excretion of metabolites of prostaglandin produced by platelet suggesting platelet activation.[17,18] There is a paucity of data on PCAD, especially smokers aged <40 years from the Indian population perspective. Thus, we conducted a study to determine clinical, social, biochemical, and angiographic profile of smokers in Indian youth with PCAD.

Subjects and Methods

The PCAD registry is a prospective, multicenter, descriptive, observational study examining a cohort of young Indian adults aged <40 years with CAD. This is registered under the Clinical Trials Registry of India (CTRI/2018/03/012544). The study protocol was approved by the Institutional Ethics Committee and informed consent form was signed by all participating patients (Dated February 23, 2018).

Inclusion criteria

Our study included all patients aged <40 years, with a history of smoking and with index admission for ischemic heart disease, as proven by

1. Documented episode of ACS by a history of typical chest pain, diagnostic electrocardiogram, cardiac biomarkers, and coronary angiogram
2. Chronic stable angina with documented evidence of CAD.

Exclusion criteria

1. Patients with myocarditis, cardiomyopathies, and pulmonary embolism
2. Patients who were previously diagnosed with CAD or on medications such as antiplatelets and statins
3. Patients with chronic kidney disease and liver failure
4. Patients with usage of oral contraceptives and steroids.

Patients who satisfied the entry criteria were enrolled. The demographic details, presence of CAD risk factors like diabetes, hypertension and family history were recorded. Presentation to hospital, window period from onset of symptoms to arrival, primary method of management, course in hospital, and echocardiogram on admission were all documented. Coronary angiographic profile and mode of intervention (if any) were also documented**.** Significant obstructive CAD was defined as ≥50% narrowing of the diameter of the lumen of the left main coronary artery or ≥70% narrowing of the diameter of the lumen of the left anterior descending coronary artery, left circumflex artery, or right coronary artery.

Biochemical and hematological profile was documented. Total cholesterol and triglycerides (TGs) were estimated using commercially available kits (Accurex Biomedical Pvt. Ltd., Mumbai, Maharashtra, India). Measurement of direct low-density lipoprotein cholesterol (LDL-C) was done by enzymatic homogeneous colorimetric assay using Cobas Gen3 C502 analyzer. Adult Treatment Panel III Classification of Lipoproteins was used to classify patients into high and low category. Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m) by the International Diabetes Federation criteria.

Statistical methods

The qualitative data were summarized by counts and percentages, while quantitative data were tabulated by descriptive statistics such as mean, median, and standard deviation. The data were analyzed by R statistical analysis and computing language version 3.5.1 (R core team, 2018).

Results

One thousand nine hundred and eighty-five patients of total of 3450 patients (57.53%) registered under PCAD registry belonged to this particular study group. The mean age of this study group was 33.96 years. Only 7 patients (0.35%) were under 20 years age group. Sixty-nine patients (3.47%) were 21–25 years. Two hundred and ninety-one patients (14.65%) were 26–30 years age. Five hundred and sixty-nine patients (28.66%) were 31–35 years age. One thousand and forty-nine patients (52.84%) were 36–40 years age [Figure 1]. All patients were male. Seven hundred and sixty-seven patients (38.63%) were residing in rural areas. Majority of them (1079, 54.35%) were working in urban areas. One thousand two hundred and nine patients (60.90%) were covered under government schemes for below poverty-line category. Majority of patients (1691, 85.18%) belonged to the Hindu community, only 91 (4.58%) were vegetarians.

One hundred and forty patients (7.05%) had diabetes mellitus and 246 (12.39%) had hypertension. Two hundred and sixty-nine (13.55%) had a strong family history of PCAD Table 1. Physical parameters showed that 796 patients (40.10%) had normal BMI, while 720 patients (36.27%) had high BMI (537 overweight, 183 obese) and 469 patients (23.62%) had BMI according to the revised BMI

classification for South Asian Indians. Going by waist–hip ratio definition, 1415 patients (71.28%) had abdominal obesity. Hemoglobin estimation showed that 37.17% (738 patients) had polycythemia, while 8.16% (162 patients) had anemia and the remaining 54.67% had normal hemoglobin levels.

