

Atherosclerosis in coronary artery and aorta in a semi-urban population by applying modified American Heart Association classification of atherosclerosis: An autopsy study

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ABSTRACT

Background: Ischemic heart disease (IHD) following atherosclerosis is a giant killer and the incidence of atherosclerosis in coronary arteries is rapidly increasing among Indians. The study was formulated to assess the histomorphological atherosclerotic changes in aorta and coronary arteries at autopsy by applying the modified American Heart Association classification of atherosclerosis based on morphological descriptions to find out the age and sex related prevalence of atherosclerosis in the semi-urban population of Kolar, a district in Southern India. **Materials and Methods:** Autopsy was conducted on 113 cases whose age ranged from 8-85 years. Autopsy was conducted by the conventional technique; heart and the aorta were removed and fixed in 10% formalin. The heart was dissected along the direction of flow of blood and aorta along the posterior surface. Microscopic assessment of the three main coronary arteries and aorta was done using the modified American Heart Association classification of atherosclerosis. Proportions were analyzed using Chi-square test. **Results:** The number of males was 78 (69%) and number of females was 35 (31%). Mean age was 37.11 ± 15.69 years. Increased incidence of intermediate lesions was noted in young individuals (15-34 yrs). Atherosclerotic lesions were more in left anterior descending artery compared to other coronary arteries and in abdominal aorta compared to thoracic and ascending aorta. Vulnerable plaques were more in right coronary artery. **Conclusion:** With cardiovascular disease attaining pandemic proportions, the study of subclinical atherosclerosis is the need of the hour to estimate the disease burden in the asymptomatic population. The increased amount of atherosclerosis (advanced and intermediate lesions) found in the young population in this study gives an indication that anti-atherogenic preventive measures need to be implemented in young individuals, so as to prevent coronary artery disease from causing premature death.

Key words: Atherosclerosis, autopsy, modified American Heart Association classification

INTRODUCTION

Atherosclerosis continues to be one of the hot topics in pathology research. Cardiovascular disease (CVD) has emerged as a major health burden worldwide with atherosclerosis being the major cause.^[1] Ischemic heart disease (IHD) following atherosclerosis is the most common cause of cardiac deaths worldwide.^[2] Atherosclerosis affects the Indian population at a younger age than in other ethnic groups with more advanced lesions.^[3] Epidemiological data of the last 5 decades indicate a significant increase in the

Access this article online	
Quick Response Code:	Website: www.jcdronline.com
	DOI: 10.4103/0975-3583.102692

prevalence of coronary artery disease in urban as well as rural India.^[3]

Autopsy is a tool of real value for assessment of pathologies, which are difficult to assess in the living.^[4] As study of atherosclerosis in the living population is difficult, invasive, and expensive especially in developing countries, autopsy studies has been proved to be a good method for assessing atherosclerosis.^[5] With the limited amount of resources available in rural and semi-urban population in India for studying atherosclerosis, autopsy plays a major role in documenting the prevalence of atherosclerosis in the population. Studying the prevalence of sub-clinical atherosclerosis in a population helps the health administrators to plan preventive measures and possible measures for reversal of atherosclerosis.^[6] Since atherosclerosis is a giant killer disease, a major financial burden on the nation's economy and health sector, even a modest reduction in its incidence goes a long way in shaping the health of the future generation of the nation. In view of race, risk factor, and geographical diversities present in India, studying the prevalence of the disease in the specific population is of great importance. To the best of our knowledge, very few studies have applied the modified American Heart Association classification of atherosclerosis based on morphological descriptions for the assessment of atherosclerosis in the Indian population. Hence, this autopsy study was undertaken to find out the prevalence of atherosclerosis in the population of Kolar district.

MATERIALS AND METHODS

The study was conducted on 113 hearts and aortas obtained from autopsies conducted by the Department of Forensic Medicine in Kolar, a district, located in the south-eastern part of Karnataka, a state in India. Cause of death and patient identification was noted in each case. Each autopsy subject was identified, examined, and post mortem study was done after obtaining consent from next of kin in case of medical autopsy and requisition from the Police/Department of Forensic Medicine in medico legal autopsies. Past/Family history was obtained from next of kin in whichever cases possible.

