



## AN OBSERVATIONAL COMPARATIVE STUDY OF RISK PROFILE AND ANGIOGRAPHIC FINDING AMONG ACUTE CORONARY SYNDROME PATIENTS WITH AGE <40 AND ≥40 YEARS OLD

### Cardiology

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### ABSTRACT

**Objective:** In this study we aimed to compare the risk factors for coronary artery disease as well angiographic profiles in patients with ACS stratified according to age.

**Materials and Methods:** Total 500 patients of ACS undergoing coronary angiography at SMS hospital Jaipur, Rajasthan India between July 2016 to December 2017 were reviewed. The patients <40 years (group 1) and ≥40 years (group 2) were compared. Both groups were compared for angiographic finding and clinical and biochemical risk factors for coronary artery disease.

**Results:** Total 500 patients were involved in this study. Two groups were made and classify study population as group 1 (<40 years) with 250 patients (mean age 33.66±3.45 years) and group 2 (≥40 years) with 250 patients (mean age 56.18±9.06 years). Smoking, Family history, and dyslipidemia were more prevalent in group 1 while diabetes mellitus, hypertension was higher in group 2. Single-vessel disease were predominant angiographic finding in group 1 whereas patients of group 2 showed involvement of multivessel disease.

**Conclusion:** Our study shows a significantly difference in risk factor profile (clinical and biochemical) as well as angiographic finding among both group. Among younger population, smoking and dyslipidemia were predominantly present as preventable risk factors for CAD. These two preventable risk factors are an important threat for our community health. So encouragement for smoking cessation, promotion of healthy life styles should be encouraged beginning from young ages.

### KEYWORDS

### INTRODUCTION

Coronary artery disease (CAD) is an extremely upsetting disease precisely because it affects an otherwise healthy person in the productive age of life that may lead to mortality or disability without warning. Particularly if the afflicted person is young adult (below 40 year of age), this create a big burden for family, friends, and occupation to cope with such unfavourable circumstances. Providentially, according to most studies only 3% of all CAD cases occurs in this particular age group and myocardial infarction (MI) and symptomatic CAD have less incidence in person age <40 year.

Here It must be pointed out that, young adults with symptomatic disease who come to medical attention may only represent few people than actual figure. when considering manifest and subclinical disease together. Because this age group (age < 40 year), asymptomatic patients typically do not undergo medical investigations so diagnosis of CAD happens only by chance on many times and the exact prevalence of the disease has been grossly underestimated.

Indeed, once rigorous intravascular ultrasound-based investigation was done in a cohort of recently transplanted hearts (mean donor age 33.4 ± 13.2 years) by Tuzcu et al. (2), the prevalence of disease was 50%, with one in six teenagers manifesting coronary lesions.

It is estimated that by 2020 more than 50% of world total patients of CAD will be present in our country. So coronary artery disease (CAD) is giving rise to a big public health problem and clinical issue particularly in Indian subcontinent (3).

It is also reported in some studies that Person living in Indian land mass may develop coronary artery disease (CAD) at an exorbitant rate and also at a younger age compare to western world (4).

Occurrence of CAD in young adults, particularly before forty year of age is contemplated as premature CAD. (5,6) The occurrence of coronary artery disease 12–16% among Indian young adult patients. It is also reported in studies that cardiovascular diseases are contributing as a leading cause for mortality in patients below the age of fifty year and about 25% of acute MI cases being reported in patients under the age of 40 yrs. (7)

Apart from severity of disease and prognosis, which were found different among young adults and older population there was also difference in clinical risk factors and biochemical risk profile among both population group (8). In many clinical studies it have been clearly

stated that compared with older patients, patients with premature CAD show predominantly involvement of one coronary vessel (9).

Patients with early CAD have as hypercholesterolemia risk factor 9–10, as well as positive family history (9–10) and cigarette smoking (11) found to be strongly associated with coronary artery disease. Same also supported by epidemiological studies that both group have different set of risk factors and clinical presentation (12–13).

