

ORIGINAL ARTICLE

Morphological Array of Cardiac and Coronary Artery Diseases in Cases of Sudden Death: An Autopsy-Based Histopathological Study in Rural Setup

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Abstract :

Cardiovascular diseases are the foremost cause of sudden death in adults. The primary objective of this study is to estimate the prevalence of various cardiac and coronary artery diseases in sudden unexpected death cases in rural setup. Estimation of age and sex-wise frequency of coronary atherosclerotic disease (CAD), and grading of CAD by applying the Modified American Heart Association (AHA) classification are secondary objectives. In this three years prospective cross-sectional study, heart specimens were studied from 136 persons whose death was sudden and unexpected. Gross dissection and histopathological examination of coronary arteries and heart were done. Diagnoses were based on both gross and microscopic findings.

CAD with or without other diseases was the most frequent pathology (n-100, 73.5%). Left ventricular hypertrophy in 45 cases (33.09%), myocardial infarction in 30 cases (22.06%), valvular abnormalities in three cases (2.2%), infective endocarditis in two cases (1.47%), aortic dissection in one case (0.74%), right ventricular hypertrophy in one case (0.74%) and cardiac myocyte atrophy in one case (0.74%) were observed. Male-female ratio of CAD was 8.09:1. Advanced CADs (type IV, V, VI) were found in 94 (94%) cases. In males, the maximum number of advanced CAD was observed in the fifth decade (n- 27, 31.76%) and in females in the seventh decade (n- 4, 44.44%). This study reveals the increasing trend of CAD in rural populations. This study adds rare entities like young-age aortic dissection and cardiac myocyte atrophy to the existing literature and emphasises the importance of autopsy in sudden death cases.

Keywords : Aortic dissection; Coronary atherosclerotic disease; Infective endocarditis; Left ventricular hypertrophy; Myocardial infarction.

Introduction :

Cardiovascular diseases (CVD) are the foremost cause of sudden death in adults.¹ In India, most of the studies carried out in sudden death cases explored coronary atherosclerotic disease (CAD) in detail. The detailed histopathological study of all cardiovascular pathology irrespective of their causality to the event of sudden death is minimal. The present study had been undertaken with the primary objective of estimating the prevalence of various cardiac and coronary artery pathology in sudden unexpected death cases autopsied at our institution. Secondary objectives are (1) The estimation of age and sex-wise frequency of CAD and (2) The grading, and analysis of CAD by applying the Modified American Heart Association (AHA) classification.

Materials and Methods :

The present prospective cross-sectional study was conducted at a teaching hospital catering to the rural population. The present study was carried out in the pathology department in collaboration with the Department of Forensic Medicine, for 3

years (Jan 2019 – Dec 2021), after getting approval from the institutional ethical committee.

All the heart specimens of sudden unexpected death cases according to the WHO definition i.e., death occurring in ≤ 24 hours of the onset of symptoms were included in the study,² irrespective of their age and past history of CVD. The autolysed heart specimens and unnatural death cases were excluded from the study.

The heart specimens were fixed in ten per cent neutral buffered formalin, weighed, and measured, and coronary arteries were dissected carefully. Then the three major coronaries were serially sectioned at 3mm intervals to examine the pathological changes. Ventricles of the heart were dissected by short-axis method, to examine myocardial pathologies. Inflow-outflow method dissection was done for the rest of the heart. (Fig.-1) Appropriate tissue sections were processed routinely and stained with haematoxylin and eosin stains. Decalcification of the calcified blood vessels was done prior to processing.

The extent of atherosclerotic changes was studied microscopically and graded according to the modified AHA classification of atherosclerosis based on the morphological description.³ A brief summary of Modified AHA classification is as follows: Type I - isolated macrophages and foam cell collections in the arterial intima, Type II (fatty streak lesions) – mainly intracellular lipid accumulation, Type III – II changes with

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Article History

DOR : 03.07.22; DOA : 07.11.22

small extracellular lipid pools, Type IV- II changes and core of extracellular lipid, Type V- lipid core and a thick layer of new fibrous connective tissue, Va- when the new fibrous tissue is part of the lesion with a lipid core, Vb- when lipid core and other parts of the lesion are calcified, Vc- when the lipid is minimal or absent and the lesion is fibrotic, Type VI – complicated lesions with fissure, haematoma and thrombus.³

Morphology and extent of atherosclerotic lesions according to age and sex were analysed. The proportions were analysed using the chi-square test where ever appropriate.