One hundred and ninety-four patients (9.77%) had total cholesterol in high range (>240 mg/dl), 1303 patients (65.06%) had HDL cholesterol in low range (<40 mg/dl), and 293 patients (14.76%) had LDL-C in high range (>160 mg/dl), while 656 patients (33.04%) had elevated TGs levels. The mean total cholesterol of the entire study population was 189.572 ± 47.11, LDL was 120.264 ± 84.81 mg/dl, HDL was 33.259 ± 9.64, and TG was 209.699 ± 87.11.

The most common index presentation of CAD in young smokers was with ST elevation myocardial infarction (STEMI) (1583 patients – 79.74%), of which 482 patients (24.28%) had delayed presented with evolved myocardial infarction. Unstable angina/non-STEMI presentation was seen in 383 patients (19.28%), of which, 49 patients (2.46%) presented with spontaneous resolution of MI. About 17 patients (0.85%) presented with chronic stable angina.

Left ventricular (LV) ejection fraction recorded for each of patient showed adequate systolic function (>50%) in 852 patients (42.92%), moderate LV systolic dysfunction (40%–50%) in 911 patients (45.89%), while severe LV dysfunction (<40%) in 222 patients (11.18%). One thousand six hundred and eighty-nine of the 1985 (85.08%) patients underwent coronary angiography. About 695 patients (41.14%) had significant obstructive CAD, of which, 77 patients (4.55%) had high thrombus lesions. Seventy-nine patients (4.67%) had normal coronary arteries, 244 (14.46%) had nonobstructive CAD, and 690 patients (40.85%) had recanalized coronaries.

Table 1: Risk factor profile of patients

Risk factor	Patients	Proportion (%)
Diabetes	140	7.05
Hypertension	246	12.39
Family history	269	13.55
Alcohol	941	47.40
Obesity	183	9.22

Table 2: Ultimate outcomes of management of premature coronary artery disease

Management	Patients	Proportion (%)
Medical management (dual antiplatelete)	1334	67.20
Medical management with triple therapy (dual antiplatelete and oral anticoagulation)	77	3.87
Death	34	1.71
PCI	515	25.94
CABG surgery	21	1.06

CABG: Coronary artery bypass grafting, PCI: Percutaneous coronary intervention

Ultimately, 1441 of 1985 patients (71.08%) were discharged after treatment with optimal medical therapy. Five hundred and thirty-six patients (27.01%) underwent revascularization (515 underwent PTCA and 21 underwent coronary artery bypass graft surgery) [Table 2]. Thirty-four patients (1.71%) went into cardiogenic shock due to severe pump failure which ultimately resulted in death.

Discussion

The present study intended to show demographic profile and clinical profile of Indian smoker population with PCAD. Smoking and low physical activity in Indians have found to be prevalent in 20–39-year-old adults.[19] In young patients (<45 years) with CAD, the prevalence of smoking ranges from 60% to 90% as compared to 24% to 56% in subjects aged 45 years and over, according to previous studies.[10,11]

In our study, 57.53% of patients admitted under the PCAD registry were smokers. The average age of this study group was 33.96 years and all patients were male. The INTERHEART study also observed that smoking was a greater risk factor in younger men than in women.[20] Our data are in accordance with previous findings in that the prevalence of smoking was high (70.6%) in young ACS patients and smoking was an independent predictor of ACS in young adults (odds ratio: 2.49 [95% confidence interval: 1.16–5.34]) after adjustment for age, gender, BMI, hyperlipidemia, hypertension, and family history of premature CAD.[21]

Predominant dyslipidemia pattern was (65.06%) low HDL cholesterol with high TGs (33.04%). Conventional lipid