The hearts and aortas were fixed in 10% buffered formalin. The heart was dissected along the flow of blood. Left anterior descending artery (LAD), left circumflex artery (LCA), and right coronary artery (RCA) were dissected longitudinally until they entered the musculature. The coronaries were examined grossly for the presence of thrombus, narrowing, and atherosclerosis. Aorta was

cut along its posterior surface and examined grossly for atherosclerosis. Bits were taken from LAD, LCA, and RCA from coronaries and ascending aorta (AA), thoracic aorta (TA), and abdominal aorta (AbA) of aorta from gross atherosclerotic lesions as well as suspicious lesions for the microscopic assessment of atherosclerosis. If no lesions were found, random bits were taken from above mentioned six sites. Bits usually measured 0.3 to 0.5 cm across in case of coronary arteries and 1 × 0.5 cm in case of aorta.

Hematoxylin and eosin-stained sections were evaluated. Microscopic grading of atherosclerosis [Figures 1 - 9] was done using the modified American Heart Association (AHA) Classification of atherosclerosis based on morphological descriptions.^[7] This specific classification was used since it offers better categorization of atherosclerotic lesions based on morphological descriptions compared to the earlier AHA classification, which was too rigid with its descriptions of lesions using Roman numerals and was not particularly useful in subdividing the intermediate lesions of atherosclerosis. Defining these intermediate lesions is of great importance as they are the precursor lesions of future advanced atherosclerosis. According to this classification the non-atherosclerotic intimal lesions are intimal thickening and intimal xanthoma, which differs based on the amount of foam cells in the intima. The progressive atherosclerotic lesions are pathological intimal thickening (PIT) + erosion, fibrous cap atheroma (FCA) + erosion, plaque rupture, calcified nodule and fibro calcific plaque. The lesions were designated as pathological intimal thickening when they had pools of extracellular lipid and their predominance is an indicator of progression to advanced atherosclerotic lesions.^[6] These intermediate lesions are comparable to the raised fatty streak described in the AHA classification.^[8] The modified AHA classification describes thick fibrous cap atheroma and thin fibrous cap atheromas (TFCA), the latter carrying higher chances of rupture and thrombosis with consequent obstruction of blood flow in the coronaries causing IHD. A noteworthy addition to the modified classification is the description of occurrence of erosion and thrombus formation even with intermediate lesions like pathological intimal thickening, which explains the thrombus formation in a few cases of sudden cardiac death where there was absence of advanced atherosclerotic lesions. Proportions were analyzed using Chi-square test.

RESULTS

The present study was carried out on 113 hearts and aortas, and the age of the subjects ranged from 8 to 85 years. Mean age was 37.11 ± 15.69 years. Majority of patients belonged

