

## Original Research Article

# Study of risk factors and its correlation with carotid intima media thickness for atherosclerosis in patients of coronary artery disease and their offspring

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### ABSTRACT

**Background:** A significant percent of cardiovascular event occurs without well-known modifiable risk. A new tool for early identification for atherosclerosis is required for early intervention. Aims and objectives of the study was to study the risk factors for CAD and its correlation with CIMT.

**Methods:** One hundred and forty subjects were studied for the risk factors of CAD in Department of Medicine of G.R. Medical College, Gwalior from 2012 to 2013. Out of 140 subjects, 100 were patients having CAD and 40 age matched subjects were included as control group. Data was also recorded from their offspring. High resolution B mode ultrasonography was performed to assess CIMT of carotid arteries. The maximum CIMT of any one side of carotid artery was taken for study.

**Results:** CAD was more prevalent among males (78%). Majority of the offspring of cases had age between 28-42 years and majority were male (73%). Most common risk factors for CAD was dyslipidemia (48%), hypertension (24%), diabetes (12%) and smoking (21%), whereas in offspring's of CAD patients, dyslipidemia was seen in 28%, hypertension in 3%, diabetes and tobacco smoking in 12% and 24% respectively. The CIMT of CAD patients was significantly increased with increasing the number of risk factors and the same pattern was also seen in controls. The CIMT of asymptomatic offspring's having positive family history was significantly more than the asymptomatic offspring without positive family history of CAD.

**Conclusions:** CIMT measurements can be used as a surrogate marker of atherosclerosis as it has showed a direct link with number of risk factors of CAD.

**Keywords:** Atherosclerosis, Cardiovascular events, Carotid intima media thickness, Ultrasonography, Smoking

### INTRODUCTION

Atherosclerosis is considered as a chronic inflammatory process of arterial wall which occurs due to imbalance between lipid metabolism, maladaptive immune response and genetic alterations.<sup>1,2</sup>

Cardiovascular Diseases (CVD) such as Ischemic Heart Disease (IHD) or stroke, has direct link to atherosclerosis and get evident in adulthood. Previous evidence suggest

that process of atherosclerosis commences in childhood and progresses to measurable vascular changes in adulthood.<sup>3,4</sup>

Smoking, hypercholesterolemia, hypertension and diabetes are the well-known modifiable risk factors for the CVD.<sup>5</sup> However, previous authors have shown that 20% of the cardiovascular events occurs without above mentioned conventional risk factors.<sup>6</sup>

Age, gender and family history of premature CVD are non-modifiable risk factors for the development of atherosclerosis. Several previous evidences suggest that family history of premature CVD is an independent risk factor for the development of CVD and significant predictor for CAD.<sup>7,8</sup>

Reports of The Third Report of the Expert Panel on Detection, Evaluation, and Treatment of the High Blood Cholesterol in Adults (ATP III) suggest that family history of premature CAD (identified as myocardial infarction or sudden death of father or other male first-degree relative before the age of 55 years or before 65 years of age in mother or other female first-degree relative) as one of the important risk factor for CAD.<sup>9</sup> In present study authors tried to evaluate the risk factors associated with atherosclerosis in patients of coronary artery disease and their offspring.

## METHODS

A prospective cross-sectional study was performed on 140 subjects of either sex having different age groups in Department of Medicine of G. R. Medical College, Gwalior for one years from 2012 to 2013.

Out of 140 subjects, 100 were patients having CAD and 40 age matched subjects were included as control group. Data was also recorded from their offspring.

Institutional Ethics Committee approval was obtained before starting the study. A written informed consent was secured from all the subjects after a through detailing of the study in their own local language.

All patients of coronary artery disease who were admitted in department of medicine were included. Any patients with chronic or acute infection like tuberculosis, pneumonia, skin disease and patients who did not give the written informed consent were excluded from the present study.

The detailed history, demographic parameters including age and sex, details of CV risk factors like history of hypertension or diabetes, addiction like tobacco chewing and/or Bidi or cigarette smoking. Baseline clinical examinations, general physical examination and systemic examination was carried out in all subjects. Fasting blood samples were collected in the morning for lipid profile, fasting glucose level which was measured using standard enzymatic methods. All the relevant blood investigations were done in Department of biochemistry and pathology of GRMC Gwalior.

High resolution B mode ultrasonography was performed to assess CIMT of carotid arteries. The maximum CIMT of any one side of carotid artery was taken for study.

