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Association between multiple cardiovascular risk factors and coronary artery disease in young individuals belonging to an Eastern Indian Population: A histopathology and autopsy-based study

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Abstract
Introduction: *Coronary Artery Disease (CAD) is a leading cause of death in men and women at a global scale. This condition has been increasingly threatening in young individuals in the recent years. In the current study we attempt to find the association of CAD with various cardiovascular risk factors among young individuals in a regional Eastern Indian population.*
Materials and Methods: *CAD status of 55 subjects, determined by Histopathological (HP) analysis, following autopsy, was correlated with risk factors they were exposed in like history of smoking, alcohol consumption, physical activity level, stress level and socioeconomic status. Data were analysed using SPSS version 23.0, Armonk, NY, IBM Corp. Chi-square test with Yates correction and Fisher exact test were applied in univariate analysis. Binary logistic regression was applied to perform multivariate analysis of factors contributing to the CAD status.*
Results: *Univariate analysis showed that smokers and alcoholics were significantly associated with higher grade of CAD (p < .05). Higher HP grade of CAD was significantly more commonly found among those who belonged to lower middle and below class of socio-economic status (p = .02). Also, sedentary physical activity status was significantly associated with higher level of HP grade of CAD (.000). However Binary logistic regression also showed that smoking, alcohol consumption and lower middle and below socio-economic status had significantly higher risk of developing higher HP grade of CAD while moderate physical activity status had a protective effect on development of higher HP grade.*
Conclusion: *There is a high incidence of CAD in the young individuals and has been significantly associated with lower socioeconomic status, history of smoking and alcohol consumption and sedentary lifestyle. Moderate physical activity however has a protective effect from the condition.*
Keywords: *Coronary Artery Disease, Risk Factors, Young Individuals, Histopathological Analysis, Socioeconomic status, Stress, Physical Activity, Smoking, Alcohol consumption.*

Introduction

Coronary Artery Disease (CAD) is a leading cause of death of men and women worldwide. Global in distribution, atherosclerosis is emerging as the single largest disease accounting for nearly on third of all deaths in India. An estimated of 1.3 million Indians died from this disease in the year 2000 alone. The death toll due to CAD rose upto 2.95 million by the year 2015, of which 14% were less than 30 years of age and 31% were less than 40 years of age. Pathologically, atherosclerosis is a diverse disease with heterogeneous mechanisms of progression where there is a gradual development of smooth muscle cell rich lipid pool lesion, referred to as pathological intimal thickening; which is a lipid driven chronic inflammatory disease of the vessel wall, in which both innate and adaptive immune response play a role[1].

Such pathological changes are triggered by multiple modifiable and non- modifiable risk factors like age, sex, socio-economic status, physical activity level, stress, any habits like that of substance abuse. The current trend in the disease progression has shown that individuals belonging to the younger age group are seen to be show a higher affection rate of non-communicable diseases as compared to their elderly counterparts. Also autopsy based study apart from having the advantage of being more cost effective, is actually more specific in determining a disease in the asymptomatic stage as compared to any other screening or diagnostic test[2].

With this backdrop the present study was conducted with the objective to find any possible association between the Histopathological (HP) changes of coronary atherosclerosis and the various risk factors in young individuals in an Eastern Indian population.

Materials & Methods

This analytical, cross-sectional, observational study was conducted in the Department of Forensic Medicine and Toxicology in association with Department of Pathology, of a tertiary care hospital in Kolkata, West Bengal on coronary artery sample obtained from 55 young individuals, belonging to the age range of 20-39 years, who died due to non-cardiac cause, with no known history of cardiac disease in the past, nor having any history of diabetes mellitus or hypertension in their family. The study was conducted during the period of July 2017 to June 2018 (1 year). Ethical clearance was obtained from the Institutional Ethical Committee. A questionnaire was designed by the principal investigator in order to get pre-mortal data of the individual about his/her history of smoking, alcohol intake, socio-economic status (SES), physical activity level and stress respectively. This data was collected from the family members or relatives accompanying the subject of study to the morgue complex during the post-mortem examination. Previous disease status of the subject was confirmed from the cases sheets/ clinical notes obtained during the post mortem examination. Any family history of disease was directly enquired about to the family members. SES was assessed using the Modified BG Prasad scale (per capita income levels for the year 2017 and 2018)[3]. Level of physical activity was assessed based on the occupation in which the subject was involved in, when alive. For eg. teachers, clerks, lawyers etc. were classified as sedentary, while housewives, industrial labourers, mason workers, rickshaw pullers etc. were said to be moderately active. The stress level of the subjects were assessed according the Holmes and Rahe Stress scale or the Social Readjustment Rating scale[4]. The coronary artery samples obtained during autopsy were histo-pathologically analysed and the results were graded according to the Histopathological grades of atherosclerosis by the American Heart Association (AHA)[5]. The current study showed results to range from grades I to VI for statistical convenience the grades has been classified as I-III as low grade and IV-VI as high grade.

Statistical Analysis: Data were analysed using SPSS version 23.0, Armonk, NY, IBM Corp. Chi-square test with Yates correction and Fisher exact

test were applied in univariate analysis. Binary logistic regression was applied to perform multivariate analysis of factors contributing to the CAD status.