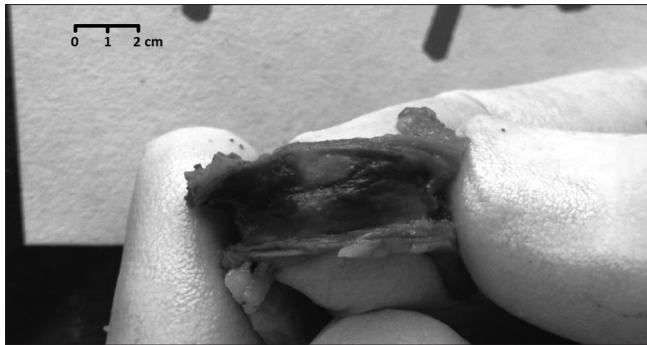


Figure 1: Gross photograph of lesion in coronary artery

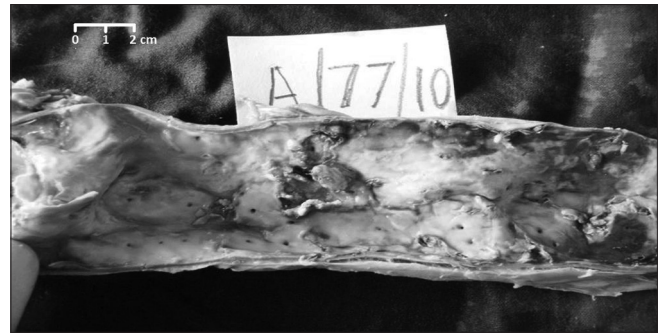


Figure 2: Gross photograph showing complicated aortic atherosclerotic lesions

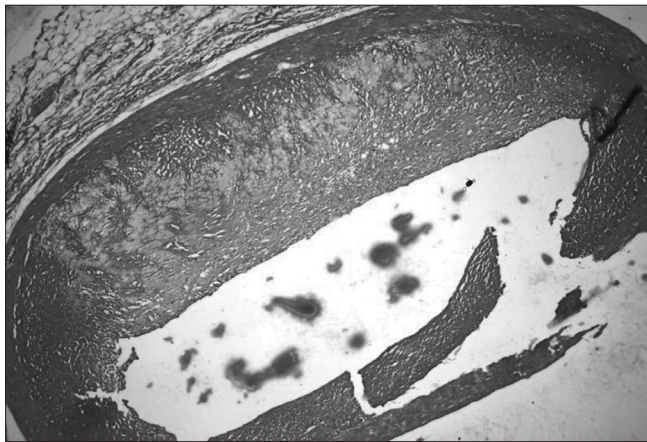


Figure 3: Microphotograph showing coronary pathological intimal thickening (H and E, × 100)

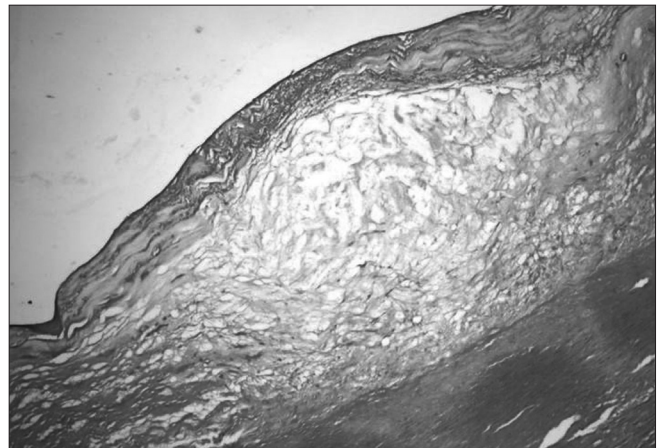


Figure 4: Microphotograph showing aortic thick fibrous cap atheroma (H and E, × 100)

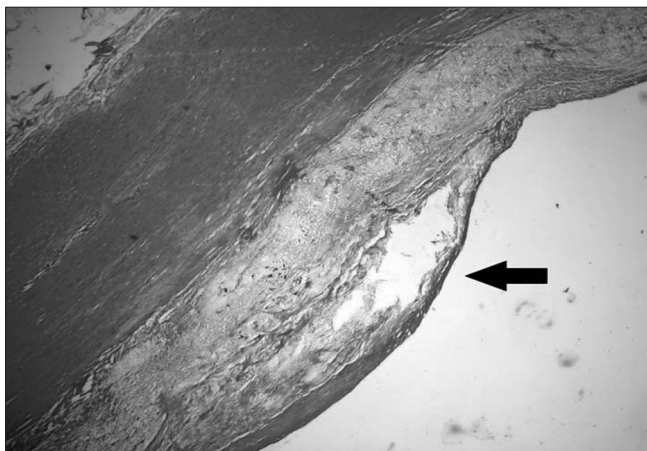


Figure 5: Microphotograph showing aortic thin fibrous cap atheroma (arrow) (H and E, × 100)

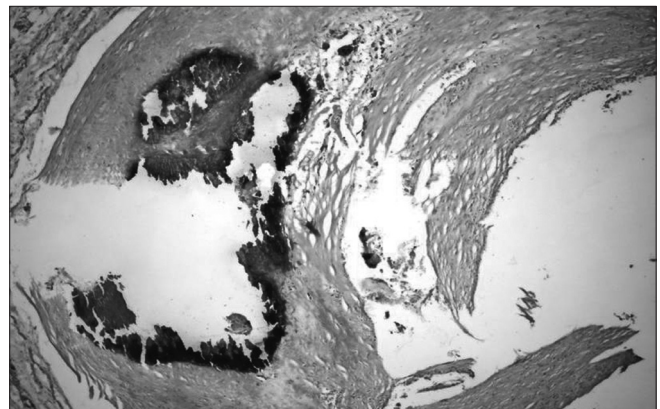


Figure 6: Microphotograph showing coronary calcified nodule (H and E, × 100)

