"HISTOMORPHOLOGICAL SPECTRUM OF CARDIAC LESIONS IN AUTOPSY CASES - A DESCRIPTIVE STUDY"

by

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Dissertation Submitted to the Kerala University of Health Sciences, Thrissur, in partial fulfilment of the requirements for the degree of

MD DEGREE in PATHOLOGY

Under the guidance of

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HMT COLONY, KALAMASSERY

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Kerala University of Health Sciences

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STRUCTURED ABSTRACT

STRUCTURED ABSTRACT

INTRODUCTION:

With the turn of the century, cardiovascular diseases (CVDs) have become the leading cause of mortality in India. Autopsy study provides an understanding of the basic process which sets a stage for clinically significant cardiovascular disease. Cardiac autopsies are performed with the aim to observe histomorphological changes that could guide to the cause of death especially when there is history of no specific disease or co-morbidities.

OBJECTIVES:

1. To describe the histomorphological patterns of cardiac lesions in autopsy specimens in a tertiary care centre.
2. To identify Coronary Atherosclerotic changes related to age and gender in the study population .

METHODS:

A descriptive study of 140 autopsy heart specimens was conducted in the Department of Pathology over a period of one year. Relevant clinical data was collected from the requisition forms received in the Department of Pathology. Formalin fixed specimens were inspected externally, emptied of clots, weighed & dissected by in inflow outflow method. Measurements of right and left ventricular wall was noted. Three major coronaries & ascending aorta were examined for atherosclerotic changes. Sections from RV wall, LV wall, three coronaries & stump of aorta were processed and stained with Haematoxylin & Eosin. Microscopic examination for myocardial changes and grading of atherosclerotic lesions was done using Modified American Heart Association (AHA) criteria . Data was compiled to look for histomorphology patterns of cardiac lesions & prevalence of atherosclerosis. Statistical analysis was done using SPSS software.

RESULTS AND DISCUSSION:

The study comprised of 140 cases in the age ranging from 18 years to 92 years. The mean age of the study population was 45.98 years. Male to female ratio was 3.5:1 with 109 cases (77.9 %) of males. The most common histopathological finding in our study was coronary atherosclerosis in 113(80.7%)cases followed by ischemic heart disease in 62 cases (44.28%) and myocarditis in 16 cases (11. 42%). There was 1 case of cardiac amyloidosis (0.71%), vaso-occlusive crisis of sickle cell disease (0.71%), & infective endocarditis (0.71%).

The frequency of coronary atherosclerosis was more in elderly and in male gender.

Triple vessel involvement was seen in 60 (42.9 %) cases. Left Anterior Descending artery was the most common coronary involved in 101 cases (72.14%) , with grade VII atherosclerosis in 28 cases (20%) being the most common grade of atherosclerosis according to modified AHA criteria.

As the study was conducted during the COVID -19 pandemic we received 15 cases (10.7%) of RT-PCR confirmed SARS-CoV-2 virus infection. Features of COVID associated cardiopathy observed in the study were microhaemorrhage in 4 (26.67%) cases , fibrin deposition in 3 (20%) cases, oedema and capillary dilatation in 12(80%) cases and inflammatory infiltrate without necrosis in 4 (26.66%)cases.

CONCLUSION:

In the present study coronary atherosclerosis was the most frequently encountered lesion followed by ischemic heart disease . The incidence of atherosclerosis was found to be 80.7%. The study highlights the importance of cardiovascular risk factors screening from a younger age. Our study adds valuable data to the literature regarding the morphology of atherosclerotic lesions.

Keywords: autopsy, atherosclerosis, coronary arteries, Histopathology

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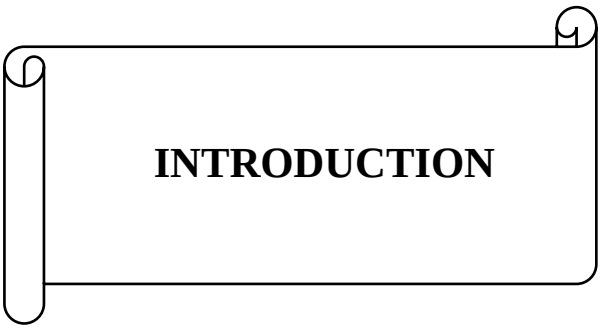