Results :

One hundred and thirty-six heart specimens of sudden unexpected death cases were received during the study period. The age of the study cases was between three months to eighty years [Mean 42.79 years, Standard deviation (SD) 16.47]. Two cases were below one year of age. Among the study cases, 77% (n- 105) of specimens were male, and 23% (n-31) from female. The maximum number of study cases were in the 41-50 years age group (n- 35, 25.74%).

The mean age for male cases was 44.36 years with an SD of 15.57. The mean age for female cases was 36.42 years, SD 19.14.

Three cases have pre-existing diagnoses and treatment histories for CVD. Those were rheumatic heart disease (RHD) with mitral stenosis (MS), ventricular septal defect (VSD) with surgical closure, and a CAD case treated with stent.

CAD in association with or without other diseases was identified in 100 cases (73.53%), which was the most frequent pathology (Table-1). Male cases affected by CAD were 89 (89%), and female cases affected by CAD were 11 (11%) with a p-value of 0.00001 (statistically significant). Male: Female ratio of CAD is 8.09:1.

Among CAD, advanced atherosclerotic lesions (type IV, V, VI) were found in 94 (94%) cases including 85 (90.43%) male cases and nine (9.57%) female cases (Image 2- a, b, c).

Above 61 years of age, all the study cases had advanced CAD. The overall relative frequency of advanced CAD in young individuals (<40 years) was 49.15% (n-29) (Graph -1).

In males, the maximum number of advanced CAD was observed in the fifth decade (n- 27, 31.76%) and in females in the seventh decade (n- 4, 44.44%) (Graph-1).

Among advanced atherosclerotic lesions, cases with complicated plaque (type VI) were 18 (19%).

Among CADs, more than 50% stenosis of the lumen by atherosclerotic lesions was found in 43 (43%) cases, in any one or more than one, of the epicardial vessels (Fig. – 2 d).

The left anterior descending artery (LAD) was the most common artery to be affected by CAD (n-93,93%). The second most common artery was the right coronary artery (n-65,65%). The least common artery to be affected by CAD was the left circumflex artery (n-42,42%).

The maximum number of cases had double vessel involvement by CAD (n-43, 43%).

The second most common pathology observed was left ventricular hypertrophy (LVH) (n-45, 33.09%) found in association with other diseases mainly CAD (n-34,25%) (Table - 1). Thirty-nine (86.67%) cases of LVH were male and six cases (13.33%) were female (Table – 2). LVH cases had left ventricular wall thickness ranging from 1.8 to 2.5 cm.

Myocardial infarction (MI) was found in 30 (22.06%) cases with the highest frequency in the fifth decade (n-11, 36.67%). Acute MI was found in nine cases (6.61%), Healed MI in 17 cases (12.5%), and acute and healed MI in four cases (2.94%).

In acute MI, grey-brown haemorrhagic areas were identified in the gross examination. In microscopy myocyte necrosis, acute inflammatory cell infiltration, congestion, and haemorrhage were made out (Fig. 3- a, b).

In healed infarcts, white fibrotic areas with thinned-out myocardium were made out in the gross examination. In microscopy fibrosis with entrapped hypertrophic myocytes and chronic inflammatory cell infiltration were made out (Fig. 4).

All 30 specimens with MI had advanced CAD. Triple vessel involvement was found in 14 (46.67%) MI cases. All 30 MI cases were male. Critical stenosis of coronary arteries (>50%) was found in 20 (66.67%) cases of MI. The youngest age of myocardial infarction was 24 years.

The youngest person affected with advanced CAD was a 19 years old male, who died of Type A ascending aortic dissection (AD) and hemopericardium (Fig. 5 – a, b). LVH was also observed in this case.