While Indian subcontinent is a large geographical area, different area have some difference in risk profile, eating and smoking habits so we conducted this study particularly in patients coming from rural Rajasthan to study coronary angiographic (CAG) profile and risk factor analysis of CAD patients at all ages because there are not enough published data from our geographic area. The present study examined the angiographic findings, conventional coronary risk factors of patients <40 and ≥40 years old with CAD

### METHODS

**AIM:** To determine the difference in angiographic and clinical profile of ACS cases below 40 yr and above 40 yr of age.

**Primary objective:** To determine the difference in proportion of cases with positive family history, dyslipidemia and pattern and number of vessels involved in ACS cases among >40yr and <40 yr of age.

**Secondary objective:** To determine other clinical parameters as sex ratio, DM, HTN, smoking, BMI, Tobacco chewing, and others among patient of ACS >40Yr and <40 Yr of age.

**Sample size:** sample size is required is 250 cases in each group at 95% confidence and 80 % power to verify the expected difference of 10% in the proportion of cases with TVD among <40yr (8%) and >40 yr (18%) of age group of ACS cases, the sample size is adequate to cover other primary variables of study.

**Study population:** Patient hospitalized with the final diagnosis of ACS (unstable angina, ST-elevation myocardial infarction, and non-STEMI) and who underwent coronary angiography in our department.

**Exclusion:** Patients with cardiac valve disease, acute or chronic liver disease, and infectious diseases. Patients with previous LBBB, on PPI, recent inflammatory illness (within the last month), history of carcinoma or secondary conditions that could precipitate angina (anaemia, arrhythmias, fever) Patients with ongoing systemic or

cardiac inflammatory processes.

Total 500 patients admitted at cardiac intensive care unit at Sawai Mansingh Hospital Jaipur rajasthan between July 2016 and December 2017 were included in study. Meticulous history was taken regarding symptoms ,their duration of onset, time to reach hospital ,prehospital treatment Information, any previous history of associated co morbid conditions like hypertension, diabetes, coronary artery disease, history of premature CAD in first degree relatives, complete clinical examination and treatment details were collected. Investigations like ECG, 2D ECHO, RFT, lipid profile were also done.

Acute coronary syndrome was defined as Acute MI (STEMI and Non-STEMI) or unstable angina. Patients divided in two group <40 year and >40 year of age.

in this study. Consecutive 500 patients including both male and female admitted into this hospital were the study subjects. Out of them 250 were <40 year age and 250 were >40 year of age. Among these patients atherogenic risk factors like smoking, Diabetes, HTN, dyslipidaemia, gender, family history of CAD and also prior history of myocardial infarction, heart failure, angina class, NYHA class, EF and angiographic pattern were studied. Patients who did not undergo CAG and patients without objective evidence of ACS were excluded from the study.

CAG were performed in all of the patients in the study group. The reasons for CAG were inadequate control of symptoms with optimal medical therapy, high risk determined with exercise or pharmacologic stress testing, prior myocardial infarction, admission with an ACS, ejection fraction<40% on echocardiogram and history of coronary artery bypass grafting surgery (CABG) or percutaneous intervention (PCI) in the past. A 70% or greater decrease in diameter of a major epicardial coronary vessel or greater than 50% decrease in diameter of the left main coronary artery was defined as significant coronary obstructive disease. Acute coronary syndrome was diagnosed on the basis of typical chest pain, diagnostic electrocardiographic findings and cardiac enzyme evolutionary patterns.

### Statistical analysis

The collected data were analysed using spss software. Categorical variables were presented as frequency and percentage and the groups were compared by using the Chi-square test . Continuous variables were described as mean value  $\pm$  standard deviation (SD) and were compared by using the Student's t-test to identify statistical differences between the groups. The p-value <0.05 was considered to indicate statistically significant difference between the groups.

### Result

The baseline demographic characteristics of patients with ACS enrolled in our study are presented by age category in Table 1.

The study population was consisted of 500 patients. Two hundred and fifty patients (229 male) with mean age  $33.66 \pm 3.45$  years were in group 1 (< 40 year age) and 250 patients (190 male) with mean age  $56.18 \pm 9.06$  years were in group 2 (> 40 year age).