INTRODUCTION

INTRODUCTION

With the turn of the century, cardiovascular diseases (CVDs) have become the leading cause of mortality in India. According to the Global Burden of Disease study age -standardized estimates, nearly a quarter of all deaths in India are attributable to Cardiovascular diseases.(1) Cardiovascular diseases (CVDs) have now become the leading cause of mortality in India. A quarter of all mortality is attributable to CVD. Ischemic heart disease and stroke are the predominant causes and are responsible for >80% of CVD deaths. The Global Burden of Disease study estimate of age-standardized CVD death rate of 272 per 1,00,000 population in India is higher than the global average of 235 per 1,00000 population.

The incidence of atherosclerotic coronary artery disease has increased two-folds in the past few decades. With nearly one-third of all the deaths in the country, it has become an epidemic and will soon emerge as the leading cause of death from a disease. A substantial proportion of the population in India is exhibiting an increasing prevalence of cardiovascular disease and associated risk factors .An estimated 1.3 million Indians died from coronary artery disease (CAD) in 2000. The projected death from CAD by 2015 was 2.95 million. Overall, around 6.4 crore cases of CAD were reported in the year 2015.(2)

Some of the most common histopathological cardiac lesions include Atherosclerotic coronary heart disease followed by Hypertensive heart disease, Hypertrophic cardiomyopathy, Myocarditis, Infective endocarditis, Rheumatic heart disease and Aortic dissection.

The autopsy study provides an of understanding the basic process which sets a stage for clinically significant cardiovascular disease. There is no valid method of sampling of living population. Therefore it is considered that death suspected due to cardiovascular pathology , probably provide the best sample of the living population for studying cardiovascular diseases.

The cardiac autopsies are performed with the aim to observe histomorphological changes that could guide to the cause of death especially when there is history of no specific disease or co- morbidities . Several autopsy studies in which state-of-the-art histological methods were used had just thrown new light on

the compositions of lesions and on the diversity of mechanisms whereby they developed . Autopsy studies are a good tool to estimate the prevalence, grading, and distribution of cardiac lesions and their correlation with various risk factors.

Advancements in medical intervention and surgical therapy along with secondary prevention have resulted in improved quality of life and better life expectancy in CAD patients, yet the prevalence still remains high. However, the exact data on the prevalence of coronary atherosclerosis or clinical CADs are extremely diverse.

The burden of cardiovascular diseases is high in Kerala, India, and a considerable proportion of these occur in young people. Within India, the rates of CVD vary markedly with highest in states of Kerala, Punjab and Tamil Nadu.(3) The overall age-adjusted prevalence of definite coronary artery disease (CAD) is 4.8 per cent in men and 2.6 per cent in women in Kerala, India. There was almost a three-fold increase since 1993.(4)

Many cardiac pathologies are concealed and found incidentally on histomorphological evaluation of samples sent after post-mortem examination. This study aims at exploring the vast spectrum of lesions which can be diagnosed on histopathology after autopsy which aids in studying the epidemiology, pathophysiology and management modalities of these diseases.


OBJECTIVES

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1. To describe the histomorphological patterns of cardiac lesions in autopsy specimens in a tertiary care centre.
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BACKGROUND

AND

REVIEW OF LITERATURE

BACKGROUND AND REVIEW OF LITERATURE

The exploration of the heart has a history of at least five millennia. In ancient China, the heart was regarded as the "origin of the pulse, the seat of joy and spirit, and the monarch of the body".(5) The model of the heart and veins represented by Aristotle (384–322 B.C.) was one of the earliest but accurate descriptions of the cardiovascular system. With his own specific metaphysical approach, restricted by his own methodology of dissecting dead animals, Aristotle was the first to accurately describe the anatomy of the heart and blood vessels in his Historia Animalium. Hippocratic Opus is a collection of medical works associated with Hippocrates' teachings (400 BCE). One such medical work on the Heart ,recorded the anatomical details of heart in depth(6).