Three cases of valvular abnormalities (2.2%) including two cases of MS and one case of calcific aortic stenosis (AS) were observed (Image 6 – a, b). In both cases of MS, mitral valves were tight and calcified. Microscopically fibrosis and calcific degeneration in mitral valves were noted. No active inflammation was detected.

Infective endocarditis (IE) was observed in a 36 year old male case and a 17 year old female case (1.47%). In both cases, mitral valve vegetations with ruptured chordae tendineae were noted (Fig. 7-a). Microscopic sections from the mitral valve vegetations showed huge mixed inflammatory cell infiltration with lots of histiocytes and multinucleated giant cells. (Fig. 7-b) In a 5-year-old male case with pigeon chest deformity, right ventricular wall hypertrophy (RVH) was found.

Small-sized heart with a weight of 50 grams was found in a 45-year-old malnourished and mentally retarded male case. On microscopy, cardiac myocyte atrophy was made out (Fig. 8 - a, b).

Discussion :

Compared with all other countries, India suffers a huge loss in the productive age group of 35-64 years due to CVD.⁴ The prevalence of CVD is high in urban populations compared to the rural population in India.⁴

In this rural setup study, CAD was the most frequent disease. Apart from that, a wide spectrum of heart lesions was encountered during this study period encompassing congenital heart diseases, IE, acquired valvular diseases, cardiac myocyte adaptations, and aortic dissection. The epidemic of CAD began in



Fig. 1: Gross examination - a) Coronary blood vessels dissection, b) Three major epicardial arteries serial sectioned and showing atheromatous plaque.

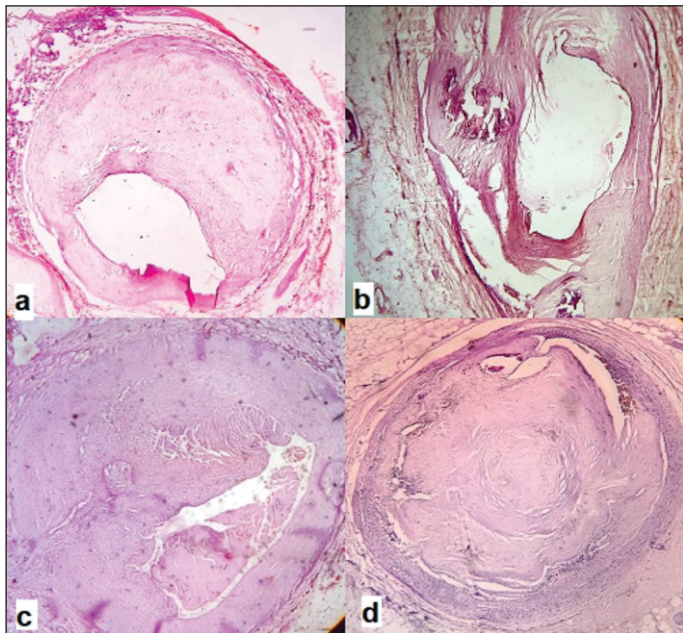


Fig. 2: Light microscopic features - a) Type Va fibro atheromatous plaque with significant lumen narrowing (H&E 4X), b) Type Vb calcified atheromatous plaque, c) Type VI atherosclerosis with plaque rupture and intraplaque haemorrhage (H & E 10X), d) Atheromatous plaque with more than 90% stenosis of the lumen (H & E 4X).

