

Factors Predisposing to Recurrence of Early Onset Coronary Artery Disease (CAD) in Adults Below 45 years of Age.

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ABSTRACT

Background: As we transition into an era with increased burden of non - communicable disease the evolution of risk factors predisposing to atherosclerotic cardiovascular disease (ASCVD) and its recurrence have gained significance. As a diagnostic category ASCVD includes coronary artery disease (CAD) which afflicts majority of our population above the age of 60 years. However, with increase in burden of both index and recurrent CAD events, assessment for CAD risk factors is now recommended as early as 20 years of age. Therefore, periodic assessment of traditional CAD risk factors like age, gender, addiction, comorbidities are now being offered to both young and old individuals. **Methods:** The current study was undertaken to assess the risk factors associated with recurrent CAD in patients below the age of 45 years. 449 patients (376 male and 73 female) were included in our study and 64 had recurrent CAD event. **Results:** We reported statistically significant correlation of diabetes mellitus and hypertension with recurrent CAD events ($p < 0.05$). We also observed association of recurrent CAD events with various parameters viz, smoking, alcohol intake, low HDL level, high triglyceride level, waist circumference and waist hip ratio, but not significant correlation. **Conclusion:** Female gender, hypertension, diabetes mellitus and low HDL cholesterol levels were predominant risk factors behind recurrent CAD event.

Keywords: Atherosclerotic cardiovascular disease, recurrent CAD, Female gender, hypertension, diabetes mellitus, low HDL cholesterol

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Introduction

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide contributing to more than 17 million deaths globally in the years 2012-2013 [1]. Although it's a disease afflicting majority of adults above the age of 60 years, studies such as

Framingham have illustrated substantial risk of CAD in young adults below the age of 45 years [2]. This epidemiological transition towards preponderance of non-communicable disease including CAD has occurred at an accelerated pace in countries such as India. Evidence suggests that CAD occurs at a younger age in Indian population leading to mortality rate attributable to CAD up to 50% [3]. India's age standardized death rate due to cardiovascular disease stands at 272 per 100,000 while the global average is much less at 235 per 100,000. According to Global Burden of Disease severity Premature mortality in India has increased by 59% in a span of 20 years from 1990 to 2010. In 2010 the premature mortality in terms of life lost stood at 37 million. [4]

Strategies' focusing on primary and secondary prevention along with advancement in treatment modalities have led to increased

survival rates after an index event. However, the incidence of recurrent CAD event has emerged as a significant obstacle in management of CVD. The incidence of recurrent events ranges from 5.7% at the end of 6 months to 14.3% at the end of six years [5]. Recent systematic review analyzing mortality and morbidity at the end of one year following index cardiovascular event found that age, gender, comorbidities including hypertension, diabetes, chronic kidney disease, peripheral arterial disease and past cerebrovascular events increased the risk of recurrent CAD [2, 6].

Although it is important to study the burden of CAD associated with these risk factors, studies in age specific cohorts are few and far between. Newer data suggests that up to one third adults with premature coronary artery disease will experience recurrent major cardiovascular event. The possibility is particularly pronounced in those with diabetes, inflammatory diseases and those of Asian and sub-Saharan ethnicity, according to a new analysis [7]. Data on prevalence and risk factor profile of young CAD demographic is difficult to obtain given their varying and migratory life style as well as ignorance regarding primary prevention. Therefore, the current study was carried out to find out the correlation between risk factors and recurrent cardiovascular events in age specific

cohorts in young atherosclerotic cardiovascular disease (ASCVD) patients below the age of 45 years. Given our resource limited setting studies like ours will help clinician in aggressively treating the underlying risk factor and curtailing the incidence of recurrent CAD in young individuals.

Material and Methods

This is a single center retrospective study, conducted in a tertiary care hospital over a period of three years. The study included record and data from adults admitted with acute coronary syndrome. The data was collected by accessing health record of patients admitted with acute coronary syndrome in Coronary care unit of GTB hospital. The diagnosis of acute myocardial infarction (AMI) was based on criteria for acute, evolving and recent AMI laid down by universal definition of myocardial infarction [8]. Early onset CAD was defined as the occurrence of an AMI or symptomatic myocardial ischemia with obstructive CAD ($\geq 70\%$ stenosis) in men and women 45 years and younger [9].