All the data analysis was performed using SPSS ver. 20 software. Frequency distribution and cross tabulation was

performed to prepare the tables. Quantitative data was expressed as mean whereas percentage was used to express categorical data. Student t-test was applied to compare the CIMT of cases and controls. ANOVA was applied to compare the variability of CIMT in between different groups among the cases and controls.

## RESULTS

Out of 100 CAD patients, majority were males (78%) followed by females (22%). Mean age of patients with CAD was 56.82±8.91 years which ranges from 34 to 64 years.

Total 100 offspring of cases were studied out of which maximum were age group 28-42 yrs. Majority were male (73%) followed by females (27%). Total 40 offspring of controls were studied out of which maximum were age group 30-40 yrs. Majority were males (62.5%) followed by females (37.5%).

Both the groups were compared for the assessment of risk factors for CAD and it was found that in CAD groups, majority of the patients had dyslipidemia (48%) followed by hypertension (24%), diabetes (12%) and smoking (21%), whereas in offspring's of CAD patients, dyslipidemia was seen in 28%, hypertension was present in 3%, diabetes and tobacco smoking was seen 12% and 24% respectively. In offspring of controls, dyslipidemia was seen in 12%, hypertension was present in 8%, diabetes and tobacco smoking were seen 6% and 18% respectively.

**Table 1: Mean CIMT of CAD patients with respect to risk factors.**

No. of risk factors	Mean CIMT value	Mean CIMT value controls
NIL	0.34±0.05	0.32±0.02
1	1.14±0.2	0.38±0.12
2	1.26±0.1	0.64±0.21
3	1.42±0.00	0.64±0.28
p value	<0.0001	0.0028

**Table 2: Mean CIMT of asymptomatic offspring with positive family history and asymptomatic offspring without positive family history.**

Asymptomatic offspring's	Mean CIMT
With positive family history	0.826±0.28
Without positive family history	0.443±0.27
p Value	<0.0001

Table 1 compare the mean CIMT values between CAD patients and of those without CAD. It was found that as the number of risk factors for CAD increases a significant increase in CIMT value was noted, similarly among control group though significant but lesser increase in

CIMT was observed suggest CIMT as an important marker in CAD patients.

Table 2 compares the role of family history for the risk of CAD, as offspring with positive family history had higher CIMT as compared to those without it. Offspring's with positive family history had CIMT of  $0.826 \pm 0.28$  whereas those without positive family history had  $0.443 \pm 0.27$ .

## DISCUSSION

Expert panel reports of National Cholesterol Education Program (NCEP) on Blood Cholesterol Levels in Children and Adolescents specify positive family history in biological parents and grandparents for CVD before 55 years of age.<sup>10</sup>

All conventional risk factors are significantly associated with the risk of CAD in Asian Indians, as in all other populations. Although the conventional risk factors do not fully explain the excess burden of CAD, these risk factors appear to be doubly important in Asian Indians and remain the principal targets for prevention and treatment.<sup>11</sup>

Smoking has emerged as a major dominant modifiable risk factor associated with young CAD. In fact, it has emerged as a sole dominant conventional risk factor associated with young CAD.<sup>12</sup> In present study 21% CAD patients were smokers whereas 24% of the offspring were smokers. In a case control study on tobacco use and risk of myocardial infarction, by Teo et al, it was found that, the effect of current smoking was much larger in younger (odds ratio=3.53) than in older individuals (odds ratio=2.55).<sup>13</sup> In an angiographic study done on premature CAD patients, in North India, smoking was found as a risk factor in 53.6% patients.<sup>14</sup> In a study done by Zimmerman et al, the prevalence of smoking in young CAD was found to be more than 90 percent.<sup>15</sup>

Hypertension is an important risk factor for all clinical manifestation of atherosclerosis. Several major prospective epidemiological studies have found that both systolic and diastolic hypertension have a strong, positive, continuous, and graded relationship to CHD without evidence of a threshold risk level of blood pressure.<sup>16</sup> In present study 24% of CAD patients and only 3% of the offspring's had hypertension.