**Table 1: Characteristic of two study group.**

| Variables              | Younger group(Group 1) <40 year N=250 | Older group (group 2) >40 year N=250 | P value |
|------------------------|---------------------------------------|--------------------------------------|---------|
| Age (mean $\pm$ SD)yrs | 33.66 $\pm$ 3.45                      | 56.18 $\pm$ 9.06                     | <0.001  |
| Age range              | 26 to 39                              | 41 to 75                             |         |
| Male ,n (%)            | 229(91%)                              | 190(76%)                             | 0.07    |
| Female n(%)            | 21(9.0)                               | 60(24%)                              | <0.01   |
| Male/female ratio      | 10.9                                  | 3.1                                  | <0.001  |

There were no significant differences between the group 1 and the group 2 in terms of frequency of anterior-wall STEMI, inferior-wall STEMI, NSTEMI, or unstable angina presentation [Table-2]. The mean ejection fraction was  $43.48 \pm 8.92$  in the younger group and  $42.99 \pm 11.63$  in the older group.

**Table 2 Comparison of clinical diagnosis between younger and older patients with acute coronary syndromes .**

| Clinical diagnosis | Group1 (n=250)   | Group2 (n=250)    | P value |
|--------------------|------------------|-------------------|---------|
| STEMI              | 210(84%)         | 170(68%)          | 0.09    |
| NSTEMI             | 25(10%)          | 52(20.8%)         | 0.12    |
| USAP               | 15(6%)           | 28(11.2%)         | 0.34    |
| EF                 | 43.48 $\pm$ 8.92 | 42.99 $\pm$ 11.62 | 0.14    |

Results in Table 3 showing that smoking, obesity, dyslipidemia and h/o premature CAD in first degree relatives were the predominant risk factor among younger group while DM, HT and female gender were more common in group 2. There was no statistical difference in overweight and obesity prevalence between the groups. Type 1 DM (insulin-dependent DM) was more common in group 1 (64.7%) while most of the patients in group 2 had type 2 DM (non insulin dependent DM) (81.3%) who frequently used oral antidiabetics compared to insulin therapy or diet alone. Besides, plasma glucose levels of diabetic patients in our study population were commonly not under control.

**Table 3. Clinical characteristics of study patients with premature coronary heart disease (Group 1) and late onset of coronary heart disease (Group 2)**

| Variables            | Group 1 (n=250) | Group 2 (n=250) | P value |
|----------------------|-----------------|-----------------|---------|
| HTN,n(%)             | 56(22.4)        | 115(46)         | <0.005  |
| DM,n(%)              | 22(8.8)         | 90(36)          | <0.005  |
| Family history, n(%) | 108(43)         | 41(16)          | <0.05   |
| Dyslipidemia , n(%)  | 128(51)         | 104(41)         | <0.012  |
| BMI>25,n(%)          | 140(56)         | 144(57)         | 0.13    |
| Smoking,n(%)         | 114(45)         | 104(41)         | 0.09    |
| Tobacco chewer, n(%) | 56(22.4)        | 68(27)          | 0.11    |

A detailed analysis of lipid profile [Table 4] revealed that the mean total cholesterol, LDL cholesterol, and triglyceride levels were significantly higher in the younger group(group 1) as compared to the older group(group 2). Further, the HDL cholesterol levels, VLDL cholesterol levels, and lipid ratios of total cholesterol to HDL cholesterol and LDL cholesterol to HDL cholesterol were non-significantly higher in the younger group(group1) .