The data included patient history and laboratory parameters along with anthropometric measurements like waist and hip circumference along with waist hip ratio. The Waist circumference, hip circumference and waist hip ration were defined according to criteria given by NCEP- ATP III 2001 and IDF criteria for metabolic syndrome. Waist hip ration of more than 0.9 in females and more than 1.0 in males was considered abnormal. Waist circumference of more than 102 cm in males and 88 cm in females was considered significant [10]. Hypertension was defined as systolic BP >130 mm Hg and Diastolic BP of more than 85 mm Hg or use of specific medication. Similarly, Diabetes mellitus was defined by criteria given by American diabetes association. Dyslipidaemia was defined as triglyceride level of more than 150 mg/dl or use of specific medication. HDL cholesterol < 40 mg/dl and <50 mg/dl in men and women respectively was considered low [10]. No sample size calculation was offered because the study used service data collected during provision of health care retrospectively. Incomplete records were excluded from the study.

Statistical Analysis

Statistical analysis was performed by using Microsoft SPSS 21 software. Data was presented as mean and standard deviation or number and percentage for continuous and categorical variables as applicable. Differences between groups were analysed using Chi-square test or t-test as applicable. For all statistical tests, $p < 0.05$ was considered as the level of significance.

Result

The base line characteristics of the study population are summarized in Table 1. In the present study, we were recruited 449 patients below the age of 45 years. There were 376 male and 73 female study participants. 64 (14.3%) patients had recurrent CAD out of which 52 (13.8%) recurrent events occurred in male patients and 12(16.4%) recurrent events were reported in female patients. A total of 96 patients gave history of diabetes mellitus and recurrent CAD was reported in 23 patients, of these diabetic patients making the correlation of diabetes mellitus with recurrent CAD statistically significant ($\chi^2 = 9.409$, $p < 0.05$). 176 patients gave history of hypertension and 35 hypertensive participants had recurrent CAD making association of hypertension with recurrent CAD, which was significant statistically ($\chi^2 = 7.514$, $p < 0.05$). We observed 5 patients had antecedent history of Cerebrovascular accident, out of which 2 had a recurrent CAD event. Smoking was the most common form of addiction among the study participants ($n = 272$), of which 45 had recurrent CAD; however we did not find statistically significant correlation between smoking and recurrent CAD. History of alcohol intake was present in 134 and 22 participants in this group had recurrent CAD, but the correlation was not statistically significant. Low HDL levels were reported by 303 patients. 51 patients with low HDL had recurrent CAD making the association with recurrent event statistically significant. Out of 182 patients with high triglyceride levels 32 had recurrent CAD but the association was not significant statistically. The mean triglyceride levels were 138.9082 ± 75.80944 mg/dl. The mean HDL level of study population was 36.93272 ± 9.902534 mg/dl. Waist circumference of more than 102 cm in males and 88 cm in females was found in 216 patients out of whom 31 patients had recurrent CAD. High waist hip ratio was found in 188 patients and 23 patients in this group reported recurrent CAD. However the correlation between these anthropometric measurements and recurrent CAD was not statistically significant.

Discussion

CAD is the most common manifestation of ASCVD constituting approximately 50% of new ASCVD events [1] Framingham study was one of the pioneering studies shedding light on the life time risk of CAD event. The study demonstrated the life time risk of CAD by following 7733 participants between the ages of 40 and 94. For individuals aged 40 years, this life time risk was 49% in males and 32% in females [2]. The INTERHEART study which was carried out in 17 countries including 4 low income countries

Table 1: Predisposing Factors in Patients with Recurrent CAD

	Recurrent CAD - Present	Recurrent CAD - Absent	Total	P value
Male	52(13.8%)	324 (86.2%)	376	0.560
Female	12(16.4%)	61(83.6%)	73	
Diabetes mellitus	23 (24%)	73(76%)	96	0.002
Hypertension	35(19.9%)	141(80.1%)	176	0.006
Past CVA	02(40%)	03(60%)	5	0.098
Smoking	45(16.5%)	227(83.5%)	272	0.085
Alcohol	22(16.4%)	112(83.6%)	134	0.392
Waist circumference	31(14.4%)	185(85.6%)	216	0.954
Waist/ Hip Ratio	23(12.2%)	165(87.8%)	188	0.299
High Triglyceride level	32(17.6%)	150(82.4%)	182	0.096
Low HDL	51(16.8%)	252(83.2%)	303	0.024

which includes 1,56,424 participants revealed that CAD related mortality in low income countries was relatively higher even though the overall prevalence was lower in comparison to high income countries [11]. Most researchers use variables of age, gender, current smoking habits, diabetes mellitus, dyslipidaemia and systolic blood pressure for assessment. A multitude of risk factor models developed over the years have used CHD (coronary heart disease) death, non-fatal myocardial infarction as endpoints for CHD risk scores [12,13]. These important risk factors also make patients susceptible to recurrent CHD events. This was corroborated by AFIJI study (Appraisal of risk factors in young ischemic patients justifying aggressive intervention), in which out of 880 people who were followed up 264 developed recurrent CAD event. Many of the patients who developed recurrence had a family history of premature CAD (40.8%), around 77.6% were active smokers and also had dyslipidemia. It also showed that smoking was associated with two fold increased risk of myocardial infarction after 1st episode [7].

