

ORIGINAL ARTICLE

Histopathological Evaluation of Cardiac Lesions in Autopsy Specimens

Clement Wilfred D¹, Chinki Anupam²

ABSTRACT

CONTEXT: Evaluation of cardiac autopsy specimens is crucial for identifying concealed cardiovascular pathology and providing insights into the pathogenesis and progression of disease. Hence, this study was undertaken to evaluate the histopathological features of cardiac lesions in autopsy specimens.

METHOD: This was a prospective cross-sectional study conducted on cardiac specimens from routine autopsies over a period of three and half years, between January 2018 and June 2021, at M.S. Ramaiah Medical College and Hospitals, Bengaluru. The hearts were evaluated grossly and microscopically to identify the various histopathological changes. **RESULTS:** A total of 250 cases, with mean age of 39±15 years and male-female ratio of 4.4:1, were evaluated. In 207 (82.8%) cases 299 morphological lesions were identified, comprised of coronary atherosclerosis (52.4%), myocardial infarction (26%), aortic atherosclerosis (21.2%), cardiac hypertrophy (12%), valvular disease (2%), aortic dissection (2%), cardiac tamponade (1.6%), pericarditis (1.2%), myocarditis (0.8%) and cardiomyopathy (0.4%). **CONCLUSION:** Cardiac lesions were detected in 82.8% in autopsies. The most frequent finding is coronary atherosclerosis with triple vessel involvement being the commonest. Severe luminal occlusion, calcification and thrombosis are most frequent in Left anterior descending coronary artery. The next most common lesion is Myocardial Infarction, the most significant pathogenetic mechanism of which is coronary atherosclerosis. There is a strong association between coronary and ascending aorta atherosclerosis. Thus, many preventable and concealed lesions are discovered at cardiac autopsies and this data is important for assessing disease trends and introducing new interventions and therapeutic management regimes.

KEYWORDS | atherosclerosis, autopsy, cardiac specimen, coronary, myocardial infarction

AUTOPSY PROVIDE AN OPPORTUNITY TO STUDY the etiopathogenesis of human diseases, to evaluate the influence of diseases on other organs systems, to correlate the macro and microscopic features of organs with clinico-laboratory findings and to determine the probable cause of death.¹

India has a high burden of cardiovascular disease (CVD) accounting for 28.1% of total deaths and 14.1% of total disability adjusted life.^{2,3} According to Global Burden of Disease study, the age standardized CVD death rate in India is 272 per 100,000 population, which is definitely higher than the global average

of 235.² Further its incidence is increasing, especially in the young urban population due to high incident rates of risk factors like obesity, diabetes, hypertension, dyslipidemia and smoking.²

Cardiac specimen is routinely sent for histomorphologic evaluation, following post-mortem examination, in order to detect any concealed CVD, especially in cases of sudden/unnatural death. Many CVD's are incidentally detected at autopsy.⁴ A wide and varied spectrum of cardiac lesions can be discerned on histopathology post autopsy and this data can provide valuable insights into the pathogenesis,

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How to cite this article

Clement Wilfred D, Chinki Anupam. Histopathological Evaluation of Cardiac Lesions in Autopsy Specimens. *Indian J Forensic Med Pathol.* 2022;15(1):25-31.

progression, epidemiology and clinical management.^{1,4} Hence the present study was conducted with the objective of evaluating the histopathological features and determining the frequency of the varied lesions identified in routine cardiac autopsy specimens.

MATERIALS AND METHODOLOGY

This was a single centre prospective cross-sectional study conducted on all cardiac specimens from routine consecutive autopsies over a duration of three and half years, between January 2018 and June 2021, at M.S. Ramaiah Medical College and Hospital, Bengaluru. Autolysed specimens and perinatal and neonatal autopsies were excluded.