It is widely agreed that the post-mortem examination can provide the best information on the disease processes present at death(7).Major advances in the understanding of cardiovascular diseases, including atherosclerosis and coronary artery disease, congenital heart diseases, and cardiomyopathies, were possible through autopsy investigation and clinicopathological correlations.(8)

Analysis of mummified humans from ancient populations has revealed that atherosclerosis was prevalent in preindustrial societies across various geographical regions and historical eras. These findings "suggest that the disease is an inherent component of human ageing and not characteristic of any specific diet or lifestyle," write Professor Randall Thompson and colleagues, who have published their report from the Horus study in the Lancet.(9)

ANATOMY OF THE HEART

The human heart is a remarkably efficient, durable, and reliable pump, propelling more than 7500 L of blood through the body each day, and beating more than 40 million times a year—the wellspring for tissue oxygenation, nutrition, and waste removal.(10)

Heart weight varies from 250 to 350 g , with an average of 300 g in males and from 200 to 300 g, with an average of 250 g in females. Cardiac weight is 0.45% of body weight in males and 0.40% in females.(11) The difference in weight between males and females appears after the age of 12 years. Adult weight is achieved between the ages of 17 and 20 years. The heart reaches 50% of its adult dimensions at birth, 75% by 5 years and 90% by 12 years. An average adult heart is 12 cm from base to apex, 8–9 cm at its broadest transverse diameter and 6 cm anteroposteriorly.(12)

MYOCARDIUM

The pumping function of the heart occurs through coordinated contraction ,during systole and relaxation ,during diastole of cardiac myocytes of the myocardium. Left ventricular myocytes are arranged in a spiral circumferential orientation to generate vigorous coordinated waves of contraction spreading from the cardiac apex to the base of the heart. In contrast, right ventricular myocytes have a less structured organization, generating overall less robust contractile forces. Contraction is achieved by shortening of serial contractile elements , sarcomeres within parallel myofibrils. Although the heart is primarily a pump, it is worth remembering that it also has other functions including endocrine function.

VALVES

The four cardiac valves - tricuspid, pulmonary, mitral, and aortic - maintain unidirectional blood flow. Valve function depends on the mobility, pliability, and structural integrity of the leaflets of the atrioventricular valves - tricuspid and mitral or cusps of the semilunar valves - aortic and pulmonary.

CONDUCTION SYSTEM

Coordinated contraction of the cardiac muscle depends on the initiation and rapid propagation of electrical impulses— accomplished through specialized myocytes in the conduction system.

The components of the conduction system include the following:

- Sino atrial (SA) node pacemaker, at the junction of the right atrial appendage and superior vena cava.
- Atrio ventricular (AV) node, located in the right atrium along the interatrial septum
- Bundle of His (AV bundle), connecting the right atrium to the ventricular septum
- Right and left bundle branch divisions that stimulate their respective ventricles via further arborization into the Purkinje network.(10)