to the 3rd decade of life (25.7%), followed by 5th decade (22%), and 4th decade (16%). Fifty-two cases were young individuals (aged between 15-34 years) of which 33 (63.5%) were males and 19 (36.5%) were females [Table 1]. Older individuals had higher degree of atherosclerosis compared to the younger individuals [Tables 2 and 3]. A total of 78 (69%) cases were male and 35 (31%) cases were female

[Table 1]. Mean age of males was 39.14 years and mean age of females was 35.91 years. Men had slightly more atherosclerosis both in coronaries and aorta than females [Tables 4 and 5].

In the current study, the most common cause of death was road traffic accidents (RTA) (46%), followed by suicidal poisoning (37.1%), burns (5.3%), and rest comprising of other causes of death like cut throat injuries,

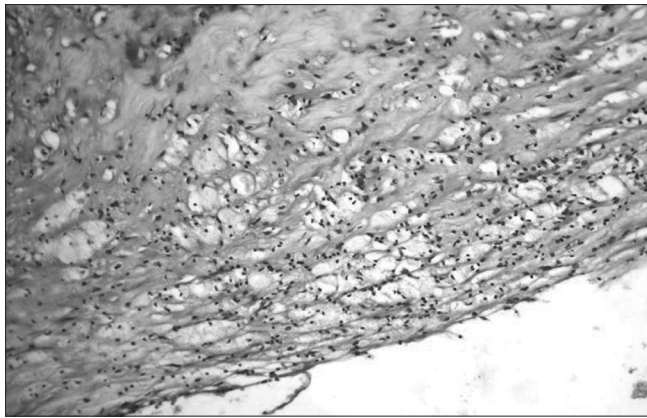


Figure 7: Microphotograph showing coronary artery with severe inflammation (H and E, x 100)

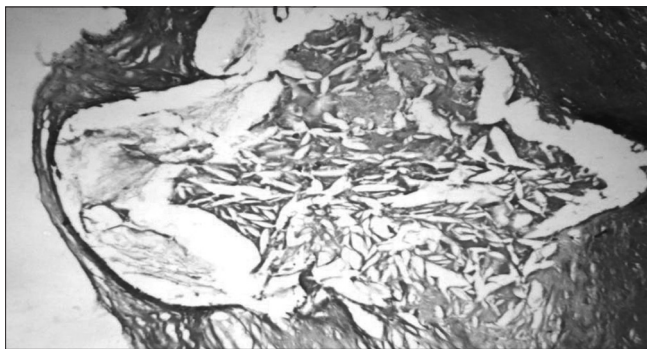


Figure 8: Microphotograph showing coronary thin fibrous cap atheroma (H and E, x 100)

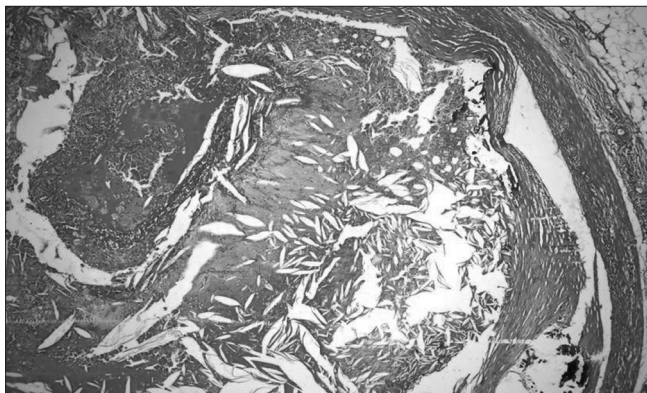


Figure 9: Microphotograph showing coronary fibrous cap atheroma with calcification and rupture. (H and E, x 100)

alcohol intoxication, ruptured uterus and hypertensive encephalopathy. Maximum victims of RTAs were males (40%) and maximum victims of burns were females (6.67%). Dividing the cause of death as suicidal and non-suicidal, there were 64 (56.6%) subjects who had died due to non-suicidal causes and 49 (43.3%) subjects who had died due to suicidal causes. Atherosclerosis in the young individuals who had committed suicide was significantly more than the young individuals who had died of non-