The specimens were received in the autopsy division of histopathology section and in every case the standard protocol for surgical grossing by "Virchoff's method" was followed. The dimensions, weight, thickness of right and left ventricular and interventricular septum were recorded. The status of the i) atrial, ventricular and septal walls (defects/infarcts); ii) chambers (normal/dilated); iii) valves (stenosis/calcification/regurgitation); and iv) tendinous cords – (thickening/fusion/rupture) were recorded. The aorta was observed for atheromatous lesions, aneurysmal dilation and dissection. The three major epicardial coronary arteries were sectioned along their entire course, starting from their ostia, every 3 to 5 mm and examined for atheromatous lesions and thrombi. For microscopic examination, representative bits were taken from the right and left ventricular walls and atrioventricular junctions, interventricular septum, apex and all the three major coronary arteries and aortic stumps. Additional bits were taken wherever necessary. The tissue bits were processed as per standard protocol and paraffin embedded blocks were cut and stained by haematoxylin and eosin (H & E). Light microscopic evaluation of the H & E stained slides was done and results were recorded. Coronary artery occlusion was graded based on narrowing in cross-sectional area as follows as follows: Grade 1- \leq 25% block, Grade 2- 26- 50% block, Grade 3- 51- 75% block

and Grade 4- \geq 76% block.⁵

The age, sex, cause of death and autopsy findings were obtained from the deceased post-mortem files.

Statistical Analysis: SPSS Version 18.0 software was used for analysis. All the continuous variables were expressed as mean and standard deviation and all qualitative variables as proportion. The percentage and frequency of each type of cardiac lesion was determined.

RESULTS

A total of 250 cardiac specimens were received, over a three and half year's duration. The mean age of the deceased was 39 ± 15 years (age range: 11 to 79 years) with male: female ratio of 4.4:1. Majority of the cases occurred in the 4th decade followed by 3rd decade (Table 1).

Cause of Death: The most common cause of death was cardiac disorders (37.2%) followed by respiratory disorders (16%). (Table 2). The unnatural cause of death is included in unintentional injuries (traffic accidents, snake bites and honey-bee stings) and in intentional injuries (homicide and suicide) (Table 2).

In 207 (82.8%) cases, 299 morphological lesions were identified depicted in Table 3, along with the age and sex distribution. In 134 cases (53.6%), multiple lesions were identified (Table 4). The most common histopathological lesion identified was coronary atherosclerosis (52.4%; 131/250) followed by myocardial infarction (26%; 65/250). There was no specific finding in 43 (17.2%) cases.

Of the 131 cases of coronary atherosclerosis, 39, 25 and 67 cases showed single, double and triple vessel diseases respectively (i.e. a total of 290 coronary arteries showed atherosclerotic plaques). (Figure1) Left anterior descending coronary artery (LAD) (40.7%; 118/290) was the most common to be involved followed by right coronary artery (RCA) (30%; 87/290) and left circumflex coronary artery (LCX) (29.3%; 85/290). Severe atherosclerosis with grade IV luminal occlusion was found most commonly in LAD. Superimposed thrombus and calcification were found in 7.6% (22/290) and 31.7%

AGE RANGE	NO. OF CASES (%)	MALES	FEMALES	M: F RATIO
10-20	30 (12%)	17	13	1.3:1
21-30	52 (20.8%)	40	12	3.3:1
31-40	67 (26.8%)	58	9	6.4:1
41-50	43 (17.2%)	40	3	13.3:1
51-60	36 (14.4%)	34	2	17:1
61-70	16 (6.4%)	10	6	1.6:1
71-80	6 (2.4%)	5	1	5:1
TOTAL	250	204	46	4.4:1

Table 1: Age and sex distribution of cases.

CAUSE OF DEATH	NO. OF CASES	
Unnatural causes	Unintentional	17 (6.8%)
	Intentional	26 (10.4%)
Natural causes	Cardiac	93 (37.2%)
	Respiratory	40 (16%)
	Neurological	10 (4%)
	Hepatic causes	27 (10.8%)
	Renal Failure	11 (4.4%)
	Sepsis	15 (6%)
	Haematological	1 (0.4%)
Unknown	10 (4%)	
Total	250	

Table 2: Distribution of cause of death

Coronary Artery	Grading of Coronary Artery Occlusion				Superimposed Thrombosis	Dystrophic calcification
	Grade I (≤25%)	Grade II (26-50%)	Grade III (51-75%)	Grade IV (>75%)		
RCA	12	36	25	14	3	30
LAD	10	37	39	32	16	35
LCX	10	32	28	15	3	27
Total	32	105	92	61	22	92

Legend: RCA - Right Coronary Artery, LCA - Left Circumflex Coronary Artery, LAD - Left Anterior Descending Coronary Artery.