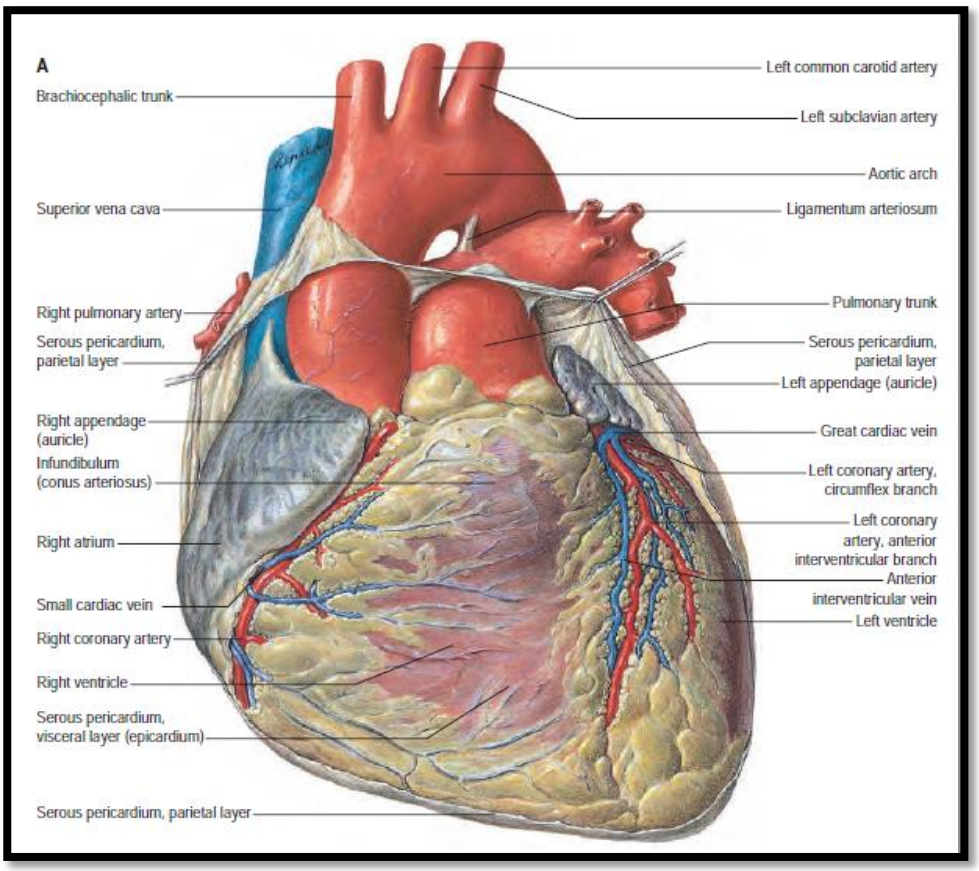


Figure 1.Anatomy of the heart.(12)

HISTOLOGY

Microscopically, the normal myocardium is a functional syncytium of myocardial fibres / cardiac myocytes that have centrally located nuclei .Cardiac myocytes are a specialized form of striated muscle . Faint dark eosinophilic intercalated discs between the myocytes form the mechanical and electrical couplings. Numerous capillaries with sparse interstitial tissue are found between the myocardial fibres .(13)

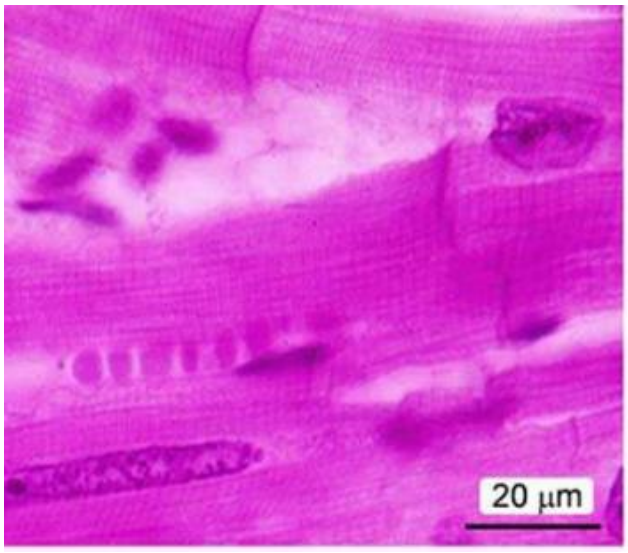


Figure 2. High power view of the striated cardiomyocytes with centrally located nuclei & dark eosinophilic intercalated discs**.**

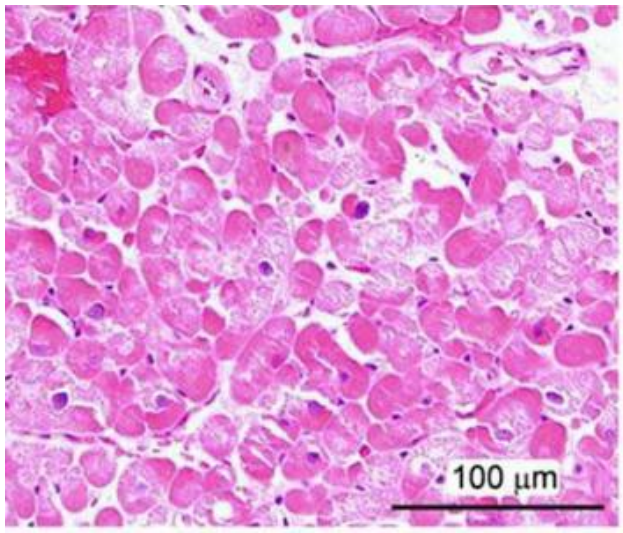


Figure 3. Sparse interstitial tissue and numerous capillaries between myocardial fiber cross-sections

BURDEN OF CARDIOVASCULAR DISEASES IN INDIA

According to the Global Burden of Disease study age-standardized estimates (2010), nearly a quarter (24.8%) of all deaths in India are attributable to CVD The age standardized CVD death rate of 272 per 100 000 population in India is higher than the global average of 235 per 100 000 population(1).