Table 1: Age distribution of the cases

Age group (years)	Male	Female	Total	Percent (%)
0-9	0	2	2	1.8
10-19	7	5	12	9.7
20-29	19	12	31	25.7
30-39	11	6	17	16
40-49	20	2	22	22
50-59	13	4	17	15
60-69	4	6	10	8
70-79	0	0	0	0
80-89	1	1	2	1.8
Total	75	38	113	100

Table 2: Distribution of atherosclerosis in young individuals

15-34 Age group (n-52)	Coronaries (%)	Aorta (%)
Non-atheromatous	40	12
Pathological intimal thickening	44	70
Advanced atherosclerotic lesions	16	18

Table 3: Distribution of atherosclerosis in older individuals

35-85 Age group (n-61)	Coronaries (%)	Aorta (%)
Non-atheromatous	27	10
Pathological intimal thickening	40	50
Advanced atherosclerotic lesions	33	40

Table 4: Distribution of atherosclerosis in females

Females (n-35)	Coronaries (%)	Aorta (%)
Non-atheromatous	50	25
Pathological intimal thickening	32	48
Advanced atherosclerotic lesions	18	27

Table 5: Distribution of atherosclerosis in males

Males (n-35)	Coronaries (%)	Aorta (%)
Non-atheromatous	48	20
Pathological intimal thickening	39	48
Advanced atherosclerotic lesions	23	32

suicidal cause [Tables 6 and 7].

The degree of atherosclerosis in LAD was significantly more when compared to the RCA and LCA [Table 8]. The number of thin fibrous cap atheromas, erosion, thrombus, and the amount of inflammation, which are indicators of vulnerable plaques, was significantly more in the RCA when compared to LAD and LCA [Table 8]. Coronaries of five cases also showed calcified nodules, indicating extensive amount of calcium deposits causing luminal stenosis.

In the present study, the degree of atherosclerosis gradually increased as we moved from ascending aorta to the abdominal aorta. The degree of atherosclerosis, amount of inflammation, and calcification were all significantly more in

Table 6: Distribution of atherosclerosis in the young individuals of the suicide group

15-34 yrs - Suicide group (n-25)	Coronaries (%)	Aorta (%)
Non-atheromatous	33	6
Pathological intimal thickening	48	72
Advanced lesions	19	22

Table 7: Distribution of atherosclerosis in the young individuals of the non-suicide group

15-34 yrs non-suicide group (n-24)	Coronaries (%)	Aorta (%)
Non-atheromatous	46	25
Pathological intimal thickening	40	60
Advanced lesions	14	15

Table 8: Artery based distribution of atherosclerosis

Lesion	LAD	LCA	RCA	AA	TA	Ab A
IT	06	02	00	00	00	00
IX	49	54	55	35	22	18
PIT	27	34	37	55	59	54
FCA	30	22	18	14	21	29
TFCA	01	01	03	09	11	12

LAD = Left anterior descending artery, LCA = Left circumflex artery, RCA = Right coronary artery, AA = Ascending aorta, TA = Thoracic aorta, Ab.A = Abdominal aorta, IT = Intimal thickening, IX = Intimal Xanthoma, PIT = Pathological intimal thickening, FCA = Fibrous cap atheroma (thick), TFCA = Thin fibrous cap atheroma

the abdominal aorta indicating the increased hemodynamic shear forces that are present in the abdominal aorta [Table 8].

DISCUSSION

CHD incidence is decreasing in Western Europe, the United States, and in Australia but is steeply increasing in Central and Eastern Europe, Asia, and Africa.^[9] The greater cause for concern is the early age of CHD deaths in the developing countries compared to the developed countries, which cripple the major work force of the nation.^[10,11] Since atherosclerosis is known to increase with ageing, the need of the hour is to assess the incidence of atherosclerosis in the young population who are being exposed to atherogenic influences like sedentary lifestyle and poor dietary habits. In the 15-34 age group (n-52), 16% of the coronaries and 18% of aortas showed advanced lesions (fibrous cap atheromas) [Table 3]. In the study by Fausto N on atherosclerosis in young people, he found that 10% of the individuals had advanced atherosclerosis.^[4] The incidence in our population is higher than the western population studied by Fausto N and highlights the fact that Indian youth are having increased incidence of atherosclerosis at a younger age. Noeman A *et al.* have reported an incidence of CAD of 5% for western population compared to 12-16% in the South East Asian population and their findings correlate with the findings of our study.^[11] The other point worth noting is the increased number of intermediate lesions