Table 5: Distribution of coronary artery atherosclerotic changes.

Cardiovascular lesions	Present study, 2021 (n=250)	Garg S et al ⁷ , 2018(n=141)	Shah SN et al ⁸ , 2019 (n=152)	Rani E et al ⁹ , 2017(n=97)	Joshi C et al ⁶ , 2016(n=115)	Kulkarni MP ¹⁴ , 2018(n=250)
Coronary Atherosclerosis	131(52.4%)	78(55.3%)	93(61.2%)	75(77.3%)	74(64.3%)	123(49.2%)
Myocardial infarction	65(26%)	20(14.1%)	67(44.1%)	3(3.1%)	33(28.7%)	62(24.8%)
Aortic Atherosclerosis	53(21.2%)	—	—	—	—	—
Myocardial Hypertrophy	30(12%)	10(7.09%)	20(13.2%)	—	60(52.2%)	14(5.6%)
Valvular Heart Diseases	5(2%)	2(0.14%)	—	—	—	9(3.6%)
Aortic Dissection	5(2%)	—	—	—	—	—
Cardiac Tamponade	4(1.6%)	—	—	—	—	—
Pericarditis	3(1.2%)	4(2.8%)	—	1(1.03%)	1(0.9%)	—
Myocarditis	2(0.8%)	5(3.5%)	—	—	11(9.6%)	—
Cardiomyopathies	1(0.4%)	—	—	—	—	3(1.2%)
Others	—	—	14 (9.2%)*	18 (18.6%)**	11 (9.6%***)	9 (3.6%****)
No specific finding	43(17.2%)	22(15.6%)	51(33.6%)	0	29(25.2%)	30 (12%)

Table 6: Comparison of morphological lesions with other studies.

"n" indicates the total no of cases studied; The percentages are calculated from the total no of cases studied; * comprises of 14 cases of congestion, ** includes chronic ischemic heart disease (13.4%), congestion (2.1%), stromal fatty infiltration (2.1%), pericarditis & cysticercosis (each 1%); *** includes sickle cell anemia (5.2%) & fatty streaks (4.4%); **** includes DIC (1.2%), acute leukemia (0.8%), papillary fibroelastoma, amyloidosis, ventricular septal defect & sickle cell anaemia (each 0.4%)

Morphological lesions	No. of lesions	Mean Age	Males	Females	M:F
Coronary Atherosclerosis	131	45± 14 (20-75)	116	15	7.7:1
Myocardial infarction	65	45± 15 (19-75)	58	7	8.2:1
Aortic Atherosclerotic Plaque	53	49± 14 (21-75)	48	5	9.6:1
Myocardial Hypertrophy	30	35± 13 (14-67)	26	4	6.5:1
Valvular Heart Diseases	5	35.8 (13-50)	5	-	-
Aortic Dissection	5	41 (27-65)	3	2	1.5:1
Cardiac Tamponade	4	53 (20-65)	2	2	1:1
Pericarditis	3	47 (31-65)	2	1	2:1
Myocarditis	2	15 (11-20)	1	1	1:1
Cardiomyopathies	1	19	1	-	-
Total	299	39±15 (11-75)	178	29	6.1:1

Table 3: Morphological lesions identified in cardiac autopsy specimens with the age and sex distribution

MULTIPLE LESIONS IDENTIFIED	NO. OF CASES
Coronary Atherosclerosis and Myocardial infarction	65
Coronary Atherosclerosis and Aortic Atherosclerotic Plaque	53
Coronary Atherosclerosis and Myocardial Hypertrophy	10
Myocardial Hypertrophy and Aortic dissection	3
Coronary Atherosclerosis and Valvular Heart Diseases	1
Cardiac Tamponade with Aortic dissection and Coronary Atherosclerosis	1
Cardiac Tamponade with Aortic dissection, Myocardial hypertrophy and Coronary Atherosclerosis	1
Total	134

Table 4: Multiple morphological lesions identified in cardiac autopsy cases.