**Table 4. Comparison of fasting glucose and lipid levels of the groups**

| Variables                         | Group 1 (n=250)   | Group2 (n=250)    | P value |
|-----------------------------------|-------------------|-------------------|---------|
| Total cholesterol, mg/dl          | 244 $\pm$ 24.8    | 181 $\pm$ 23.35   | <0.05   |
| LDL-cholesterol ,mg/dl            | 142 $\pm$ 28.12   | 119 $\pm$ 13.8    | <0.05   |
| HDL-cholesterol, mg/dl            | 40 $\pm$ 10.20    | 42 $\pm$ 16.35    | 0.12    |
| Triglyceride, mg/dl               | 162 $\pm$ 16.5    | 119 $\pm$ 14.15   | <0.05   |
| Ratio of total cholesterol to HDL | 4.95 $\pm$ 1.57   | 4.65 $\pm$ 1.51   | 0.170   |
| Ratio of LDL to HDL cholesterol   | 3.11 $\pm$ 1.37   | 2.82 $\pm$ 1.15   | 0.106   |
| VLDL cholesterol (mg/dl)          | 25.45 $\pm$ 14.07 | 24.31 $\pm$ 10.47 | 0.21    |

The coronary angiographic profile [Table 5] revealed that younger patients with ACS were significantly more likely to have normal vessels than that in the older patients. Eleven patients (4.4%) of group 1 had normal coronary arteries and 29 patients (11.6%) had noncritical coronary lesions in case of ACS while two patient(0.8%) had normal coronary arteries and eight patient (3.2%) had noncritical lesion in group 2 Single-vessel disease was the most common phenomenon in younger patients, while multi-vessel disease was more common in older patients. Distribution of the subjects by the number of coronary artery involvement is depicted in [Table 5]] for in both the groups. LAD was the most common coronary artery involved with angiographic stenosis or occlusion among younger patients(group 1), while LCx ,LAD and RCA were equally involved among older patients (group 2). There was no statistically significant difference between the two groups in the frequency of left main coronary artery stenosis. Coronary angiographic findings between the two groups are shown in Table 5.

**Table 5. Coronary angiography findings of the study patients with premature coronary artery disease (Group 1) and late onset of coronary artery disease (Group 2)**

| Variables                                        | Group 1<br>(n=250) | Group 2<br>(n=250) | P value |
|--------------------------------------------------|--------------------|--------------------|---------|
| <b>Extent of luminal narrowing</b>               |                    |                    |         |
| Significant, n                                   | 210                | 240                | 0.08    |
| Noncritic, n                                     | 29                 | 8                  | <0.05   |
| Normal, n                                        | 11                 | 2                  | <0.05   |
| <b>Number of arteries significantly involved</b> |                    |                    |         |
| Single vessel, n                                 | 142                | 104                | <0.05   |
| Multivessel, n                                   | 68                 | 162                | <0.05   |
| <b>Involvement of coronary arteries</b>          |                    |                    |         |
| Left anterior descending artery, n               | 172                | 179                | 0.10    |
| Right coronary artery, n                         | 81                 | 145                | <0.05   |
| Circumflex artery, n                             | 87                 | 151                | <0.05   |
| Left main coronary artery, n                     | 5                  | 15                 | <0.05   |

## DISCUSSION

Premature CAD has been defined as having an age of onset ranging from 30 to 56 years in various studies. We selected an age cut-off of 40 years to define a premature CAD based on previous epidemiologic studies (14).

In literature, about 200 risk factors for coronary artery disease have been recognized or hypothesized. Majority of these risk factors are treatable or preventable (15). Accordingly, these risk factors can be classified into class I (preventable risk factors), class II (requires intervention to lower cardiovascular risk), class III (factors if modified might lower cardiovascular risk) and class IV (unmodifiable risk factors) (15). In this study, we determined the differences in the characteristics of class I-IV risk factors and angiographic profile between younger and older patients with ACS. We selected an age cut-off of 40 y to define a premature CAD, based on previous Indian (8,17) and Indian subcontinent studies (7,8,16).

In our study, the youngest patient presented with coronary heart disease was 26 years old, suggesting an early onset of disease and requiring an alarming attention. Further, the most obvious finding in our study was a very high prevalence of ACS among men as compared to women. The proportion of males among ACS patients who underwent coronary angiography was ten times than that of females in the younger group and three times than that of females in the older group. Although the significant male predominance observed in the present study is in line with other studies (18,19), this should be considered as an indication of the skew in exposure to cardiovascular risk factors that males have been subjected to.