(pathological intimal thickening) seen in the coronaries of young Indians. These raised lesions are precursors of future advanced atherosclerotic lesions.^[7] Early implementation of anti-atherosclerotic measures can help prevent the development of these raised lesions and future CHD.

The hypothesis proposed and pioneered by Dr. David Barker states that the 20th century epidemic of coronary heart disease in Western countries might have originated in fetal life.^[12] He reported that the deaths from ischemic heart disease were commoner in men who had been small at birth and at 1 year of age. This has been attributed to permanent metabolic and endocrine changes caused by impaired nutrition in fetal life, which would have been beneficial if nutrition remained scarce after birth. If nutrition becomes plentiful after birth, it predisposes to obesity and impaired glucose tolerance, which are a few of the major causes of atherosclerosis. Indian babies are usually small, with a mean birth weight of only 2,700 gms and 30% have a birth weight of 2,650 gms or less.^[12] Since the birth weight of cases autopsied were not available, a correlation could not be made. Nonetheless, low birth weight generally seen in many babies born in a semi-urban and rural population like ours could play role in the development of early atherosclerosis.

Human immunodeficiency virus too can cause accelerated atherosclerosis as was seen in a 35-year-old male who was not on highly active anti-retroviral therapy.^[13] Due to the improved treatment regimes and infection control, people infected with HIV are living longer and the incidence of chronic diseases caused by atherosclerosis have risen, which need to be controlled by anti-platelet and lipid controlling drugs.

Among the population which was aged between 35-85 yrs [Table 3], the incidence of atherosclerotic lesions in aorta was 90% with 40% being advanced atherosclerotic lesions. In the coronaries, the incidence of atherosclerotic lesions was 73% with 33% being advanced lesions. Puri N *et al.* have reported an incidence of 86% atherosclerosis in their study on Indian population of Haryana.^[3] The wide difference between the present study and the study by Puri N *et al.* might be due to the fact that they used the earlier AHA classification and considered even grade I and II lesions as atherosclerotic. In the present study since we have used the modified AHA classification of atherosclerosis, the earliest lesions like intimal thickening and intimal xanthoma were not considered as atherosclerotic lesions, partly explaining the difference in the incidence of atherosclerosis. Yazdi *et al.* have reported an incidence of 71.2% in another study on Asian population using the earlier AHA classification.^[2]

As has been seen in other studies conducted both on Western and Indian populations, the incidence of atherosclerosis was more in males compared to females.^[2,14-17] In the coronary atherosclerotic lesions seen in our study, 50% were females and 62% males, which is comparatively lesser than that seen in the population of Iran where 61.6% females and 73.1% males had atherosclerosis, as reported by Yazdi SAT *et al.*^[2] The reasons for such a difference could be due to the fact that majority of the cases in the present study were from the semi-urban population, in whom, the degree of atherosclerosis and the incidence of CHD is said to be low compared to the urban population.^[18-20] Singh H *et al.* have reported the incidence of atherosclerosis in the coronaries to be 68% in males and 27% in females.^[15] The frequency of atherosclerotic lesions was 28.9% in a study by Golshahi *et al.*^[17] In the present study, the incidence of atherosclerotic lesions in males [Table 3] in the aorta was 80% of which 32% were advanced atherosclerosis and coronaries showed 62% atherosclerotic lesions of which 23% were advanced lesions. The incidence of atherosclerotic lesions in females [Table 4] in the aorta was 75% of which 27% were advanced lesions. In the coronaries of females, the incidence of atherosclerotic lesions was 50% of which 18% were advanced lesions.

