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Original Research Paper

Pathology

HISTOPATHOLOGICAL SPECTRUM OF VARIOUS CHANGES IN HEART – AN AUTOPSY BASED STUDY

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ABSTRACT

Introduction: There has been a significant rise in cardiac-related casualities globally during the last few decades, especially among urban population. In India, ischemic heart disease has become prevalent, affecting roughly 10% of the population. The role of pathologist is to study the various disease process which lead to death and to establish the cause of death. Autopsies are crucial in evaluating the underlying causes responsible for such mortalities. As post-mortem analysis of heart is the the main diagnostic tool to study gross and histopathological changes in healthy or diseased heart, an autopsy study of heart was therefore planned to observe various histopathological changes. **Aim and Objectives:** The objective of this research was to examine the histomorphological characteristics of different heart lesions, including both gross and microscopic observations, in heart specimens obtained post-mortem at the Department of Pathology, RNT Medical College, Udaipur, over a one-year period. **Materials and Methods:** A prospective study was conducted in the department of pathology, RNT Medical College Udaipur over a period of one year. We examined a total of 157 autopsies, regardless of the cause of death, with 7 cases being too autolyzed for inclusion. Therefore, our study included 150 whole heart specimens. These specimens underwent gross examination, and microscopic sections stained with H&E were analyzed to identify various histopathological alterations. The observed findings were then clinically correlated. **Results:** Atherosclerosis emerged as the predominant cardiac lesion, evident in 67 out of 150 autopsied hearts (44.66%), followed by ischemic heart disease observed in 26 cases (17.33%). Myocardial hypertrophy was present in 21 cases (14%), while myocarditis was noted in 6 cases. Additionally, changes indicative of electrocution were found in 2 cases, tuberculosis in 3 cases, stenosis of the aortic valve in 4 cases, and metastasis from lung carcinoma in 1 case. Age-related alterations were detected in 15 cases, while congestion was observed in 19 cases. Two cases each of rheumatic heart disease and congenital anomalies were also identified. Notably, the cause of death remained undetermined in 47 cases (31.33%) despite comprehensive macroscopic and microscopic examination. Among the major vessels, the left anterior descending artery was the most frequently affected (37.31%), followed by the right coronary artery (32.83%) and the left circumflex artery (29.85%). Of the three major vessels, 18.37% exhibited single-vessel involvement, while 34.32% and 47.31% of cases showed involvement of two and three vessels, respectively. Correlation analysis between age and atherosclerosis revealed a significant p-value of less than <0.05. Although males exhibited a slightly higher prevalence of atherosclerotic changes, the difference was not statistically significant. **Conclusion:** Ischemic heart disease emerged as the predominant cause of morbidity and mortality within our society, with atherosclerosis being the prevailing observation. The most frequent pattern of involvement was identified as three-vessel disease

KEYWORDS : Autopsy, Heart, Coronaries, Histopathology, Atherosclerosis

INTRODUCTION:

Cardiovascular disease (CVD) represents a significant global health challenge and has become the primary cause of illness and death in India. The incidence of ischemic heart disease in the country has risen to approximately 10%.[1] These conditions often impact individuals during their most productive years, leading to significant social and economic consequences. The occurrence of sudden death poses a considerable challenge for autopsy pathologists. Since cardiac autopsy serves as the primary diagnostic method to examine histomorphological changes in both normal and diseased hearts, a thorough examination often reveals a wide range of concealed cardiac pathologies incidentally. Therefore, meticulously performed autopsies and histopathological analyses are essential tools to assess potential diseases or injuries, determine the cause and manner of death, and contribute to the study of the epidemiology, pathogenesis, and management approaches for various cardiac lesions.[2] Given the lack of a reliable method for sampling living populations, autopsies, particularly histopathology, remain the most dependable approach for determining the cause of death and verifying the accuracy of clinical diagnoses, diagnostic procedures, and death certification.