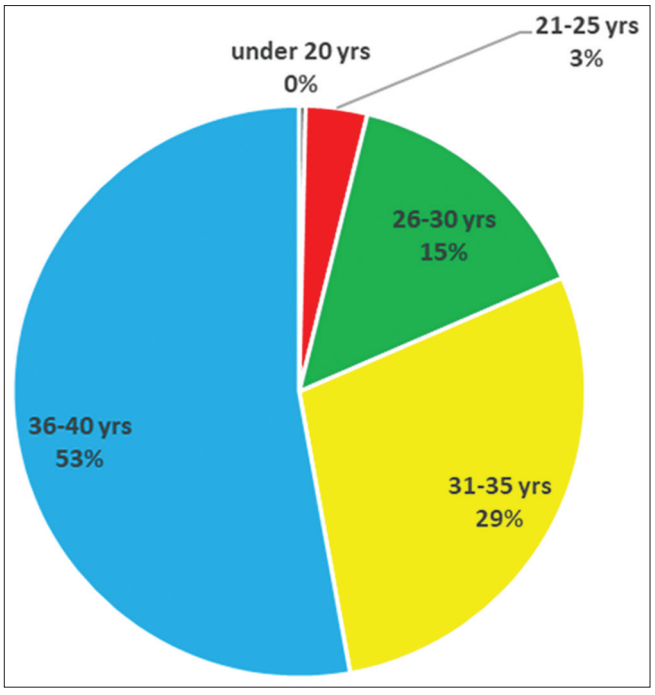

Figure 1: Graph of age distribution of patients

parameters fail to explain the higher occurrence or severity of CAD in the young Indian population. With respect to the entire study population as a whole, LDL as an independent entity did not seem to be a strong risk factor. Hence, among all the conventional lipid parameters, low HDL-C along with high TGs seems to be the main contributing factor for premature coronary artery in Indians. Furthermore, risk assessment that considers the entire lipid profile will identify more high-risk individuals than evaluating LDL-C alone. Some epidemiologic data suggest that instead of measuring the cholesterol in LDL or HDL, measuring their respective apolipoproteins apoB-100, apoA-I and their ratios have been better predictors of CHD risk.[22]

Smoking can trigger myocardial infarction in individuals with minimal atherosclerosis or even with normal coronary arteries, especially among the young,[23,24] promoting temporary coronary vessel occlusion, as a result of thrombus formation, coronary artery spasm, or both.[24] Pathophysiological effect of smoking on increasing hypercoagulability is much more than accelerating atherosclerotic plaque development. It is associated with a procoagulant state with effects on increased platelet activation and aggregation, increased circulating levels of fibrinogen, and increased thrombin generation. This pathophysiology is reflected in the point that 99.15% of patients presented with ACSs and the most common index presentation was with STEMI (79.74%), and very negligible number of patients presented with chronic stable angina (0.8%).

Coronary angiogram was performed in 85.08% of all patients in the group, and it revealed that majority of the patients had insignificant CAD (58.86%) and ultimately, 71.08% of patients were treated and discharged on optimal medical therapy alone. These findings support the hypothesis that the pathogenesis of STEMI in smokers may be predominantly thrombogenic than atherogenic, making it more amenable to medical therapy. This gives rise to an unexpected favorable short-term outcome to such patients which controversially is labeled as the "smoker's paradox."

Another aspect of CAD in smokers, is 'smokers' polycythemia' as a result of decreased plasma volume and secondary polycythemia (high plasma red blood cell concentration), which is due to chronic carbon monoxide (CO) exposure from tobacco smoke.[23,24] CO binds to hemoglobin with an affinity 250 times that of oxygen, thereby interfering with the systemic delivery of oxygen to tissues. In addition, CO binds to cytochrome oxidase and exacerbates cellular hypoxia. Among chronic smokers, this prolonged state of reduced systemic delivery of oxygen to body cells leads to a compensatory phenomenon called erythrocytosis (increased RBC). In this study, it was observed that a significant number of patients (37.17%) had polycythemia.

Conclusions

There is increasing incidence of CAD in the younger population and smoking is one of the greatest risk factors. Since a predominant number of young smokers presenting with CAD had insignificant CAD on coronary angiogram, medical management also plays an important role in these sets of patients. In the era of primary percutaneous coronary intervention being the norm for treating ACSs, future research is needed to develop novel pharmacological strategies to treat these set of patients who respond well to medical therapy.

Limitations of the study

It is purely an observational cross-sectional study which does not give any information regarding long-term clinical outcomes of the disease in these subsets of patients.

Acknowledgment

We would like to thank Research Coordinator, Mrs. Rani B J, and Research Assistant, Mr. Prateesh, for technical help.

Financial support and sponsorship

This study was financially supported by Sri Jayadeva Institute of Cardiovascular Sciences and Research.

Conflicts of interest

There are no conflicts of interest.

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