The World Health Organization (WHO) has estimated that, with the current burden of CVD, India would lose $237 billion from the loss of productivity and spending on health care over a 10-year period (2005–2015).7 Reasons for the high propensity to develop CVD, the high case fatality, and the high premature mortality include biological mechanisms ,social determinants, and their interactions.(3)(1)

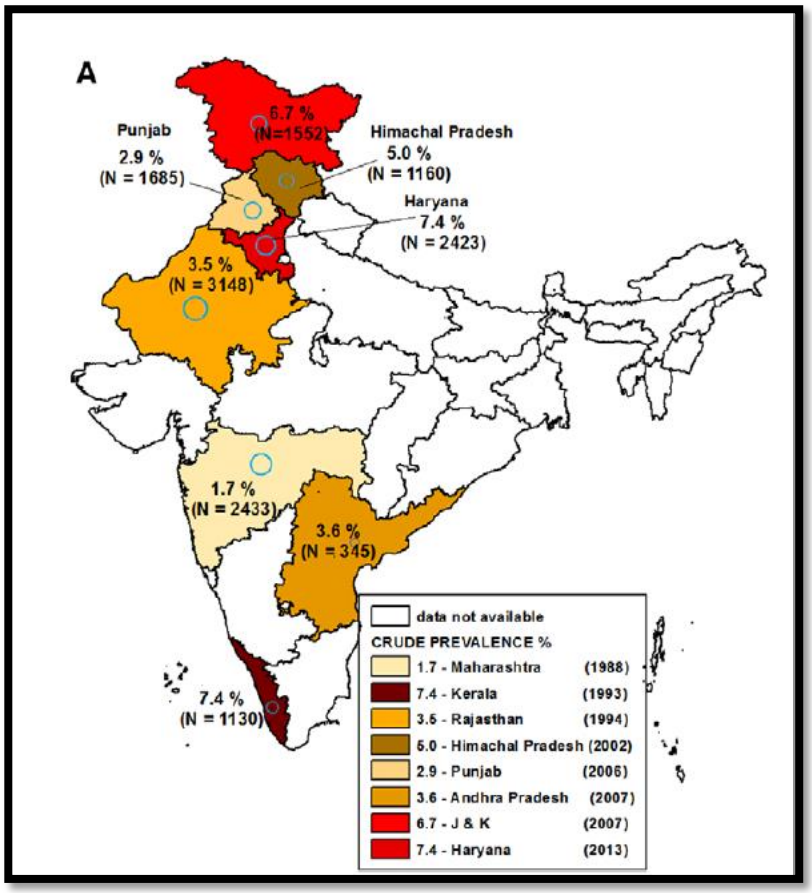


Figure.4 Ischemic heart disease prevalence rate in rural India.