Against this backdrop, this study was conducted to ascertain the extent of the issue by determining the cause and characteristics of cardiac death, establishing correlations, and observing various histomorphological changes in 150 whole-heart autopsy specimens. Additionally, the severity and distribution of some of these lesions were examined in bodies undergoing autopsy at our institute, which encompasses a diverse representation of all social classes.

AIMS AND OBJECTIVES:

1. To study the spectrum of histopathological heart lesions.
2. To analyze the demographic attributes of the study cohort.
3. To examine and assess changes in the heart and blood vessels through macroscopic and microscopic examination.

MATERIALS AND METHODS:

This prospective study was conducted at the Department of Pathology, RNT Medical College, Udaipur, Rajasthan, spanning from October 2022 to September 2023, covering a duration of 12 months. A total of 157 autopsies, including cases with whole heart specimens submitted for post-mortem examination to determine the cause of death, whether associated with known or unknown cardiac diseases, were analyzed. The study encompassed individuals from all age

groups, sexes, religions, and castes. Among the 157 specimens, 7 were deemed unsuitable for analysis due to poor preservation and complete autolysis, and were therefore excluded from the study. Consequently, 150 whole-heart specimens were included for analysis. Epidemiological data and post-mortem findings were gathered from post-mortem requisition documents, police records, and case histories.

Gross examination of heart

Formalin-fixed specimens, preserved in 10% formalin, underwent external inspection for visible pericardial pathology, scar marks, discolored areas, and were weighed. The hearts were dissected using the inflow-outflow method of cardiac dissection, supplemented by short-axis and other relevant techniques as needed. After removal of extraneous vessels and residual postmortem blood clot, the hearts were re-weighed.

All four chambers were carefully examined for blood clots and gross pathology of valves, including stenosis or calcification, as well as the endocardium for vegetations, thrombi, or plaques. Measurements of ventricular wall thickness and interventricular septum were taken, and cut surfaces were inspected for signs of myocardial ischemia such as loss of luster, mottling, or scarring. Areas of ischemia were serially sectioned and noted for location and size.

The three main vessels—right coronary artery (RCA), left circumflex artery (LCA), and left anterior descending artery (LAD)—were examined through serial transverse sections at regular intervals of 3-4 mm for evidence of hardening, blockage, or plaque. The aorta was longitudinally opened and inspected for atheromatous plaque, calcification, thickening, or aneurysm.

Microscopic Examination

Samples were extracted from the right and left ventricular walls, interventricular septum, apex, right and left coronary arteries (including both branches), valves, and aorta stump. Additional sections were obtained as needed from suspected pathological lesions. These tissues underwent processing and were paraffin-sectioned at a thickness of 4 μm. Subsequently, routine hematoxylin and eosin staining was applied. Special stains such as Van Gieson, Masson Trichrome, and Von Kossa were employed as required based on the nature of the lesion. Microscopic observations were recorded and clinically correlated..

Statistical analysis

The study findings underwent statistical analysis using Statistical Package for the Social Sciences (SPSS) version 20 (IBM Corp. SPSS statistics for windows). Quantitative variables were presented as mean ± standard deviation and range, while categorical variables were expressed as numbers and percentages. Differences in variables were assessed using the Chi-square test, with a p-value of < 0.05 considered significant for all statistical analyses.

RESULTS:

One hundred fifty specimens were included in study and underwent for gross, microscopic examination and demographic variables.

Age & sex distribution

All cases were categorized into age groups based on the age at the time of death. The youngest case was a newborn male of one and a half months, while the oldest was a 90-year-old male, resulting in an age range of 0-90 years. The mean age for males was 42.46 years and for females was 35.63 years. Out of 150 autopsies, 114 (76%) were males and 36 (24%) were females (refer to Table 1). In the present study, it was noted that the maximum number of cases were observed in the age group of 41-50 years, comprising 41 cases (27.33%) (refer to Table 2).