(92/290) of the lesions. The distribution of coronary atherosclerotic changes with extent of luminal occlusion and secondary changes are depicted in Table 5.

The aortic stump (ascending aorta) showed fatty streaks and atherosclerotic plaques in 76 and 53 cases, respectively. Of the atherosclerotic plaques, 3.8% (2/53) were complicated with surface erosions and 7.5% (4/53) showed calcifications. The 65 cases of myocardial infarction comprised of 22 (33.8%) recent infarcts and 43 (66.2%) old and healed infarcts (Figure 2).

Myocardial hypertrophy was seen in 30 cases with mean weight of 378±88 gm (range: 300-650 gm), mean left ventricular thickness of 1.7± 0.2 cm (1.3- 2.2cms) and mean right ventricular thickness of 0.7± 0.2 cm (0.4-1.3cms) (Figure 3A).

DISCUSSION

Histopathologic evaluation of heart in autopsies has greatly furthered our knowledge, providing valuable insights into the pathobiology of various cardiovascular diseases especially, congenital heart diseases, coronary atherosclerosis and myocardial infarctions.¹ The only way to study cardiac morphological features and correlate it with clinical features is via autopsy, as it is not possible to do this in the living.⁴ These autopsy studies not only provide valuable information regarding the cause and nature of death, but also provide valuable epidemiological information.⁶

The comparison of various morphological lesions identified in our study with other studies is shown in Table 6.

In the Present study cardiovascular lesions were identified in 82.8% of the cardiac autopsies similarly in the study by Garg S *et al.* 84.4% of the cardiac specimens showed lesions.⁷ Where as in studies by Shah SN *et al.* and Joshi C *et al.* cardiac lesions were found in 66.7% and 74.2% of the autopsies respectively.^{6,8} The male: female ratio was 6.1:1 in our study emphasising that males have a higher risk of cardiovascular disease. Similarly, many other cardiac autopsy

studies showed male predominance: Dhankar V *et al.* Joshi C *et al.* Shah SN *et al.* and Garg S *et al.* found male: female ratios of 2.7:1, 6.8:1, 3.1:1 and 12.8:1, respectively in their studies.^{4,6-8}

The commonest morphological lesion identified was coronary atherosclerosis (52.4%) which is in sync with studies by Dhankar V *et al.* (61.5%), Joshi C *et al.* (64%), Garg S *et al.* (55.3%), Shah SN *et al.* (61.2%), Rani E *et al.* (77.3%) and Karanfil R *et al.* (75%).^{4,6-10} Secondary changes like dystrophic calcification and superimposed thrombosis were present in 31.7% and 7.6% of the atherosclerotic lesions, respectively, in our study. Similarly, Marwah N *et al.* observed thrombosis in 7.5% of the lesions.¹¹ In other studies the frequencies of calcification and thrombosis ranged from 17% to 53.3% and 5% to 10.8%, respectively.⁶⁻⁸ In our study triple vessel involvement was most frequent followed by single vessel and double vessel involvement. However, in studies by Venkatesh K *et al.* and Sudha ML *et al.* triple followed by double and single vessel involvement was observed.^{5,11,12} Literature review revealed that the most frequently involved artery is LAD (45-64%) followed by RCA (24-46%) with LCX being least affected (3-10%).^{5,8,11,12} Our experience also is similar with LAD being the most frequently involved and LCX being the least involved. We observed that severe luminal occlusion (Grade IV stenosis), dystrophic calcification and superimposed thrombosis are most frequent in LAD, which is in sync with studies by Venkatesh K *et al.* and Marwah N *et al.*^{5,11} Thiripurasundari R *et al.* evaluated coronary arteries from 77 cases of unnatural deaths and observed that LAD shows maximum narrowing (49.4%) compared to other arteries.¹³ Unlike our findings, Shah SN *et al.* observed these changes more commonly in the LCX.⁸ Such discrepancies in frequency of lesions, among studies, could possibly be attributed to a selection of cases and handling of tissues (if meticulous sampling is not done atherosclerotic lesions, being focal, can be missed).¹¹