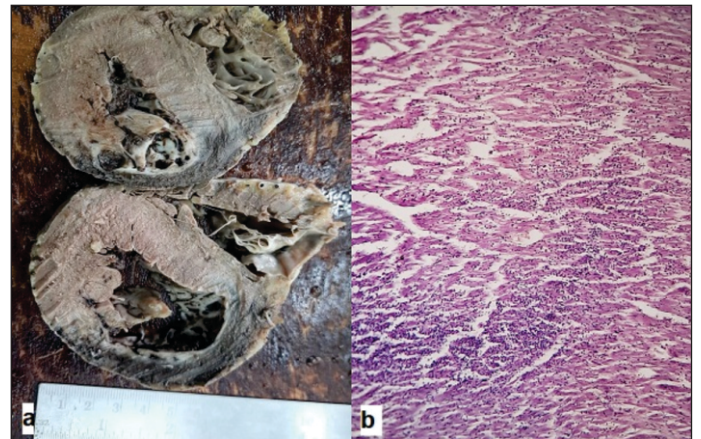


Fig. 3: Acute myocardial infarction - a) Gross examination showing massive infarct in the anterior wall of the left ventricle, b) Microscopic picture showing myocyte necrosis and acute inflammatory cell infiltration (H & E 10X).

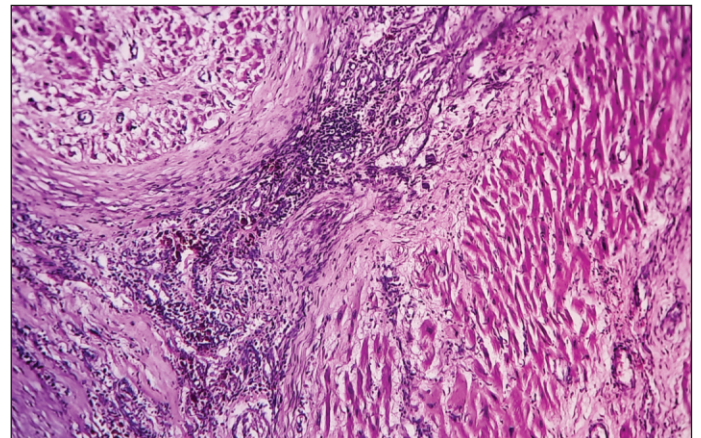


Fig. 4: Chronic myocardial infarction – Microscopic feature showing fibrosis, chronic inflammatory cell infiltration, and entrapped hypertrophic myocytes (H & E10X).

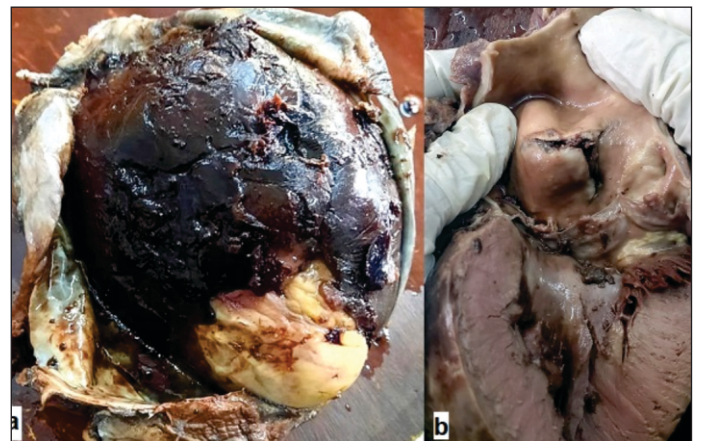


Fig. 5: a) Hemopericardium in a case of ascending aortic dissection, b) Ascending aortic dissection.

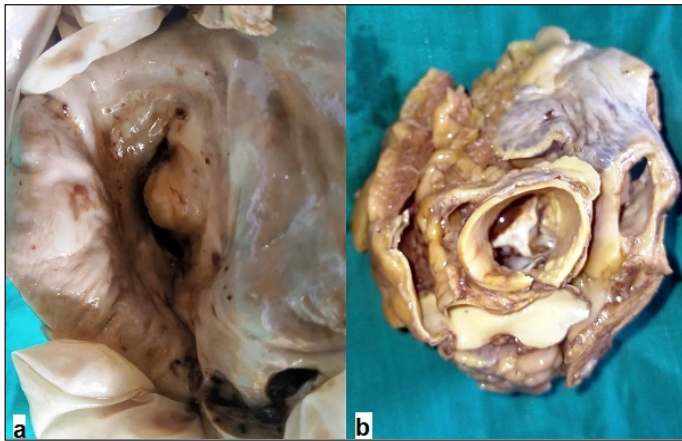


Fig. 6 : a) Mitral stenosis with the tight and calcified mitral valve, b) Aortic stenosis with calcified aortic valve.