Heart Weight distribution

In males, post-fixation heart weights ranged from 20 grams to 680 grams, while in females, they ranged from 32 grams to 530 grams. The average heart weight was 269.63 grams. The mean heart weight for males was 298.48 grams, and for females, it was 256.65 grams. Cardiomegaly, defined as an increase in heart weight exceeding 300 grams in females and 350 grams in males, was noted.[3]

Histopathological changes in heart

A diverse array of histopathological alterations were identified upon microscopic examination. Coronary atherosclerosis (CA) emerged as the most prevalent finding, observed in 67 cases (refer to Figure 6), followed by ischemic heart disease (IHD) in 26 cases (refer to Figures 2, 3, 4). Myocardial hypertrophy was detected in 21 cases, while myocarditis was present in 6 cases. Ventricular rupture was identified in one case (refer to Figure 5), and two cases exhibited electrocution-related changes. Additionally, tuberculosis involvement with varying extents affecting the pericardium and myocardium was observed in 3 cases. Four cases exhibited calcification of the aortic valves, and one case showed metastasis from lung carcinoma (refer to Figures 7, 8). Age-related changes were noted in 15 hearts, including abundant lipofuscin accumulation in 12 cases (refer to Figure 14) and marked fatty infiltration in three cases, characterized by diffuse fat infiltrates exceeding 50% of the myocardial wall without thinning or dilatation, which contrasted with normal hearts. Severe myocardial congestion was evident in 19 cases, with myocardial fibrosis observed in 11 cases, and left anterior descending (LAD) stents noted in five cases.

Notably, in 47 cases (31.33%), no significant pathological changes were detected in the heart (refer to Table 3). Two cases each of rheumatic heart disease (occurring at 15 years of age) and congenital anomalies were also documented. Microscopic examination of the heart and vessels in the 0-10 years age group revealed no remarkable findings.

Atherosclerosis

The current investigation revealed the presence of atherosclerosis in the coronary arteries and/or great vessels in a total of 98 cases (65.33%) within the age group of 11 to 90 years. Specifically, atherosclerosis was observed in the coronary arteries in 67 cases, in the great vessels in 31 cases, and in both locations in 11 cases. Notably, no cases were identified in individuals under the age of 10 years, and there was a notable increase in both the number and severity of atherosclerosis observed after the third decade of life. Additionally, all cases aged over 65 years exhibited significant atherosclerosis (refer to Table 4).

Among the three coronary arteries, the left anterior descending (LAD) artery was the most commonly affected vessel, observed in 25 cases, followed by the right coronary artery (RCA) in 22 cases, and the left circumflex artery (LCA) in 20 cases (refer to Table 5). Secondary changes in the coronary arteries, such as calcification, thrombus formation, and plaque rupture, were noted in a total of 24 cases. Specifically, 18 cases exhibited calcification, 4 cases showed thrombus formation, and 2 cases demonstrated plaque rupture (refer to Table 6).

Out of the 67 cases of atherosclerotic coronary artery disease (CAD), 76.45% showed some degree of stenosis. Among these cases, 8 exhibited critical narrowing (>90% lumen block). The majority of cases (47.76%) revealed triple vessel disease, followed by double vessel disease (34.32%) and single vessel disease (17.91%) (refer to Table 7).

Aortic lesions

Out of 34 cases, aortic atherosclerosis was noted in 31 cases (20.36%) (**figure1**), followed by 2 cases of aortitis and one case of aneurysm were also seen.