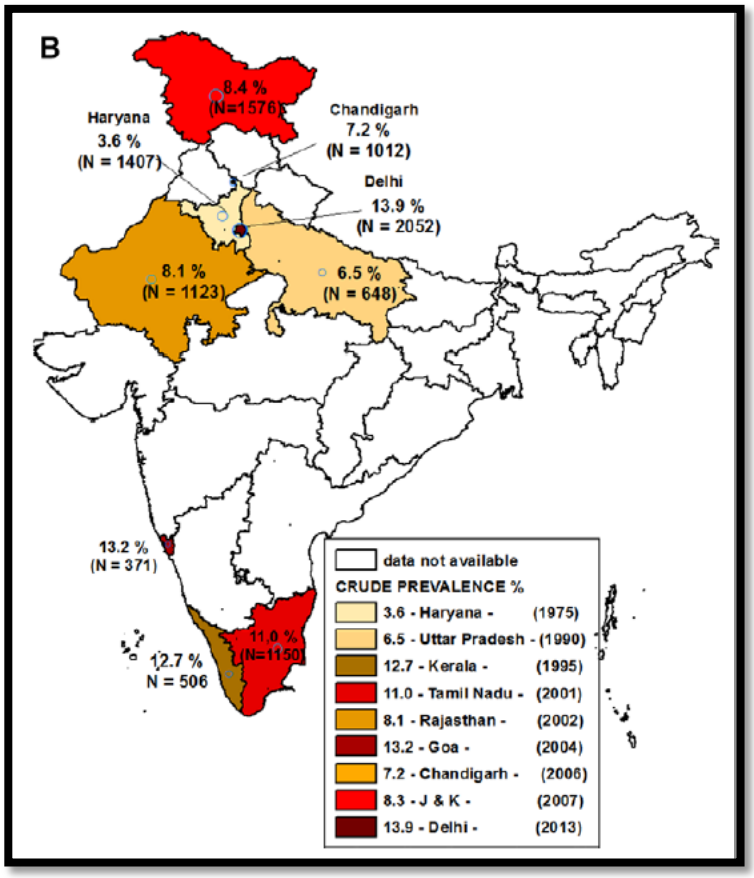


Figure 5. Ischemic heart disease prevalence rate in urban India

BURDEN OF CARDIOVASCULAR DISEASES IN KERALA

Kerala, with a population of over 33 million, is the most advanced state in epidemiological transition and has the highest prevalence of CAD risk factors in India(4) . The state has been reported to be the harbinger of what the rest of India is going to face in the near future .Although the CAD risk factor prevalence is the highest in the state of Kerala, there are no recent studies on the prevalence of CAD in this state. The only one community based study in 1993 from the rural area of the southernmost district of the state reported a CAD prevalence of 7.4 %(4). The environment in Kerala is conducive for increasing the CAD risk factors which is likely to result in an increase in the CAD prevalence.(14)

METHODS OF DISSECTION OF HEART

Many older methods are impractical for routine diagnostic pathology. Only the inflow-outflow and short axis / bread slice methods have withstood the test of time; the latter technique is applicable to virtually any form of heart disease.(15)

1. **Inflow-Outflow Method**

   This technique is suitable primarily for normal hearts. For each side of the heart, the atrium is opened first, and then the ventricle is opened along its inflow and outflow tracts, following the direction of blood flow.

2. **Short-Axis Method**

   This is the method of choice not only for the evaluation of ischemic heart disease but for virtually any other cardiac condition, because the slices expose the largest surface area of myocardium. They correspond to the short-axis plane produced clinically by two-dimensional echocardiography.

3. **Four-Chamber Method**

   Beginning at the cardiac apex, a cut is extended through the acute margin of the right ventricle, the obtuse margin of the left ventricle, ventricular septum & extended through the mitral, tricuspid valves and through the atria. This will divide the heart into two pieces, both of which show all four chambers.

4. **Long-Axis Method**

   The plane is best demarcated with three straight pins. The first pin is placed in the cardiac apex, the second in the right aortic sinus and the third near the mitral valve annulus, between the right & left pulmonary veins. The heart can then be cut along this plane, from the apex toward the base.

5. **Base Of heart Method**

   This method displays all four valves intact at the cardiac base. The technique is best applied to hearts with prominent valvular disease, including prosthetic valves.

6. **Window Method**

   This method is useful for the preparation of dry cardiac museum specimens, using paraffin and other materials or plastination

7. Unrolling Method

This technique can be used to demonstrate opacified epicardial arteries in a single plane.

8. Partition Method

Partitioning techniques are used to weigh each ventricle separately for detailed assessment of ventricular hypertrophy.

9. Injection-Corrosion Method

Plastic or latex is injected into the coronary vasculature or into the cardiac chambers and great vessels. Casts made from silicon rubber are resilient and nonadhesive and can therefore be extracted from the coronary arteries or cardiac chambers without resorting to corrosion of the specimen.

