ORIGINAL ARTICLE   CODEN: AAJMBG

Histopathological study of the coronary arteries in young individuals and its relation to their age, in a tertiary care hospital in Kolkata, West Bengal

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Abstract: *Background:* Coronary artery disease (CAD) is a leading cause of death of women and men worldwide. Global in distribution, atherosclerosis is emerging as the single largest disease accounting for nearly one-third of all deaths in India. *Objectives:* A Post-mortem study done to evaluate the incidence of CAD in the Young Individuals and to correlate it with their age. *Methodology:* In the present study heart specimen from 55 bodies were selected, over a period of one year (randomly selected based on the inclusion and exclusion criteria), which were sent to the Department of Forensic Medicine & Toxicology, NRS Medical College, Kolkata for medicolegal autopsy, belonging to the age group of 20-39 years of age, having no previous history or family history of any cardiac disease or Diabetes Mellitus. Tissues of coronary arteries were collected from the proximal part of the LAD, as it has the highest propensity to develop CAD and were studied histo-pathologically and results graded according to the AHA criteria. *Results:* Out of the 37 cases belonging to the age group of 30-39 years, 7(18.9%) cases have grade I-III change and 30(81.1%) cases have grade IV-VI changes [$\chi 2$ (5) = 30.65 p = 0.000]. Thus, age and CAD changes are positively correlated. *Conclusion:* The data obtained may form a baseline for the forthcoming studies, especially if done on a multi-centric basis.
Keywords: Atherosclerosis, Autopsy; American Heart Association, Coronary Artery Disease, Coronary Vessels.

Introduction

Coronary artery disease (CAD) is a leading cause of death of women and men worldwide. Global in distribution, atherosclerosis is emerging as the single largest disease accounting for nearly one-third of all deaths in India. Deaths from this group of diseases are likely to amount to be a staggering 34 lakh. An estimated 1.3 million Indians died from this disease in 2000. The death from coronary artery disease by 2015 was 2.95 million, of which 14% were <30 years of age and 31% were <40 years.

Aging is associated with structural and functional changes of the vessel wall, which results in decreased vascular distensibility and elevated arterial stiffness. As a consequence of arterial stiffness, systolic blood pressure increases, causing a rise in left ventricular workload and subsequent hypertrophy, and diastolic blood pressure decreases, leading to an impaired coronary perfusion. Chronic systemic inflammation has been implicated in atherogenesis, and may play a role in destabilizing vulnerable coronary plaques, thereby precipitating acute thrombosis and clinical coronary vessel events [1].

The incidence of atherosclerosis has been increasing in the younger age group, of late recently. More so there is very few clinical data available in the eastern part of India with this regard. In order to assess the magnitude of the problem, a prospective study of autopsied patients for the presence of atherosclerotic lesions of the coronaries artery and myocardial infarction (MI) was undertaken for one year in the NRS Medical College & Hospital, Kolkata. In order to assess the effect of the epidemiological risk factors exclusively on Coronary atherosclerosis, cases with previous medical complications or having a medical history of any such was excluded. An autopsy study gives a good measure of the prevalence and the gradation of atherosclerotic lesions in the different age groups.

Material and Methods

Heart specimen from 55 bodies were selected randomly, over a period of one year, for the present study, which were sent to the Department of Forensic Medicine & Toxicology, NRS Medical College, Kolkata for medicolegal autopsy. In order to find the exclusive relation between the age and the incidence of CAD in them, (in reported/documented non-diseased individuals, and also who did not have any family history of any disease precipitating CAD) following were the Inclusion & Exclusion Criteria:

Inclusion Criteria:

1. Age group of the deceased between 20-39 years.
2. Death due to non-cardiac cause.
3. No known cardiac history in the past.

Exclusion Criteria:

1. Deceased of any age greater or lesser than the abovementioned age group.
2. The deceased having any known cardiac history.
3. Family history of Hypertension and Diabetes.
4. Death due to any cardiac cause detected after autopsy.
5. Decomposed body.
6. Cases where history cannot be properly elicited.
7. Any injury on the chest is present where heart is partly or completely damaged.

The medical history and the relevant clinical history of the said deceased was taken to correlate with the findings of the coronary arteries. Even if cases were selected as per the above criteria, if previous medical history could not be properly described by the patient party, such cases could not be taken for our purpose.