The second most common lesion identified was MI (26%), which is in accordance with

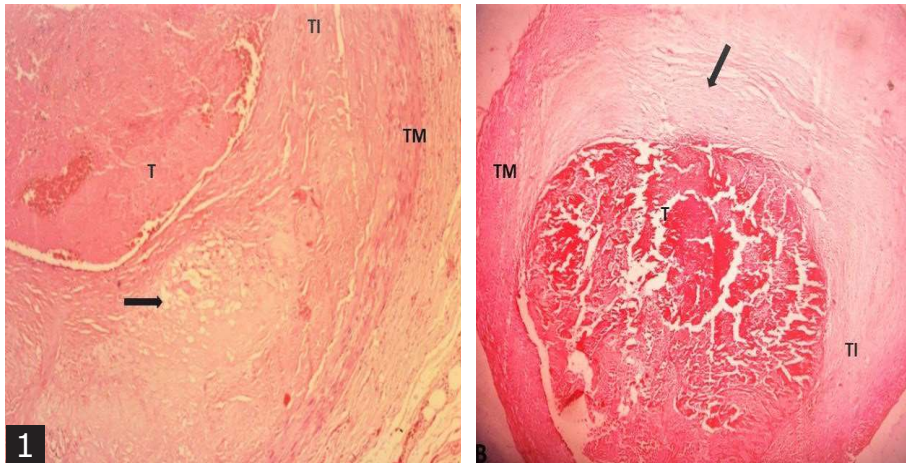


Figure 1: Coronary atherosclerosis with superimposed thrombus. Arrow shows atherosclerotic plaque. T- thrombus, TI- tunica intima, TM- tunica media (H&E stain; A- x10; B- x5).

Figure 2: Myocardial infarction. 2A shows recent infarction with necrotic cardiac myocytes and interstitial neutrophilic infiltrates. 2B shows old/ healed infarct (arrow) with replacement fibrosis and scarring (H&E stain; A- x10; B- x5).