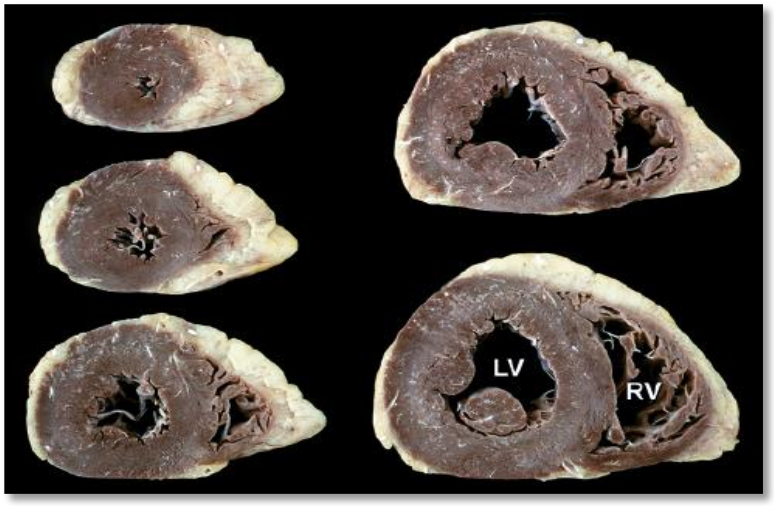


Figure 6. Short axis method of dissection of heart

The standard histologic examination of the heart

- Myocardium : take mapped labelled blocks from a representative transverse slice of the ventricles to include the free wall of the left ventricle , the ventricular septum, and the free wall of the right ventricle, as well as right ventricular outflow tract. Left ventricular myocardial sections should include the papillary muscles. Additionally, one block from each atria and any area with significant macroscopic abnormalities should be taken. Haematoxylin & eosin and a connective tissue stains like Elastic van gieson , trichrome or Sirius red are standard. Other special stains and immunohistochemistry should be performed as required.

- Coronary arteries: in the setting of coronary artery disease, the most severe focal lesions should be sampled for histology in labelled blocks and stained as above.
- Other cardiac samples such as valvular tissue, pericardium, and aorta are taken as indicated.(16)

CATEGORIES OF HEART DISEASES

A. DISORDERS OF THE ENDOCARDIUM

1. Infective Endocarditis

Infective endocarditis (IE) is an infection of the endothelium of the heart. It has an annual incidence of 3–10/100,000 of the population with a mortality of up to 30% at 30 days. The modified Duke criteria is used to help establish a diagnosis of endocarditis. (17)

Staphylococcus aureus typically produces acute endocarditis, whereas Streptococcus viridans produces subacute endocarditis. Several organisms normally found in the oral cavity are also causative, and been referred to as the Gram-negative HACEK organisms (Haemophilus aphrophilus, Actinobacillus actinomycetem comitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae).

Staphylococcus epidermidis also causes infective endocarditis, more common in the setting of prosthetic valves. Healed infective endocarditis leaves residual valve damage, often fenestrations, usually with a hemodynamic jet lesion and adjacent endocardial fibrosis.

2. Nonbacterial Thrombotic Endocarditis

Marantic endocarditis ,produces small rarely larger than 0.5 cm, pink, bland, and sterile vegetations attached to the valve surface at the lines of closure . It is typically seen in cachectic patients with a hypercoagulable state e.g., Trousseau syndrome.

3. Libman–Sacks Endocarditis

Libman–Sacks Endocarditis seen in 4% of cases of systemic lupus erythematosus and is characterized by flat, pale tan, spreading bands of vegetations located on both surfaces of the valves or chordae tendineae . Affected, in order of frequency, are the tricuspid, mitral, pulmonic, and aortic valves.

4. Rheumatic Heart Disease (RHD)

Rheumatic Heart Disease is a sequela of rheumatic fever (RF) caused by Streptococcus pyogenes (group A or beta- hemolytic streptococcus). Aschoff nodules (ANs) are a characteristic feature and appear as interstitial collections of plump mononuclear cells with occasional neutrophils arranged in a granuloma-like formation, although the presence or number of ANs does not correlate with clinical course or activity of the rheumatic process. The most characteristic cellular component of ANs is the Aschoff giant cell, which has two or more nuclei with prominent nucleoli.Another characteristic feature is the presence of Anitschkow cells, which are mononuclear histiocytes that are often arranged in a palisade around the center of the granuloma.