Table:1 Sex wise distribution of cases

Sex	Frequency	Percentage%
Male	114	76
Female	36	24

Table:2 Age wise distribution of cases

Age Range (yrs)	No. of Patients	Percentage%
0-10 Yrs	4	2.66
11-20 Yrs	8	5.33
21-30 Yrs	14	9.33
31-40 Yrs	31	20.66
41-50 Yrs	41	27.33
51-60 Yrs	29	19.33
61-70 Yrs	17	11.33
71-80 Yrs	4	2.66
81-90 Yrs	2	1.33
Total	150	100

Table:3 Spectrum of histopathological changes in autopsied hearts

Pathological Findings	Number of Cases	Percentage%
Coronary artery diseases	67	44.66
Ischaemic heart disease	26	17.33
Myocardial hypertrophy	21	14
Aorta		
Atheromatous plaque	31	20.66
Aortitis	2	1.33
Aneurysm	1	0.66
Age related changes		
Lipofuscin	12	8
Fatty infiltration	3	2
Myocarditis	6	4
Congestion	19	12.66
Myocardial fibrosis	11	7.33
Ventricular rupture	1	0.66
Rheumatic heart disease	2	1.33
Tuberculosis	3	2
Aortic stenosis	4	2.66
Metastatis	1	0.66
Congenital anomaly	2	1.33
Coronary stent	5	3.33
Electrocution	2	1.33
Normal heart	47	31.33
Autolyzed specimens	7	4.66

Table:4 Age wise distribution of atherosclerosis and it is correlation

Age Groups	Atheromatous Plaque		Present Percentage	P Value
	Present	Absent		
0-10 Yrs	0	4	0	<0.05
11-20 Yrs	1	7	12.5	
21-30 Yrs	3	11	21.42	
31-40 Yrs	9	22	29.03	
41-50 Yrs	20	21	48.78	
51-60 Yrs	18	11	62.06	
61-70 Yrs	11	6	64.70	
71-80 Yrs	3	1	75	
81-90 Yrs	2	0	100	

Table:5 Types of vessels involved in atherosclerosis

Vessel Type	Number of Cases	Percentage
LAD	25	37.31
RCA	22	32.83
LCA	20	29.85

Table:6 Atherosclerosis with secondary changes in coronary vessels

Findings	No. of Cases (67)	Percentage%
Atherosclerosis only	43	64.17
Atherosclerosis plus calcification	18	26.86
Atherosclerosis plus thrombosis	4	5.97
Atherosclerosis plus rupture	2	2.98

Table:7 Pattern of vessels involvement in atheroscerosis

Number of Vessel	Atherosclerosis Present	Percentage
Single	12	17.91
Double	23	34.32
Triple	32	47.76

Table:8 Types of myocardial infarction

Types	Number of Cases(26)	Percentage
Old MI showing fibrosis	15	57.69
Recent MI	11	42.30

Table:9 Frequency distribution of area involved in ischaemic heart disease

Wall Affected	Acute MI Cases (Percentage)	Old healed MI Cases(Percentag.)
Only RV	0 (0)	0 (0)
Only LV	1 (9.09)	0 (0)
Only IVS	0 (0)	1 (6.66)
LV and IVS	3 (27.27)	2 (13.33)
Apex	2 (18.18)	4 (26.66)
ALL	5 (45.45)	8 (53.33)

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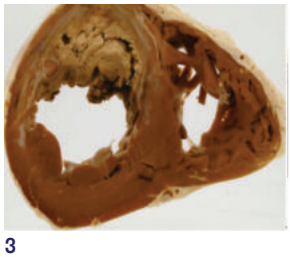

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Gross Findings, Fig.1: Aortic atherosclerosis, Fig.2: Mottled area of recent MI and white fibrous area of old infarction, Fig.3 Transmural necrosis of recent MI and white fibrous area of old infarction, Fig.4 White fibrous area of old myocardial infarction.

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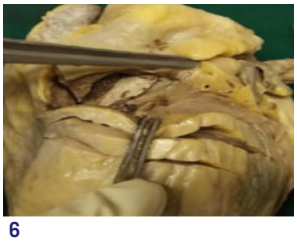

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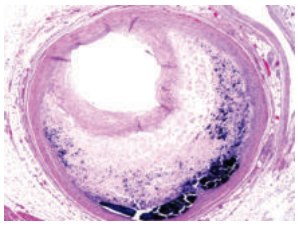
Gross Findings, Fig.5: Left ventricular wall rupture, Fig.6: Atherosclerosis of coronary, Fig.7: Outer surface of metastasis heart from squamous cell carcinoma lung, Fig.8: Cut section of metastasis heart from squamous cell carcinoma lung.