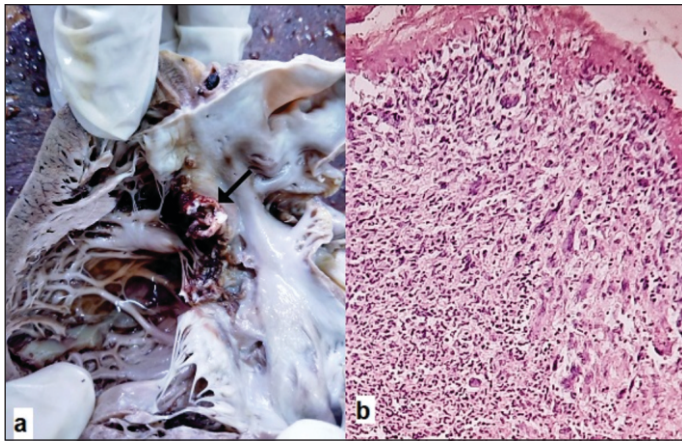


Fig. 7 : a) Infective endocarditis with mitral valve vegetations and ruptured chordae tendinae b) Microscopic picture showing mitral valve vegetations with huge mixed inflammatory cell infiltration, histiocytes and multinucleated giant cells (H & E 40X).

developed countries during the last century with a declining phase there now. But it is assuming a serious dimension in developing countries like India now. The prevalence rate of CAD in India is 6.4% (6.1% in males, 6.7% in females) in urban areas and 2.5% (2.1% in males and 2.7% in females) in rural areas.⁴

The most frequent pathology identified in the present study is CAD (73.5%) which is comparable with other similar autopsy studies.⁵⁻⁸ (Table -3) CAD was the single largest cause of death accounting for 119 deaths among 204 study cases (41%) in the study of Dayananda R et al.⁹ to find out the pattern of the causes of sudden natural deaths.

The percentage of CAD-related deaths is highest in subjects over 40 years of age.¹ In the present study, the maximum number of sudden unexpected death cases were in the 41-50 years age group (n- 35, 25.74%). Male dominance in study subjects is seen in many autopsy-based cardiac and coronary disease studies.⁵⁻⁸

There was a significantly increased prevalence of CAD observed in males than females in the present study (Male female ratio 8.09:1). The male-female ratio of Ekta rani et al.⁵ and Rao et al.¹⁰

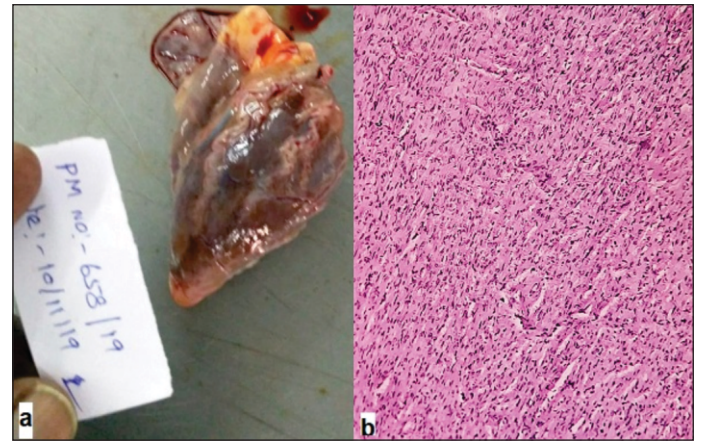


Fig. 8 : a) Small-sized heart b) Microscopic picture showing cardiac myocyte atrophy (H & E 10X).

Table - 1 Distribution of various cardiovascular pathology with their relative frequency.