The weight of the heart of the said deceased was noted. Any atherosclerotic change at a macroscopic level in any of the coronary blood vessels was noted. Dissection along the cross-section of the Left Anterior Descending Artery was done, near its root (at the point of bifurcation of the Left Coronary Artery into Left Anterior Descending Artery and Left Circumflex Artery) up to 1 cm distance. This is as per the literature [2] which clearly points out the propensity of higher incidence of Coronary Atherosclerosis in the Proximal part of LADA at an early age. The transverse section given at a gap of not more than 0.3 cm in length each. The dissected part was fixed using 10% formol-saline. The dissected tissue was taken to the Dept. of Pathology, NRS Medical College & Hospital for microscopic examination (Histopathological Examination). After routine processing & paraffin embedding 4 micro-meter sections were taken, stained adequately and microscopic findings noted.

The findings were graded according to the Histopathological Grades of Atherosclerosis as given by the American Heart Association which is mentioned as below:

- Type I: Isolated intimal foamy cell (minimal change)
- Type II: Numerous intimal foamy cells often in layers (fatty streaks)
- Type III: Pools of extracellular lipids without a well-defined core (intermediate lesion or pre-atheroma)
- Type IV: Well defined lipid core with luminal surface covered by normal intima (atheroma or fibro-plaque)
- Type V: Lipid core with a fibrous cap with or without calcification (fibroatheroma)
- Type VI: Fibroatheroma with cap defect such as haemorrhage or thrombosis
- Type VII: Calcification prominent
- Type VIII: Fibrous tissue change prominent

Results

For our convenience of result interpretation and discussion, the age of the individual cases were categorised into two age groups: 20-29 years (3rd decade) and 30-39 years (4th decade). In the present study 18 cases belonged to the 3rd decade whereas the other 37 cases belonged to the 4th decade (Table 1).

Table-1: Distribution of cases according to age groups:	
No. of cases in age group 20-29 years (Group 1) (3rd Decade)	18
No. of cases in age group 30- 39 years (Group 2) (4th Decade)	37
Total no. of cases	55

When the age of the subjects were plotted against the various histopathological grades of Coronary Atherosclerosis (as suggested by the American Heart Association) we found they were statistically significantly and positively correlated (r= 0.617; p= 0.000). We also see that out of the total 18 cases belonging to the Group 1, 16 (88.9%) have grade I-III change, whereas only 2 (11.1%) have grade IV-VI changes, whereas out of those 37 cases belonging to Group 2, 7(18.9%) cases have grade I-III change and30(81.1%) cases have grade IV-VI changes.

Thus we see in the present study that age is significantly associated with increase in HP grade [$\chi 2$ (5) = 30.65 p = 0.000]. This clearly indicates that *higher the age, higher is the incidence of Coronary Artery Disease*, as is evident from the above findings (Table 2 &Figure 1).

Table-2: Histopathological Grade of CAD cross tabulated with Age:

	I-III (AHA Grade)	IV-VI (AHA Grade)	Total No. of Cases
20-29 years (Group-1)	16(88.9%)	2(11.1%)	18
30-39 years (Group-2)	7(18.9%)	30(81.1%)	37

Fig-1: Histopathological Grade of CAD cross tabulated with Age (Bar Chart)
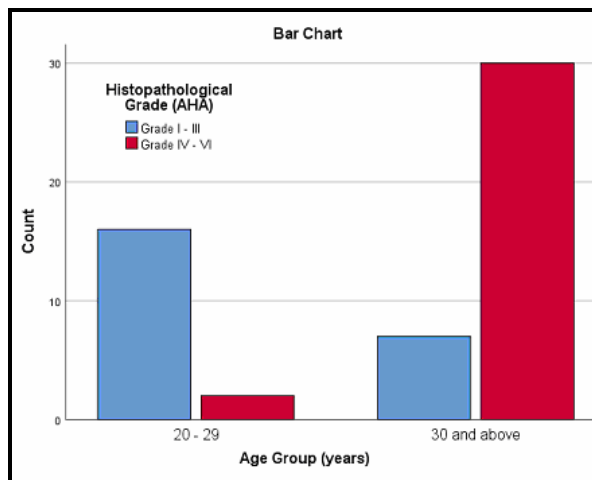
Discussion

Coronary artery disease is a rising problem globally, more so in the last quarter it has risen to explosive proportions, more so in the developing countries (3rd world countries) of the world. With the shift of the global health focus from the infectious disease to the non-infectious ones as the major *'killers'* in the society, CAD takes the pivotal position among all the other problems that we face. As seen in the other studies in India and abroad, CAD has a major incidence among the population.