Results

In the current study out of 55 subjects of the study 73% (40/55) were male, and 27% (15/55) female. In these, 33% (18/55) belong to age group of 20-29 years, whereas 67% (37/55) cases belong to the age group of 30-39 years. 58.18% (32/55) individuals were affected with Grade IV-VI (higher grade) atherosclerotic change while the remaining 41.82% (23/55) had grade I-III (lower grade) change. In the current study 82% (45/55) of subjects were smokers while 80% (44/55) were alcoholic. In 90.9% (50/55) of subjects there was incidence of mild to moderate stress whereas 67.3% (37/55) of them belonged to middle socioeconomic status or above. When their pre

mortal physical activity level was assessed, it was seen that 56.4% (31/55) of them were sedentary workers while the rest were moderate workers (43.6%). Univariate analysis showed that smokers and alcoholics were significantly associated with higher grade of CAD (p < .05). Higher HP grade of CAD was significantly more commonly found among those who belonged to lower middle and below class of socio-economic status (p = .02). Also, sedentary physical activity status was significantly associated with higher level of HP grade of CAD (.000). (Table 1)

However Binary logistic regression also showed that smoking, alcohol consumption and lower middle and below socio-economic status had significantly higher risk of developing higher HP grade of CAD while moderate physical activity status had a protective effect on development of higher HP grade. (Table 2)

Table 1: Factors associated with histo-pathological grade of CAD

Factors	HP Grade		p value
	Lower (I – III)	Higher (IV – V)	
Non-smoker (n = 10)	8 (80.0)	2 (20.0)	.018
Smoker (n = 45)	15 (33.3)	30 (66.7)	
Non-alcoholic (n = 11)	9 (81.8)	2 (18.2)	.02
Alcoholic (n = 44)	14 (31.8)	30 (68.2)	
Stress level* Mild to moderate (n = 50)	23 (46.0)	27 (54.0)	.07**
Severe (n = 5)	0	5 (100)	
Socio-economic Status*** Middle and above (n = 37)	20 (54.0)	17 (46.0)	.02
Lower middle and below (n = 18)	3 (16.7)	15 (83.3)	
Physical activity status Sedentary (n = 31)	1 (3.2)	30 (96.8)	.000
Moderate (n = 24)	22 (91.7)	2 (8.3)	

*As per the Holmes & Rahe Stress Scale   **Fisher exact test   ***as per Modified B.G. Prasad Scale

Table 2: Logistic regression analysis of factors associated with HP grade of CAD

Factors	Adjusted Odds Ratio (95% CI)	p value
Non-smoker	1	.018
Smoker	1.96 (1.31 – 4.83)	
Non-alcoholic	1	.02
Alcoholic	4.91 (1.4 – 13.1)	
Stress level Mild to moderate	AOR undefined	.083
Severe (n = 5)		
Socio-economic Status Middle and above	1	.02
Lower middle and below	5.02 (1.71 – 17.3)	
Physical activity status Sedentary	1	.000
Moderate	0.04 (0.01 – 0.13)	

Discussion

The current study shows a high incidence of coronary artery disease among young individuals in the 3rd and 4th decade of life. Individuals who are currently asymptomatic have a high probability of developing frank atheroma and subsequently complete stenosis in future. In the current study, higher HP grade of CAD was significantly more commonly found among those who belonged to lower middle and below class of socio-economic status (p = .02). Phillips JE et al. [6] found that individuals with lower SES experienced higher rates of morbidity and mortality due to CAD. Similarly, Fiscella et al.[7] showed that the SES status of an inversely related to the CAD status of an individual as chronic psychosocial stress associated with the lower SES individuals promotes this disease. Also in the similar study by Janati et al.[8] pointed out that lower educational level in lower SES individuals promote higher CAD grades in those individuals. The above studies have findings similar to our study.

In the current study we found that Sedentary physical activity level was significantly associated with HP grades of CAD (0.00), whereas moderate physical activity status had a protective effect on development of CAD. According to AHA statistical update on Coronary Heart Disease (9), in 2015 National Health Interview Survey the amount of time of children sitting idle other than school work has risen significantly from 24.9% to 41.7% from 2009 to 2015. This further triggers CAD in these young individuals. This data supports our study result.

In the current study it was seen that smokers and alcoholics were significantly associated with higher grade of CAD (p < .05). Vliestra RE et. al. [10] showed by using discriminant function analysis that cigarette smoking along with other factors like high blood cholesterol contribute to high incidence of CAD from a very early age. Berenson GS et al[11] pointed out smoking increased intimal surface fibrous plaque involvement in aorta (1.22% smokers v/s 0.12 %

in non-smokers, p=0.22) and fatty streaks in coronary vessels (8.27% vs 2.94%, p= 0.04). Similar findings were seen in Mc Mahan CA et al., Mc Gill HC et al. (both of which are part of the cooperative multicentre study namely Pathobiolological Determinants of Atherosclerosis in Youth [PDAY]), Rissanen VJ et al. and Auerbach O. et al. [12,13,14,15] respectively.

Literature have also suggested that people drinking alcohol more than 16 days per month have more probability of developing atherosclerotic lesions in the aorta than those drinking for 3 days per month or less[16]. Djousse L et al.[17] gives similar findings. These studies hence support our findings.

Conclusion

Young individuals, especially of those more than 20 years are at high risk of developing CAD and succumbing to the disease at a time that's extremely less expected. This is directly related to the risk factors associated with the disease, even if they do not have any family history as such. It is advised regular screen tests for such from a very early age, more so in those who are more pre disposed to the risk factors. Such studies in future are highly forth coming to devise some kind of preventive measure in the more susceptible individuals.

Limitations

The primary limitation of the study was the scarcity of sample size. This was probably because of the stringent inclusion and exclusion criteria, and the fixed time period of study. Secondly this study was done in only on medical college of Kolkata, and thus is not representative of the entire region.

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