Novel Atherosclerotic Risk Factors and Angiographic Profile of Young Gujarati Patients with Acute Coronary Syndrome

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Abstract

Objectives: In this study we aimed to analyse the frequency of atherosclerotic risk factors with focus to novel risk factors for coronary artery disease and angiographic profile in young (≤ 40 years) acute coronary syndrome (ACS) patient with healthy controls in Gujarat, India.

Methods: Between January 2008 and December 2012, 109 consecutive young patients aged ≤ 40 years old, diagnosed to have ACS were included in the study. All ACS patients underwent diagnostic coronary angiography. An equivalent age and sex matched population without coronary disease with similar risk factors without tobacco considered a control group. All angiographic patients were evaluated for conventional risk factors for coronary artery disease like diabetes mellitus, hypertension, smoking, obesity as well as novel atherogenic risk factors like high sensitivity C-reactive protein (Hs-CRP), Lipoprotein(a) [LP(a)], homocysteine, apolipoprotein A1 (ApoA1) and B (ApoB).

Result: In a study group, out of 109 young patients, 90 (82.6%) patients were presented to our hospital as ST-segment elevation myocardial infarction (STEMI), 10 (9.2%) presented as known non-ST-elevation myocardial infarction (NSTEMI) and 9 (8.3%) presented as unstable angina (UA). Serum cholesterol, triglycerides, LDL, LP(a) and lipid tetrad index were significantly higher in the study group whereas the HDL levels significantly lower as compared to the control group.

Conclusion: A quite common risk factors of premature CAD are smoking, high Hs-CRP, high LP(a), hyperhomocysteinaemia and positive family history in the young ACS. Most common presentation of ACS in young was STEMI. On angiography, single vessel involvement was the most common finding.

Introduction

Acute coronary syndrome (ACS) is a major cause of morbidity and mortality worldwide.1 Worldwide, about 4% of patients presented with ACS are younger than 40 years of age.2 The burden of ACS can be substantial if the individual is relatively young as they are commonly breadwinners of the family and in the prime of their working life with significant contributions to the society. Premature CAD disease is defined as occurring below the age of 40 years.

Cardiovascular disease (CVD) is posing a major public health hazard and clinical problem in South Asia (India, Pakistan, Bangladesh, and Nepal). Estimates from the Global burden of Disease Study suggest that by the year 2020 this part of world will have more individuals with atherosclerotic CVD than any other region.3 There is documented evidence that South Asian people develop CAD at a higher rate and also at an early age.4

In India, 12%–16% of CAD patients are young. Half of the CVD related deaths (52% of CVDs) in India occur below the age of 50 years, and about 25% of acute myocardial
infarction (AMI) in India occurs under the age of 40 years. Indians have a 3-fold risk of developing AMI before age of 46 compared to Malays (1.25-fold risk) and Chinese (0.7-fold risk) respectively. In general, myocardial infarction (MI) develops 5-10 years earlier in Asian Indians than in other populations, and its occurrence in patients under 40 is 5 to10-fold higher.

Young ACS patients frequently have characteristics that are different from those seen in older patients. While conventional risk factors clearly play a major role in the predisposition to ACS, a significant number of young patients with ACS do not have any of the conventional risk factors.

There are few data available regarding novel atherosclerotic risk factors in patients with premature onset acute coronary syndrome in South Asia. So this study was designed to analyse the frequency of different risk factors for coronary artery disease with focus on novel risk factors in young (≤ 40 years) population presented with ACS in Gujarat, India.

**Material and Methods**

**Study Population**

This study was carried out in the Department of Cardiology, U.N. Mehta Institute of Cardiology and Research, from January 2008 to December 2012. This institute is tertiary care centre situated in Ahmedabad, Gujarat, India. A total number of 109 patients aged up to 40 years with clinical, biochemical and ECG features suggestive of ACS were included. The diagnosis of ACS is defined by at least one of the following: (1) Occurs at rest or minimal exertion and usually lasts > 20 minutes (if nitroglycerin is not administered) (2) Being severe and described as frank pain and of new onset (i.e., within 1 month) (3) Occurs with a crescendo pattern (more severe, prolonged, or increased frequency than previously). An equivalent age and sex matched population without coronary disease with similar risk factors without tobacco considered a control group. The study protocol was approved by the institutional ethics committee and a signed; informed consent was obtained from every enrolled patient.