Garg M. et al, the study comprises of the cases in age group of 15 to 85 years. 46.4% showed significant atheroma. Left Anterior Descending was most commonly involved artery [3]. Atheroma have been seen above the age of 15 years, but significant atheroma appeared after third decade onward, as is seen in our current study, atheromatous change is seen from 20 years of age and significant atheromatous changes (Type IV and beyond) seen beyond 30 years of age (4^{th}decade). Sharma S. et al study pointed out atheroma was seen above the age of 20 years but significant atheroma appeared after third decade, which finding is consistent with our study [4]. Vyas P. et al [5] study pointed out the 3rd decade of life appears to be a watershed line in the pathogenesis of coronary vascular atherosclerosis, as we observed in our present study a steady increase in overall frequency and severity of atherosclerosis from the3rd decade onwards.

Deorajpuri R. et al [6] study writes in males the mean thickness of the Tunica Intima and Tunica Adventitia was found to be greater in males as compared to females in the age group of 21-40years. It is explained that In the Tunica Media, with advancing age, there is fibrosis of the Tunica Media, characterised by increase in the collagen & ground substance in the Tunica Media of the artery. Also the Internal Elastic Lamina (IEL) acts as a barrier for the entry of the lipid macromolecules and cells into the tunica intima. With advancing age there is fraying, splitting, fragmentation of the IEL, thus this protective barrier is lost. The IEL splits into two in between 31-40 years of age thus enclosing the adjacent smooth muscle layer, this being called the musculoelastic layer. This finding being consistent with our study, as atheromatous changes are more pronounced beyond 30 years of age.

Neil K. et al [7] study pointed out that the findings of coronary atherosclerosis in necropsy is not linearly related with age and increases at an exponential rate after 30 years of age, very similar to our study. Singh H. et al [8]a necropsy based study, found that significant coronary atherosclerosis is seen from 17 years of age onwards, although our study was done for cases more than 20 years of age, thus this finding is slightly inconsistent with our study. McGill H.C. et al [9] study for Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group) approximately 19% of 30 to34-year-old men and 8% of 30 to 34 year old women had atherosclerotic stenos is, 40% in the LAD, again being consistent with the findings of our study, although in our case we did not do any sex based differentiation in our findings.

Hathila R.N. et al [10] study showed most common age group for atherosclerotic changes was found to be 31-40years, findings of which are again consistent with the present study. Wig K. et al. [11] study pointed out that significant coronary atherosclerosis is seen from 20 years of age onwards, which is practically seen in our study as well. Dhruva G.A. et al [12] study clearly pointed out Atheroma have been seen above age of 20 years, but significant atheroma appeared after third decade onwards and thereafter there is a gradual increase in both its frequency and severity from second to sixth decade. This again is highly consistent with our study.

In Joseph A. et al. [13] study, out of the 111 autopsy cases with respect to Coronary Artery Atherosclerosis post Korean war having a mean age group of 26 +/- 6 years (all cases of age <35 years), it was seen that signs of coronary atherosclerosis were seen in 78.3% of the total study group. Proximal involvement was more common except in the right coronary artery, which was as frequently involved distally. In the present study only the proximal 1cm of the LAD was chosen, hence, the case being consistent with our study. Also in our study, the involvement of CAD is in 100 % of the cases, which is higher than the above study results. Maru M. [14] conducted an autopsy study of 124 Ethiopian patients for atherosclerotic lesions, found Fatty streaks in the coronary arteries were detected after the age of 19 years. Our study however focuses on age group beyond 20 years of age, and thus this result is taken consistent with our study. Porwal V. et al [2] study wrote Left anterior descending artery (LADA) was most frequently involved vessels (46.6%), thus this vessel was selected for the above study. The current study also took the same vessel (proximal 1 cm from its bifurcation) as its study sample.

Kumar S. et al [15] autopsy of 50 cases were done within 12 hours of death due to some unnatural cause. In the age group between 30-40 years Out of 21 male and 2 female of age group 30-40 years, 18 (85.71%) male 1(50%) female were affected. In our study however 100% cases are affected, showing higher propensity of development of atherosclerosis with respect to age in our study.

Conclusion

The study showed unexpectedly high prevalence of atherosclerosis in India, more specifically in the South-Eastern Part of West Bengal. This study highlights the importance of cardiovascular risk factors screening from early ages of third decades, as its important to note that all the cases chosen for our study neither had any history of Myocardial Infarction, nor did they have any chronic disease like Hypertension of Diabetes Mellitus during their lifetime (reported/documented), that could have explained such a change in their Coronary Arteries, post mortem.

Our study aids valuable data to the literature regarding the morphology of atherosclerotic lesions. The study of human atherosclerotic lesion is an extremely difficult task in a living subject and autopsy study is the best possible way to work on it. Though our study involved only a small number of cases, most of our observation correlated with the many similar studies. Such studies if done with higher sample size, on a multi-centric basis, the results may be higher yielding and may be applicable for baseline reference value for further study on Coronary atherosclerosis.

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