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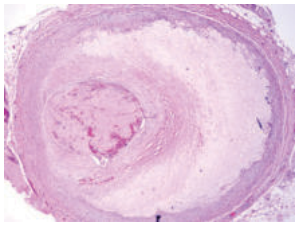

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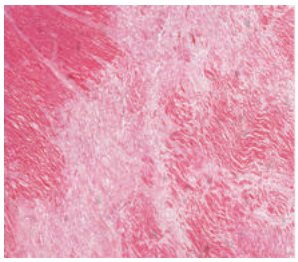

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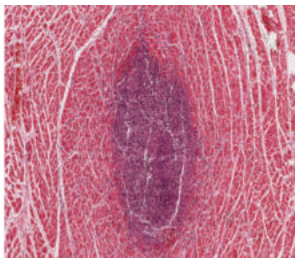

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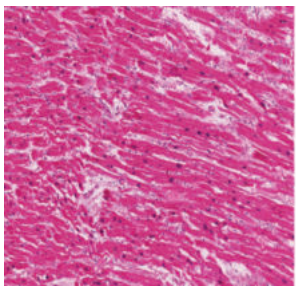
Microscopic Findings, Fig.9: Coronary artery with large atheromatous plaque containing central lipid rich core with some calcification, Fig.10: Coronary artery with atheromatous plaque and recent luminal thrombus formation, Fig.11: Section of ventricle showing features of recent myocardial infarction, Fig.12: Section of ventricle showing features of old myocardial infarction with area of fibrosis.



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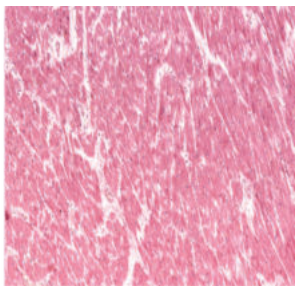

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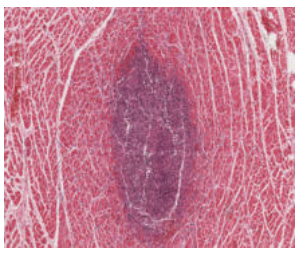

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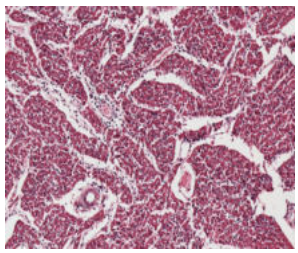

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Microscopic Findings, Fig.13: Section of ventricle showing hypertrophied muscle fibres, Fig.14: Age related brown yellow lipofuscin pigments in cardiac myocytes, Fig.15 and Fig.16: Features of acute myocarditis in ventricle musculature.

DISCUSSION:

Heart samples obtained from autopsies contribute significantly to our understanding of cardiovascular anatomy and pathophysiology, thereby advancing modern cardiovascular research. Autopsies serve as invaluable educational tools for diagnosing and evaluating treatment options for contemporary cardiovascular diseases. By correlating pathological findings with clinical contexts, autopsies offer unparalleled insights, especially considering the absence of valid methods for sampling living populations. Histopathological examination of the heart plays a crucial role in determining whether death is attributable to cardiac disease or other causes, as well as in characterizing the nature of the cardiac disease.

With the ongoing advancements in diagnostic and treatment technologies, the management of coronary heart disease (CHD) is becoming increasingly successful. For patients undergoing CHD treatment, cardiac autopsies provide valuable insights into the effects of various surgical interventions and the anatomical and pathological foundations of associated complications.[4.]