In various studies done on different age groups, the frequency of atherosclerosis were reported to be between 16% to 75%.^[2,14,15,17] The reason for this diversity could be the variability of race, culture (varied dietary habits, different economic status), and various other environmental factors.^[17] Atherosclerosis being a chronic phenomenon, starting in childhood and extending into adulthood, the cause of death seems to play a minor role in explaining the difference in degree of atherosclerosis except for in individuals who have committed suicide, since suicide is an indicator of depression and stress in the individual. Stress can be defined as a threat to homeostasis provoked by environmental, psychosocial, or physiological stressors.^[21] In humans, psychological stress and hopelessness can be risk factors for cardiovascular catastrophes such as stroke, coronary ischemia, and myocardial infarction, which occur secondary to increased atherosclerosis.^[21-24] These conditions can be silent killers, as seen in subjects who are extremely fit and without known risk factors for cardiovascular disease but suffer sudden catastrophic events such as heart attacks under conditions of sustained stress.^[17] In the present study, the number of deaths due to suicide was 49 (43%) and due to other causes were 64 (57%). The majority of suicides were due to consumption of poison and a few were due to burns. Since atherosclerosis is an age dependent phenomenon, the difference in degree of atherosclerosis between cases more than 34 years between

the suicide group and non-suicide was not significant (P value > 0.05). In cases who were equal to or less than 34 years, a significant (P value < 0.05) difference in atherosclerotic patterns were seen with cases that had died of suicide having more atherosclerosis than the cases that had died of other causes.

This increased amount of atherosclerosis in suicide cases could be explained by the increased amount of psychological stress in patients who committed suicide. The increased stress leads to endothelial dysfunction, which is a major cause for initiation and development of atherosclerosis.^[22-24] Altered hypothalamic pituitary adrenal axis and impaired platelet function of platelets have also been implicated as mechanisms by which chronic psychological stress can cause increased atherosclerosis leading to increased CHD.^[22,23] Positive affect is defined as the experience of pleasurable emotions such as joy, happiness, and contentment is associated with increased survival, lower risk of diabetes and hypertension.^[25] Increased positive effect is said to be protective against 10-year incident CHD.^[25] Stressors in the suicide patients could be one of the causes for the increased atherosclerosis in our study but such a deduction would require detailed psychiatric history of the patients, which was not available.

The increased amount of atherosclerosis in left anterior descending artery and abdominal aorta as seen in this study has been seen and documented in many other studies. Regarding the increased amount of vulnerable lesions in the right coronary artery, the possible reason could be the increased amount of hemodynamic stresses. This might have occurred due to anatomical variations specific to this population. The other possible reason could be the antemortem cardiovascular risk factors like cigarette smoking, information about which was not available.

No information regarding the cardiovascular risk factors was available in the patients autopsied, which is a major limitation of the study. The strength of the study is that, to the best of our knowledge this is one of the first Indian studies where the modified AHA classification has been used. This classification defines intermediate lesions, which are indicators of future burden of disease better than the earlier AHA classification. In this study, we came across three cases that died of rare coronary artery anomalies, which were proved only after a detailed study of the coronary arteries at autopsy which highlights the use of autopsy. The cause of death in one of these cases was the unusual origin of right coronary artery from the left circumflex artery leading to kinking of the artery.^[26] Dominant left coronary artery with total absence of right

coronary artery is a very rare coronary anomaly, which was the cause for the sudden death in one of the case.^[27] Myocardial bridging is said to be protected from the hemodynamic shear stress hence from development of atherosclerosis, but this unusual combination was seen in one of the cases.^[28]

CONCLUSION

Autopsy-based studies for studying the prevalence of atherosclerosis in a population are cost-effective procedures and help in estimating the future disease burden in the population. This helps in proper planning of preventive measures and ensures that it is directed at the right population. An increased prevalence of atherosclerosis was found in the present studied population, specifically the young individuals indicating that preventive measures should be instituted early in Indians. The data obtained here would act as baseline data for further studies to study atherosclerosis in relation to risk factor incidence in this population.

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How to cite this article: Thej MJ, Kalyani R, Kiran J. Atherosclerosis in coronary artery and aorta in a semi-urban population by applying modified American Heart Association classification of atherosclerosis: An autopsy study. *J Cardiovasc Dis Res* 2012;3:265-71.

Source of Support: Nil, **Conflict of Interest:** None declared.