Pathology	No of cases	Percentage
Coronary arterial atherosclerotic disease (CAD) alone	32	23.53%
Acute/healed myocardial infarct (MI) with CAD	21	15.44%
Acute/healed myocardial infarct (MI) with CAD and Left ventricular hypertrophy (LVH)	9	6.62%
Left ventricular hypertrophy (LVH) with CAD	34	25%
Surgically closed Ventricular septal defect (VSD)	1	0.74%
Rheumatic mitral stenosis	1	0.74%
Mitral stenosis (MS)with CAD	1	0.74%
Calcific aortic stenosis (AS) with CAD with LVH	1	0.74%
Infective endocarditis (IE) with early CAD	1	0.74%
Infective endocarditis (IE)	1	0.74%
Aortic dissection (AD) with CAD with LVH	1	0.74%
Cardiac atrophy	1	0.74%
Right ventricular hypertrophy (RVH)	1	0.74%
Normal study	30	22.06%
Total	136	100%

are 11:1 and 10:1 respectively, which is closer to the present study results.

In the present study, advanced CAD was observed in males from the second decade onwards, and its frequency consistently increased as the age advanced and a maximum number of cases were in the fifth decade. In the studies of Udasimath S et al.⁶ and Rao et al.¹⁰ the maximum number of CAD was observed in the sixth decade. It is well established that the risk for CAD is less in females during reproductive years. In the present study advanced CAD in females was observed from the fourth decade onwards and a maximum number of cases were in the seventh decade.

In their study on grading and occurrence of coronary artery stenosis in different age groups D. Ganesh Rajahan et al. observed > 50% of lumen stenosis in 38.7% (n-24) of cases which is comparable with our study result of 43% (n-43).¹¹

LAD was the most common artery to be affected by atherosclerosis in the studies of Suwarna Patil et al. (88.2%),⁸ Bhanvadia et al. (42%),¹² Kumar S et al. (68%),¹³ Lakshmi Sudha et al. (47%).¹⁴ In the present study also LAD is frequently

Table- 2 Frequency of left ventricular hypertrophy according to age and sex.

Age group in years	No of cases	Relative frequency	Male		Female	
			No of cases	Relative frequency	No of cases	Relative frequency
11-20	1	2.22%	1	100%	-	-
21-30	2	4.44%	2	100%	-	-
31-40	11	24.44%	9	81.82%	2	18.18%
41-50	13	28.89%	13	100%	-	-
51-60	8	17.78%	7	87.5%	1	12.5%
61-70	7	15.56%	5	71.43%	2	28.57%
71-80	3	6.67%	2	66.67%	1	33.33%
Total	45	100%	39		6	

Table - 3 Comparison of the relative frequency of coronary atherosclerotic disease with other studies.

Ekta rani et al ⁵	77.3% (n-75)
Udasimath S et al ⁶	84.16% (n-574)
Sanjay D.Gaiwale et al ⁷	90.14% (n-101)
Suwarna Patil et al ⁸	90.7% (n-68)
Present study	73.5% (n-100)

involved by CAD (93%).

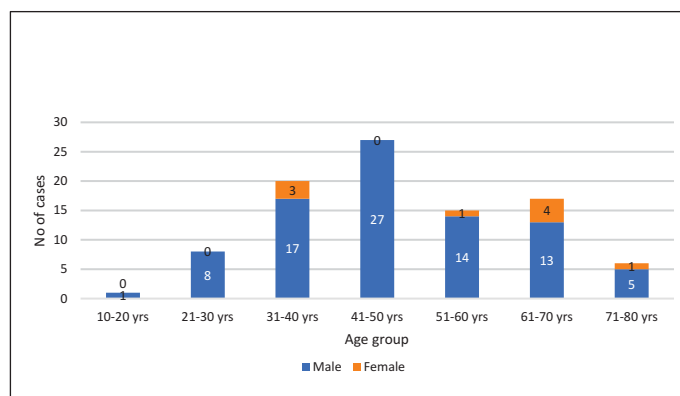
In the present study, MI was found in 30 cases (22.06%) with the highest frequency in the fifth decade which is comparable with the observations of Suwarna Patil et al. 23 cases (30.7%).⁸ The youngest person dying of MI was 24 years old in the present study, which was 26 year old in the study of Suwarna Patil et al.⁸ The frequency of acute and healed MI in this study (acute MI - 6.61%, healed MI - 12.5%, both acute and healed - 2.94%) is comparable with the studies of Udasimath et al. (n- 682 acute MI - 12.02%, healed MI - 15.15%),⁶ Ekta rani et al. (n- 97 acute MI - 3.09%, healed MI - 13.4%).⁵ The frequency of MI is relatively low in the study of Siddiqui MI et al. (n- 430 acute MI - 0.4%, healed MI - 1.16%).¹⁵ This may be due to that more than half of their study subjects were in the 11–30 years age group.