The current study included a total of 150 autopsies, with 114 being male (76%) and 36 female (24%), revealing a higher prevalence in the 41-50 year age group. This trend may be attributed to factors such as the westernization of Indian society, sedentary lifestyles, poor dietary habits, and a lack of regular medical check-ups. Additionally, there is an increased prevalence of smoking and alcohol consumption among males, whereas females benefit from the vasoprotective effects of estrogen. Age emerges as a significant risk factor for heart disease development, with the likelihood increasing with age. These observations align with previous studies demonstrating a similar male predominance, distribution across age groups, and the influence of advancing age on sudden cardiac death, as noted by **Chandrakala Joshi.,**[5] and **Bardli and Falzi et al.**[6], as well as **Karnafil R et al**.[7], reported a similar pattern with the highest number of cases occurring in the 41-50 years age range. **Rao D et al.**[8] observed a peak in the 50-60 years age group, while **Chug SS et al.**[9] noted a peak in the 50-59 years age range. Male predominance has been consistently reported in numerous autopsy studies conducted by **Sonawane et al., Wang et al., Garg et al., and Gaikwad et al** [9-12]. This comparison underscores an epidemiological shift towards older ages in heart disease incidence, a trend that correlates with urbanization, sedentary lifestyles, and inappropriate dietary habits.[13]

In our study, coronary atherosclerosis emerged as the most common histopathological finding, present in 67 cases (44.66%). While all studies consistently identify atherosclerosis as the predominant histopathological finding in heart autopsies, the reported percentages vary widely across different studies. For instance, **Ramazan Karanfil et al** [7]. reported a prevalence of 75%, **Chandrakala Joshi** [5]64%, **Dhankar Khare et al.**[14] 61.5%, and **Patel et al.**[15] 27%. These discrepancies in the frequency of atherosclerotic changes can likely be attributed to differences in demographic variables and characteristics of the populations studied, including socioeconomic status, diet, lifestyle, race, culture, and age range.

Furthermore, the correlation of age with atherosclerosis yielded a significant p-value (<0.05) (refer to Table 4), indicating that the atherosclerotic process begins at a young age and progresses with increasing age. Similar trends have been reported in previous studies.[16] This underscores the importance of early screening and intervention to mitigate the serious consequences of atherosclerosis later in life.

In our study, secondary changes such as calcification were observed in 18 cases (26.86%), thrombus formation in 4 cases (5.97%), and plaque rupture in 2 cases (2.98%) (refer to Figures 9 and 10). **Garg S et al.**[18] reported calcification in 53.3% of cases, while **Marwah Nisha et al.**[17] observed thrombosis in 7.5% of cases. Plaque calcification is more commonly found in advanced lesions, although it may also occur in small amounts in earlier lesions, typically appearing in the second and third decades of life. Histopathological investigations have revealed that plaques with microscopic evidence of mineralization tend to be larger. However, the

relationship between arterial calcification and the likelihood of plaque rupture remains unknown.[19]

In our study, the left anterior descending artery (LAD) was the most commonly involved vessel, with a frequency of 37.31%, followed by the right coronary artery (RCA) at 32.83%, and the left circumflex artery (LCA) at 29.85%. Gradwhol cited the ranges from various published analyses, reporting the frequency of involvement as follows: LAD ranging from 45-64%, RCA being the next most frequently affected vessel with a range of 24-46%, followed by the left circumflex artery with a range of 3-10%. The left main coronary artery was observed to be the least affected.[20]

In our investigation, triple vessel involvement was the most prevalent, accounting for 47.76% of cases, followed by double vessel involvement at 34.32%, and single vessel involvement at 17.91%. This finding is consistent with the study conducted by **Porwal et al.**[21], which reported triple vessel involvement in 40% of cases, double vessel involvement in 37%, and single vessel involvement in 15%. Similarly, **Garg M et al**.[11] also found triple vessel involvement to be the most common pattern at 44.4%. However, contrary results were reported by **Virmani et al.**, who showed that single vessel involvement was the most common at 44%.[22]