**Methods**

All patients were investigated for novel atherosclerotic risk markers like Hs-CRP, LP(a), homocysteine, ApoA1 and ApoB. Quantitative estimation of LP(a) was done by turbidimetry. Total cholesterol, triglycerides (TG) and high density lipoproteins (HDL) were estimated by standard procedure; low density lipoproteins (LDL) Cholesterol levels were estimated using the Friedwald Formula. Lipid tetrad index is calculated by the product of cholesterol, triglycerides and LP (a) values divided by the HDL level. [Total cholesterol x triglycerides x LP(a)/HDL]

Patients with valvular heart disease, congenital heart disease, hypertrophic cardiomyopathy and coronary artery anomalies were excluded from the study.

**Statistical Analysis**

The collected data were tabulated and analysed by using the Statistical Package for Social Sciences (SPSS for Windows version 20.0; Chikago, IL, USA). Quantitative data were expressed as mean value ± SD. The independent student’s t-test has been used to carry out significant changes quantitative data. Also, Chi-square and Fisher exact test have been used to carry out significant change in qualitative data. The p value < 0.05 consider as a statistically significant.

**Results**

The baseline characteristics of the study group (n=109) and the control group ( n=109) are shown in Table 1 and Figure 1. The two groups were matched with respect to the age and sex as control without coronary disease but similar risk factors without tobacco. The present study included 109 young patients (≤ 40 years) with ACS with age ranged from 30 to 40 years. Out of 109 young ACS patients 98 (89.9%) were male and 11 (10.1%) were female. As per modified Prasad classification 15 out of 109 patients, 72(66.1%) belonged to lower socioeconomic class, 45(41.3%) belonged to middle class and 5(4.6%) belonged to upper class. Table 2 and Figure 2 showed the clinical presentation and angiographic findings of studied patients.

All patients were evaluated for conventional risk factors as well as novel atherogenic risk factors. The mean value of total cholesterol, LDL levels, HDL levels, TG levels and mean lipid tetrad index were 160.3 ± 44.2 mg/dL, 95.1 ± 45.1 mg/dL, 36.5 ± 11.3
mg/dL, 139.9 ± 75.3 mg/dL and 27809.0 ± 44549.2 respectively, in study group as shown in Table 3. There were 45 (41.3%) patients had lipid tetrad index > 20,000.

There was a significant difference in levels of TG, TC, HDL, LDL, LP(a), Hs-CRP and BMI (p < 0.05), but no remarkable difference in other factors between the CAD group and the control group (p >0.05)

**Discussion**

Tobacco smoking is an established conventional coronary risk factor for CAD. Casual association between tobacco chewing (smokeless tobacco) and CAD is found in some case control studies. Tobacco increases the risk of cardiovascular disease by raising blood pressure, damaging vascular endothelium, increasing LDL-cholesterol oxidation, and lowers the HDL-cholesterol. On an average, 50-150 mcg of nicotine is absorbed through lungs and oral mucosa with each puff of tobacco or about 1 to 2 mg per cigarette. As per National Family Health Survey (NFHS-3) in Gujarat; prevalence of tobacco use by any form is 60.2% in men and 8.4% in women. Tobacco consumption was found to be most common addiction in young ACS patients. It was found in 65.3% which is comparable to study done by Rohit V. Ram and Atul V. Trivedi in Gujarat. In our study majority of patients were tobacco chewer rather than smoker.

The excess burden of CAD among South Asians appears to be primarily due to dyslipidaemia that is characterised by: high levels of ApoB, triglycerides, Lipoprotein(a), Lipid tetrad index, borderline high levels of LDL (low-density lipoprotein) cholesterol, low levels of HDL (high-density lipoprotein) cholesterol and ApoA1. Total cholesterol levels and LDL levels are correlated with extent and severity of CAD in Asian Indians as in whites. But at any given total cholesterol or LDL level, Asian Indians have a greater CAD risk than whites. Therefore; Asian Indians with dyslipidaemia should be treated as aggressively as if they had a CAD risk equivalent—similar to the treatment of patients with diabetes or heart disease. Thus, while a total cholesterol level of < 200 mg/dL is desirable according to the Framingham model for those with 0 to 1 risk factor, the goal for the Asian Indian population should be < 160 mg/dL. An LDL level of <160 mg/dL is appropriate for most Americans with 0 to 1 risk factor, but a level of < 100 mg/dL is optimal for Asian Indians. HDL levels of 60 mg/dL are considered optimal in both whites and Asian Indians. HDL levels are considered low when they drop below 40 mg/dL. However, most experts consider a level < 50 mg/dL to be low in women. The acceptable “normal” level of triglycerides was decreased from < 200 mg/dL to < 150 mg/dL from the Adult Treatment Panel (ATP) II report to the ATP III classification.