STEMI was the most frequent presentation in young (84%) and older (64%) patients with ACS. The most common anatomical location of the myocardial infarction was anterior wall (40.6% and 33.8% in younger and older groups respectively) trend in types of coronary heart disease reported in the present study is similar to previously published articles.(5,18,19,21)

Obesity is an alarming concern among young adults (7). The present study also showed that the mean BMI in younger patients with ACS was comparable to that in older patients with ACS. Further, the proportion of overweight and obese patients was nearly similar between two age groups, suggesting high incidence of obesity at young age. Analysis of other conventional risk factor revealed that dyslipidaemia alone was a significant risk factor in 51% of individuals in younger group and 41% in older each age groups of patients. Hypertension was two-times more common in older patients than in younger patients with ACS. While diabetes mellitus is a well-known risk factor of ACS, we found that prevalence of diabetes was three time more common in older group . On the contrary, family history of premature CAD was more common among young patients.

In our study, nearly half of the patients in both the age groups were either tobacco chewer or cigarette smoker. Although our study demonstrated a stronger association between smoking, hyperlipidaemia, obesity and ACS in younger patients, DM, hypertension, dyslipidemia and positive family history of premature

CAD were the only discriminatory risk factors between the two age groups. This is in agreement with other studies of similar nature (7,19,20).

It is widely established that lipid levels are correlated with the extent and the severity of ACS in Asian Indians as in whites, irrespective of age (5). We found that lipid levels, particularly total cholesterol, LDL cholesterol, and non-HDL cholesterol, were significantly higher among young patients than in their older counterparts. Other lipid parameters were also non-significantly higher among young patients with ACS, suggesting a significant concern about abnormal lipid levels at younger age. We emphasize that such individuals should be treated aggressively.

The present study indicates that <40 years patients have unheralded acute onset of symptoms, a higher frequency of angiographically less extensive disease and single vessel disease compared with their counterparts. Similar results have been reported by other authors (21). Histopathologic studies have demonstrated that atherosclerotic plaques in young patients with CHD are characterized by a large amount of lipid-containing foam cells and relative lack of a cellular scar tissue. This data suggest that soft plaques seen in young patients may have been present for a shorter time of period than plaques in older patients, which have a large content of fibrous tissue and are responsible for most episodes of major coronary thrombosis (22). The less extensive CHD observed in younger patients in our study might suggest that premature CHD is associated with rapid disease progression rather than with a gradually evolving process. This is in agreement with the finding that ACS is the common first presentation in younger patients (21-22)

Most of our patients with premature CAD were free of any complications during hospitalization period. Early death with the time of ACS was observed in four patients. Most series have shown a favorable short-term prognosis for young patients with an ACS (23-24). Furthermore, prognosis was found to be inversely related to age (23).

ACS, being an uncommon entity in individuals aged <40 years, constitutes an important challenge for both the patient and the treating physician (7). Lynch et al., have recently reported that the knowledge of CVD risk factors is extremely low among young adults (25). Hence, we highlight that identification and control of potential risk factors is very crucial in the primary and secondary prevention of cardiovascular disease in young individuals. Emphasis should be given on diagnosis and management of dyslipidaemia, diabetes mellitus, hypertension and cessation of smoking, which have been identified as the major modifiable risk factors in our study. Although the benefit of risk factor reduction is widely reported in older patients, such evidence in younger age group is a significant concern and warrants attention (16).

## CONCLUSION

Our study shows a significantly different clinical, angiographic and biochemical profile in <40 years patients with CAD compared with ≥40 years ones. Patients with premature CAD commonly have unheralded acute onset of symptoms, less extensive CAD and better short term prognosis than the older ones. Consistent with epidemiologic studies; positive family history, smoking, elevated total cholesterol, LDL-cholesterol and triglyceride levels and low HDL-cholesterol level were also associated with premature CAD.

Dominance of smoking and dyslipidemias that are the preventable risk factors in premature CAD patients is an important threat for our community health. Healthy life styles should be encouraged beginning from young ages and new precautions about smoking must be taken.

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