In present study majority of the CAD patients had dyslipidemia (48%) and 28% of their offsprings had dyslipidemia. Isser et al, studied lipid levels in 50 consecutive young north Indian patients (age less than 45 years) with myocardial infarction and sex-matched controls.<sup>17</sup> There was no significant difference in the levels of total cholesterol and LDL-C however; HDL-C was significantly lower in young patients with myocardial infarction ( $30.16 \pm 9.45$  mg/dl) as compared to controls ( $46.8 \pm 8.04$  mg/dl). Triglyceride levels were also significantly higher in patients as compared to controls

( $202 \pm 76$  mg/dl). In addition, in clinic-angiographic studies it was shown that the lower HDL-C and higher triglyceride levels in younger cases appear to be a hallmark of the Indian population.<sup>18</sup> Enas et al, studied the risk factors for CHD in first-generation Asian Indian immigrants to United States of America, and found that only 14% Asian Indian men and 5% Asian Indian women had the optimal HDL-C levels.<sup>19</sup> Younger patients were found to have even lower levels of HDL-C. In an analytical study done by Karthikeyan et al, over 80% of both cases and controls in South Asia had low HDL-C levels compared to 50% in rest of Asia.<sup>20</sup> In this study, among South Asians, a tendency towards weaker protection afforded by normal or high levels of HDL-C was also observed.

In present study the CIMT of CAD patients was significantly increased with increasing the number of risk factors and the same pattern was also seen in controls. According to Kuo, plasma lipoprotein metabolism, as manifested in several types of dyslipidemia, are known to contribute to atherosclerotic cardiovascular disease.<sup>21</sup> These types of abnormalities give rise to increased intimal media thickness which can act as surrogate marker of coronary atherosclerosis. According to Holland et al, as the number of risk factors for atherosclerosis are increased, chances of becoming symptomatic CAD are also increased.<sup>22</sup> In this study also, as the number of CAD risk factors increased, the value of CIMT was higher which is an indirect indication of increased risk of symptomatic CAD. According to Andersdottir et al, reported coronary events were attributable to family history of coronary artery disease.<sup>23</sup> In this study also, the CIMT of asymptomatic offspring's was also more, who were having positive family history in comparison to patients who didn't have the positive family history. So, the risk of symptomatic CAD is more in the offspring of the cases in comparison to age matched controls.

Assessment of Carotid artery Intima-Media Thickness (CIMT) is well-recognized as a surrogate marker of atherosclerosis.<sup>24</sup> National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) stated that CIMT could be used as an adjunct in CHD risk assessment. The finding of an elevated CIMT (e.g.,  $\geq 75^{\text{th}}$  percentile for age and sex) could elevate a person with multiple risk factors to a higher risk category. The CIMT of maximum number of cases was between 0.9-1.2 mm where their offspring had CIMT between 0.5-0.6 mm. The CIMT of maximum number of asymptomatic controls was between 0.5-0.6 mm where their offspring had 0.5-0.6 mm. The mean CIMT of cases was significantly higher than controls ( $p < 0.0001$ ). Mean CIMT of CAD patients increased when number of risk factors responsible for atherosclerosis were increased.<sup>25</sup>

According to world heart federation, if a first-degree male relative (e.g. father, brother) has suffered a heart attack before the age of 55, or if a first-degree female relative has suffered one before the age of 65, you are at greater

risk of developing heart disease. If both parents have suffered from heart disease before the age of 55, risk of developing heart disease can rise to 50% compared to the general population. Studies have shown a genetic component for both hypertension and abnormal blood lipids, factors related to the development of cardiovascular disease. In present study the CIMT of asymptomatic offspring's having positive family history was significantly more than the asymptomatic offspring without positive family history of CAD. A positive family history of coronary artery disease is an important predictor of impaired endothelium-dependent coronary blood flow regulation in humans. The influence of a positive family history is independent of other well-known risk factors, and it aggravates endothelial vasodilator dysfunction associated with hypercholesterolemia and increased age, suggesting important additive effects of genetic and environmental risk factors. Andresdottir et al, reported that 15% of coronary events were attributable to family history of coronary artery disease, when they used history of myocardial infarction at any age (not premature coronary artery disease) in first-degree relatives.<sup>26</sup> It is interesting that despite using a broader definition of family history of coronary artery disease, the reported prevalence was lower (16.8% in men and 21.6% in women) compared to other studies that could be because about 20% of men and women did not know their family history, but was still much less than was reported in a recent Canadian study where 67% of women reported positive family history.<sup>27</sup> Although the authors did not verify the family history in participants, it appears that the population of this cohort was well educated and reported proper family history of coronary artery disease in first degree relatives compared to other cohorts where patients may include the history of coronary artery disease in second and third degree relatives that thereby exaggerated the family history but diluted its significance.

## CONCLUSION

CIMT is associated with CVD risk factors, prevalent CVD, incident CVD, and the degree of atherosclerosis in several different arterial beds. Progression of CIMT may be attenuated or reversed with risk factor interventions, in association with a reduced risk of future CVD events. These findings provide support to the concept that CIMT measurements can be used as a surrogate marker of atherosclerosis.

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