Lipoprotein (a) appears to be a major risk factor in Asian Indians as compared to whites. Elevated LP(a) found in 35-40% of all Indians. High LP(a) levels are highly correlated with the severity of ACS, recurrent events, poor prognosis, and increased mortality. A high level of LP(a) is shown to the most prevalent dyslipidaemia in our young patients with premature CAD. LP(a) levels are governed almost exclusively by race, ethnicity, and genetics, unlike other lipids, where the levels are influenced by age, gender, diet, and other environmental factors. The effect of LP(a) on the atherogenicity is not additive but multiplicative.
which is well demonstrated by the lipid tetrad index. A high index (> 20,000) would indicate the presence of a highly atherogenic lipid profile and increase CV risk. Lipid tetrad index may be the best estimate of the total burden of dyslipidaemia as it eliminates the need for various cut-off points and ratios involving the lipid subsets. Although LP(a) levels > 30 mg/dL are generally considered the threshold at which high risk of premature CAD increases rapidly, levels below 20 mg/dL are considered optimum, particularly in Asian Indians. Modestly elevated LP(a) levels of 20 mg/dL to 30 mg/dL are associated with a 2- to 3-fold higher risk of ACS or restenosis following coronary angioplasty and bypass surgery. This risk increases 10-fold when an LP(a) level > 50 mg/dL occurs in persons with high cholesterol levels. In the present study 26 (21.5%) patients had very high level LP(a). In DVD and TVD patients, LP (a) level was significant difference (p < 0.05) compared to low risk SVD patients.

Homocysteine levels are higher among Asian Indians than others. In India, most people adhere to a vegetarian diet and vegetarians have 3.0 times higher risk of hyperhomocysteinaemia compared to those who eat non-vegetarian. Homocysteine levels > 15 μmol/L are found in 75-84% of subjects in India. The prevalence of hyperhomocysteinaemia in our study is comparable to study conducted in younger subject by A.K. Puri et al. in India.19

Strong evidence indicates that Hs-CRP is associated with CAD events. Moderate, consistent evidence suggests that adding Hs-CRP to risk prediction models among initially intermediate-risk persons improves risk stratification. However, sufficient evidence that reducing Hs-CRP levels prevent CAD events is lacking.20 Mean Hs-CRP level in our study were 16.7 ± 22.7 mg/L which correlates with study done by Tenzin Nyandak et al. Delhi, India.21 We have found very high Hs-CRP probably because of we have evaluated in ACS patients which was itself inflammatory condition.

There is now compelling evidence that the ApoB/ApoA1 ratio is a better index of the likelihood of vascular events than any of the corresponding cholesterol indices: the total cholesterol/high-density lipoprotein cholesterol (HDL-C) ratio, non-HDL-C/HDL-C ratio, or low-density lipoprotein cholesterol (LDL-C)/HDL-C ratio. ApoB/A-1 ratio > 1 associated with increased CV risk. Relation between risk and ApoB is continuous, whereas at the extremes of HDL concentration in plasma the relation to risk is not certain. Appreciating these distinctions should allow appropriate use of the ApoB/ApoA1 ratio as a simple, single, summary index of the lipoprotein-related risk of vascular disease.22 In our study mean Apo B/A1 ratio is only 0.76. This could because of most of our patients have very low HDL.

In our study ratio of TC and HDL was 5.1 ± 3.3 in the study group and 3.9 ± 1.4 in the control group. Our study correlates with study done by Daulat Manurung. 23

Conclusions

A quite common risk factors of premature CAD are smoking, high Hs-CRP, high LP(a), hyperhomocysteinaemia and positive family history in the young ACS. Most common presentation of ACS in young was STEMI. On angiography, single vessel involvement was the most common finding.

References

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