In UAE, another study was conducted over 8 years showed the incidence of recurrent cardiovascular disease in male to be 84.6/1000 and female to be 119.8/1000. 27% of the patients were actively smoking despite the first event, 43% of the patients had uncontrolled hypertension, 62.5% patients had diabetes, 38.4% were overweight and 27.3% were obese of which predominantly females [13].

As disproportionately scarce data is available regarding recurrence in young CAD patients from Indian sub-continent, our study endeavours to bridge this gap. 449 patients were part of our study including 376 males and 73 females. 64 (14.3%) recurrent CAD events were reported in our study out of which 52 (13.8%) occurred in male patients (n=376). Recurrent MI rates of up to 6.3% have been reported in studies. Our study found a slightly higher prevalence which may be attributed to novel risk profile of south East Asian population [11, 6]. We found that females had relatively higher risk of recurrent CAD at 16.4%. The finding was corroborated by similar studies and it has been postulated that a combination of factors such as Diabetes, hypertension, and obesity may fuel the adverse risk factor profile for women [14-16]. Sociocultural barriers also prevent females from seeking preventive health care making them vulnerable to recurrent CAD at young age [8,13,14].

Diabetes mellitus (24%) was the most common comorbidity associated with recurrent CAD followed by hypertension (19.9%). Both diabetes and hypertension have been implicated as significant risk factors for both index and recurrent CAD events [17, 18]. 5 patients have history of cerebrovascular accident out of which 2 had a recurrent CAD episode. Literature suggests the overwhelming association between ASCVD disease and smoking [13]. Therefore we expected statistically significant correlation between smoking and recurrent CAD. In our study 16.4% smoker suffered from recurrent CAD but the association was close to statistically significant (P=0.085). Long term randomized control trials emphasizing the role of alcohol consumption in CAD are not available. As such the effect of alcohol consumption seems to be confounding as the available observational studies have only compared characteristics of alcohol users with those of non - users. In our study history of alcohol consumption was present in 16.4% participants however its association with recurrent CAD events was not statistically significant.

Waist circumference is an indicator of central obesity and thus can be used to ascertain CAD risk. Its importance is underlined by the fact that studies have shown that central obesity has a direct bearing on mortality in CAD [20,21]. In our study 14.4% patients with

increase waist circumference had a recurrent CAD event but the association was not statistically significant. The population of Indian Subcontinent defers from Caucasians and African Americans in terms of higher intra-abdominal fat mass and excess subcutaneous truncal fat thus making truncal obesity an important but modifiable risk factor [1,22].

Dyslipidemia is well researched culprit behind young and premature CAD and its prevalence being as high as 75-80% when compared against age and sex matched control group where the prevalence is 40-48% [23]. In our study low HDL levels were a significant marker of recurrent CAD as suggested by previous studies [24]. However increased triglyceride levels did not show significant impact on the recurrent event even though hypertriglyceridemia is a major risk factor for premature CAD.

In conjunction with existing research we had expected a positive correlation between recurrent events in young CAD with Diabetes mellitus, Hypertension and low HDL level. We had postulated a similar association with smoking, hypertriglyceridemia and central obesity. However the study results don't show significant correlation with these modifiable risk factors.

The clustering of different demographic and clinical factors are responsible for recurrence of CAD in young patients. Literature suggest that aggressive intervention aimed at these risk factors will go a long way in preventing recurrence especially in resource limited setting where access to health care is major concern [25]. Application of preventive measures in this demographic is of utmost importance as they constitute the major workforce in the society and disease affliction this demographic has long term socioeconomic implication on family and society as a whole.

Conclusion

Our study concluded that significant predictors of recurrent CAD in young are female sex, Diabetes Mellitus, Hypertension and low HDL cholesterol levels. Secondary preventive measure in this cohort will go a long way in keeping our population safe.

Our study came across few limitations; the patients were recruited from a limited geographic and sociocultural profile thus making generalizability of results a bit difficult. We did not consider sociodemographic parameters such as education, family income and family history of CAD. We hope to include these parameters in future studies.

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