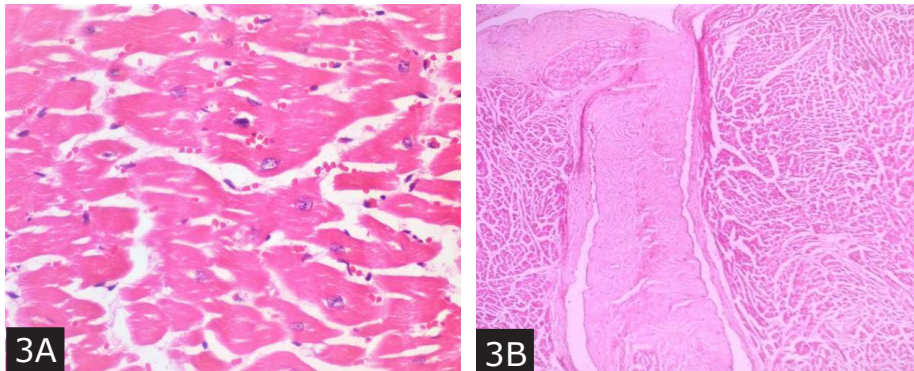
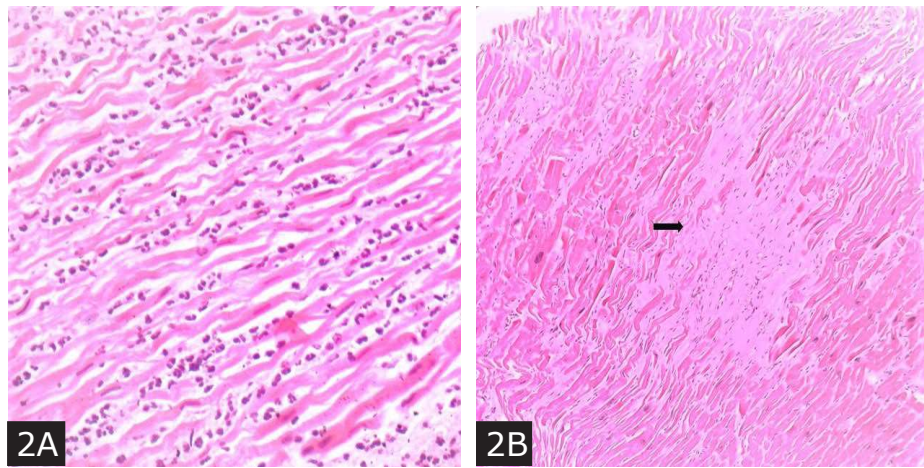
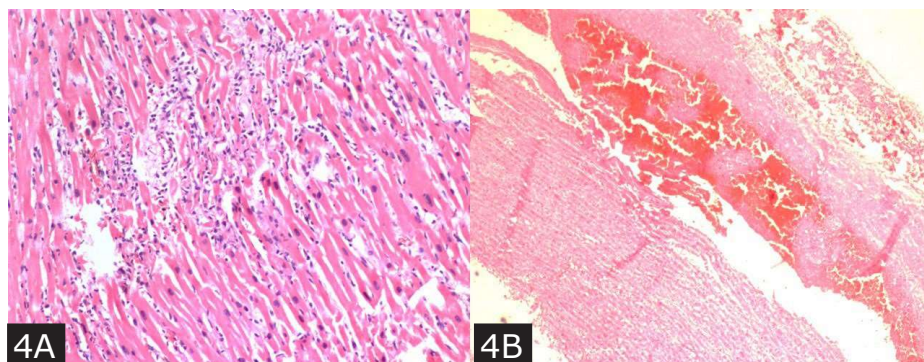


Figure 3A: Shows myocardial hypertrophy. 3B shows serofibrinous pericarditis (H&E stain; A- x10; B- x5).

Figure 4A: Shows myocarditis. 4B Shows aortic dissection (H&E stain; A- x10; B- x5).



studies conducted by Joshi C *et al.* (28.7%) and Kulkarni MP (24.8%) *et al.*^{6,14} higher frequency was reported by Shah SN *et al.* (44.1%) and lower frequency was quoted by Garg S *et al.* (14.1%).^{7,8} The differing frequencies among studies may be attributed to the time variability between onset of myocardial ischaemia and time of death.⁷ The morphologic features of MI, and hence its identification, depends on the time interval between infarction and death.¹⁵ It is well documented in literature that the single most important pathogenic mechanism of MI is coronary atherothrombosis.^{11,15} In accordance with this, all our cases of myocardial infarction had significant coronary atherosclerosis.

In 21.2% of the cases, atherosclerotic plaques were found in ascending aorta. Concurrent coronary atherosclerosis was present in all these cases. Many studies have shown significant association between coronary and aortic atherosclerosis, further risk factors are similar for development of these lesions.^{16,17}

In this study myocardial hypertrophy was present in 12% of cases. Literature review reveals varying frequencies of cardiac hypertrophy, ranging from 5.6% to 66%.^{6-8,10,14}

We observed 5 cases of valvular heart disease comprised of 3 cases of chronic rheumatic heart disease and 2 cases of infective endocarditis. Garg S *et al.* identified 2 cases of valvular heart disease comprised of 1 case each of aortic stenosis and infective endocarditis.⁷

Five cases of aortic dissection (AD) were detected in our study; one was associated with Marfan syndrome and four (80%) cases showed concentric left ventricular hypertrophy, suggestive of hypertension (Figure 4B). Literature review reveals that hypertension is the most important risk factor for AD.¹⁸ Huynh N reviewed 336 cases of AD over 6 decades.¹⁹ They identified hypertension (84%), prior cardiovascular surgery (38%), bicuspid valve (14%), and connective tissue disease (9%) as the most prevalent risk factors.¹⁹ More than 60% of their cases were not detected clinically and were first identified at autopsy.¹⁹