In our current investigation, myocardial infarction (MI) was observed in 26 cases (17.33%) (refer to Figures 11 and 12). Among these cases, old healed MI was the predominant type, noted in 15 out of 26 cases (57.69%), followed by recent MI in 11 out of 26 cases (42.30%) (refer to Table 8). **Ahmad et al.**[23] categorized MI into two groups, recent and old, and reported old MI in 35.1% of cases and recent MI in 20% of cases. In the study by **Garg S et al.**[18], 1myocardial infarction was present in 20 cases (14.1%). Conversely, **Ramazan et al**.[7] reported a higher incidence of myocardial infarction in 48% of cases, whereas Wang et al. noted ischemic heart disease in only 7% of cases, which is lower than our findings. This discrepancy may be attributed to the temporal variability between the onset of ischemia and the time of death, as microscopic features are influenced by the duration between ischemia onset and death.[8]

In cases of ischemic heart disease (IHD), we aimed to determine the frequency distribution of involvement in various areas by examining at least one section from each of the left ventricle (LV), right ventricle (RV), interventricular septum (IVS), and apex. Thirteen out of the 26 cases (50%) of IHD exhibited involvement of all the areas, followed by combined involvement of the left ventricular wall and interventricular septum in 5 cases (19.23%). Isolated involvement of the right ventricle was not observed (refer to Table 9). Our findings align with those reported in the literature.[3,7,]

The second most common lesion identified in this study was myocardial hypertrophy, observed in 21 cases (14%) (refer to Figure 13). **Wang HY et al.**[10] reported an incidence of 7%, whereas Ramazan **Karanfil et al. and Chandrakala et al**. reported a much higher incidence of cardiac hypertrophy in 66% and 52% of cases, respectively**. Basso et al.**[24] defined ventricular hypertrophy as cases exceeding the reference range, specifically a left ventricular (LV) wall thickness >1.4 cm and a right ventricular (RV) wall thickness >0.5 cm. In our study, similar criteria for cardiac hypertrophy were adopted, with histopathological confirmation.[25]

Myocarditis was detected in 6 (4%) cases (refer to Figures 15 and 16). Different authors have reported variable percentages of myocarditis, with **Chandrakala Joshi et.al.**[5] reporting 9%, and others reporting figures ranging from 5% to 30%. Additionally, in the present study, one case demonstrated the metastasis of a squamous cell carcinoma of the lung. A study conducted by **Dhankar et al.**[14] reported a case of metastatic squamous cell carcinoma with the presence of atypical squamous cell nests in the myocardium. Furthermore, in a study by **Verma et al.** four cases of carcinoma were identified.[26]

Out of the total cases, 47 (31.33%) did not reveal any discernible cause of death despite conducting a comprehensive gross and microscopic autopsy. In the studies conducted by **Verma et al. and Singal et al.**, 11% and 25% of cases, respectively, also did not yield an identifiable cause of death.[26,27]

CONCLUSION:

The current study examined histomorphological changes in autopsied whole hearts across various age groups. Ischemic heart disease emerges as a leading cause of death, with coronary atherosclerosis representing a significant pathogenetic mechanism and three-vessel disease being the most prevalent pattern of involvement. These findings are consistent with those emphasized by other authors. Additionally, the study underscores the observation that ischemic heart disease is more commonly encountered in males and its incidence escalates with advancing age. Atherosclerosis emerges as the predominant pathology identified in the study and substantially contributes to the burden of chronic illness, particularly among the elderly population. Therefore, preventive measures targeting atherosclerosis at a younger age through awareness programs become pivotal therapeutic modalities.

Moreover, various diseases and pathological processes such as myocardial hypertrophy and myocardial fibrosis, while seemingly subtle, can contribute directly or indirectly to the cause of death or morbidity. Thus, during autopsies, thorough examination of the cardiovascular system is imperative to ascertain the cause of death accurately. Autopsy reports should meticulously correlate pathological findings with the clinical history, including circumstances of death and any other investigations conducted close to the time of death.

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