LVH is a common finding in autopsies, which could be the cause of arrhythmogenesis.¹⁶ In the present study, LVH was the second most common pathology (n-45, 33.09%) observed.

Calcific AS is the most common of all valvular abnormalities. It is a consequence of recurrent chronic injury due to hyperlipidaemia, hypertension, inflammation, and other factors similar to those implicated in atherosclerosis.¹⁷ The material that deposits in the valves is hydroxyapatite. In the present study, one case of calcific AS was found (0.74%). The prevalence of AS in the present study is lower than the general population prevalence which is 2%.¹⁷

In developing countries like India, the most common cause of MS is RHD, the prevalence of which is 5-7% in India.⁴ The relative frequency of MS in the present study is 1.47%.

AD is very rare in the younger age group. Risk factors for AD in the younger age group are congenital CVDs, connective tissue disorders, trauma, pregnancy, hypertension, and idiopathic.^{17,18} In their ten years retrospective study done from the database of State wide Planning and Research Cooperative System, New York State, the occurrence of AD in ≤ 21 years of age was 0.37% (n-45).¹⁸ The relative frequency of AD in the present study is 0.74%

**Graph 1 - Age and sex distribution of advanced coronary atherosclerotic diseases.**

(n-1) which was observed in a 19-year-old male. LVH and grade V coronary atherosclerosis were also found in the same case. However full clinical workup including connective tissue disorders had not been carried out for this case.

IE is a relatively rare condition but has a high mortality rate. It is caused by microbial infection of the heart valves and endocardium. Aortic and mitral valves are the most commonly involved valves. There are several risk factors for IE including structural heart diseases, prosthetic cardiac valves, intravenous drug abuse, and RHD. In developing countries, RHD is the most common risk factor.¹⁹ In the two cases of IE (1.47%) observed in the present study, the mitral valve was affected by vegetation. Both were of young age (< 40 years).

With an incidence of 2–5%, VSD is the most common congenital malformation of the heart and VSD repair is the most commonly performed surgery in children.²⁰ A study by J W Roos- Hesselink et al concluded that late survival after VSD repair is poorer than the general population.²¹ Causes of mortality were arrhythmia, heart failure, endocarditis, during valvular surgery, pulmonary hypertension, noncardiac causes, and unknown causes.²² In the present study, one case of VSD (18 years/Female) was observed, for which surgical closure had been done before 5 years.

From the studies done on starved and malnourished people, it became apparent that cardiac muscles undergo atrophy in the state of chronic malnutrition.²³ In the present study, cardiac myocyte atrophy was observed in a mentally retarded and malnourished individual.

Conclusion :

Based on the results of the present study, it could be stated that CAD is increasing in trend in India's rural population. Even though the frequency of CAD increases with age, significant CAD has been observed from the second and third decades onward in the present study. Awareness regarding CAD, its risk factors, and lifestyle modifications have to be reinforced among the general public.

Apart from CAD, in sudden death cases, other rare CVDs have also been reported in this study, which emphasises the importance of autopsy in sudden unexpected death cases. Establishing a post-mortem diagnosis will facilitate the family members to be

screened for risk factors, early diagnosis, and treatment.

The present study also adds valuable data regarding rare entities like young age presentation of aortic dissection and cardiac muscle atrophy to the existing medical literature.

Ethics clearance: A prior approval was obtained from the institutional ethical committee

Conflict of interest: The authors declare that there is no conflict of interest

Source of funding: None to declare

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