There were 4 cases (1.6%) of cardiac tamponade, in our study, with myocardial

rupture and hemorrhage in the pericardial cavity. Microscopic examination of the ruptured site revealed interstitial hemorrhage, acute inflammatory infiltrates and necrotic myocytes. Two of these cases were associated with aortic dissection. The remaining cases, probably, were consequence of ruptured MI. Dhankar V *et al.* reported 5 cases of (9.6%) cardiac tamponade.⁴ One of their cases was due to blunt trauma and the remaining 4 cases were attributed to possible ruptured acute MI.⁴

Pericarditis was found in 3 (1.2%) of the cases, both of which were serofibrinous type (Figure 3B). Literature review revealed variable frequencies of pericarditis, detected at autopsies, ranging from 0.9% to 2.8%.^{6,7,9} Pericarditis usually is associated with a systemic disorder (infections, rheumatic fever, autoimmune diseases like systemic lupus erythematosus, uremia, cancer) or other cardiac disease (MI, post cardiac surgery), primary pericarditis is rare and usually of viral etiology.^{6,7,15}

Myocarditis was found in only 2 (0.8%) cases (Figure 4A). Both of these cases showed mild to moderate perivascular and interstitial infiltrates of lymphocytes with an occasional myocyte apoptosis. The frequency of myocarditis reported in literature ranges from 3.5% to 29%.⁷ The major causes of myocarditis are infections (predominantly viral) and immune mediated reactions and should be differentiated from MI which also shows inflammation and myocyte necrosis.¹⁵

We had one case (0.4%) of hypertrophic cardiomyopathy, which was characterised by cardiac hypertrophy (weight: 820gm), asymmetrical septal hypertrophy involving the subaortic region and compression of left ventricular cavity. On microscopy, myocyte disarray, myocyte hypertrophy and patchy interstitial fibrosis were present. Data on cardiomyopathy detected at autopsy is sparse. Dhankar V *et al.* reported a single case (1.9%) of dilated cardiomyopathy and Kulkarni MP reported three cases with cardiomyopathy.^{4,14}

Rare lesions were identified by some authors. Kulkarni MP *et al.* reported one case each of papillary fibroelastoma and

amyloidosis; Dhankar V *et al.* reported one case each of metastatic squamous cell carcinoma and tuberculosis and Garg S *et al.* reported one case of cysticercosis.^{4,7,14} Thus unknown and unexpected lesions can be diagnosed on autopsy studies. However, we did not identify any such rare lesions in our study.

CONCLUSION

Our study highlights the varied histopathologic spectrum of cardiac lesions on autopsy. The frequency of detecting cardiac lesions is 82.8%. The most common finding is coronary atherosclerosis, with triple vessel involvement being most frequent, which is in accordance with other studies. Severe luminal occlusions, calcification and thrombosis are most frequent in Left anterior descending coronary artery. The second most common lesion is MI, the most significant pathogenic mechanism of which is coronary atherosclerosis, a fact emphasized by many other authors. As widely established in literature, there is a strong association between

coronary and ascending aorta atherosclerosis. The other less frequent lesions identified are valvular heart disease, aortic dissection, cardiac tamponade, serofibrinous pericarditis, myocarditis and hypertrophic cardiomyopathy, in that order. Thus, many preventable and concealed lesions are discovered on cardiac autopsies. Such studies provide a better understanding of cardiovascular diseases. These insights into the pathophysiology are indispensable for assessing disease trends and introducing new interventions and therapeutic management regimes in patients with cardiac diseases. **IJFMP**

Acknowledgment:

The authors have made no acknowledgment in this article.

Conflict of Interest:

The authors declare that there is no commercial or financial links that could be construed as conflict of interests.

Source of Funding:

The author declares that there is no funding for this project.

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