5. Endocardial Fibroelastosis

is an uncommon condition that can result in restrictive cardiomyopathy. Pearl-white fibroelastic thickening, caused by accumulation of collagen and elastic fibers typically in the left ventricular endocardium , is often associated with aortic valve obstruction. The disease occurs either focally or diffusely in children from birth to age 2 years.

6. Loeffler Endocarditis

Loeffler Endocarditis is also known as fibroelastic parietal endocarditis with blood eosinophilia. The disease is a component of broader cardiac involvement as part of the hypereosinophilic syndrome.(13)

B. DISORDERS OF THE VALVES-

1. Myxoid Change

Stromal accumulation of glycosaminoglycans as a sign of degeneration . The layered architecture is preserved. If the architecture is absent or distorted, the differential diagnosis should include RHD. The chordae tendineae are thinned and elongated in myxomatous degeneration, whereas in RHD they are shortened and thickened.

2. Tricuspid Valves

Tricuspid valves are most commonly removed for insufficiency or infectious endocarditis.

3. Pulmonary Valves

Pulmonary valves are usually excised because of stenosis due to congenital heart disease ,most commonly as a component of tetralogy of Fallot.

4. Mitral Valves

Mitral valves are removed for acquired post-inflammatory stenosis and may show commissural fusion, cusp scarring, and dystrophic calcification . RHD vegetations are composed mainly of fibrin and are usually no more than 2 mm in size. Cases of mitral insufficiency or myxomatous degeneration show a floppy valve with redundant and ballooned leaflets with abundant myxoid change.

5. Aortic Valves

Aortic valves are removed for stenosis and are typically heavily calcified, sometimes with commissural fusion , senile calcific aortic stenosis , post inflammatory scarring, or calcification due to a congenitally bicuspid valve .

6. Carcinoid Heart Disease

Carcinoid heart disease seen in about 50% of patients with carcinoid syndrome, typically affects the heart's right side, particularly the ventricular outflow tract. Tricuspid valve regurgitation , often with stenosis and pulmonary valve stenosis, often with regurgitation are common. Gross findings include prominent hypertrophy and plaque-like thickening of the endocardium. Microscopically, the

valvular cusps show proliferation of smooth muscle and collagen deposition, without valve destruction. There are no carcinoid tumor cells in the lesion.

C. DISORDERS OF THE MYOCARDIUM

1. Myocarditis

Myocarditis is an inflammatory disease of the myocardium that is an established cause of sudden death for both adult and paediatric populations alike. The clinical presentation of myocarditis varies drastically from asymptomatic to cardiogenic shock and sudden death. (18)

The Dallas criteria provide consensus-derived histologic criteria: "an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of ischemic damage associated with coronary artery disease." However, many have speculated that less pronounced histologic abnormalities may be present and that additional molecular, immunologic, and immunohistochemical diagnostic criteria can be used productively.(19)

The WHO/International Society and Federation of Cardiology (ISFC) defines myocarditis as a minimum of 14 infiltrating leukocytes per mm2, preferably T cells, with as many as four macrophages , also known as the Marburg criteria. The diagnosis of active myocarditis classically requires the presence of an inflammatory infiltrate ,usually lymphocytic and myocyte necrosis/degeneration or damage not characteristic of an ischemic event. Borderline myocarditis indicates the absence of necrosis or damage and can be applied to any form of inflammatory infiltrate.

One of the most controversial issue in the recent SARS-CoV-2 virus infection cardiac pathology is to know if myocarditis is a common manifestation of the disease . In a study conducted by Ferrer Gomez et al , only one patient (3.3%) showed focal myocarditis characterized by both myocyte necrosis and inflammation in absence of ischemic changes. The frequency of the diagnosis of myocarditis varies among series, probably due to different diagnostic criteria among authors.(20)

A. Primary Viral Myocarditis

Primary Viral Myocarditis accounts for most cases of myocarditis in developed countries. Cardiac involvement typically follows the primary viral infection by several days. The most commonly associated agents are enteroviruses Coxsackie A and B, adenovirus, and parvovirus B19.Less common causes are echovirus, hepatitis C, herpesvirus 6, influenza viruses A and B, and HIV. The infiltrate is composed mainly of lymphocytes with associated myocyte damage . Eosinophils are typically not seen. Primary viral myocarditis is often divided into four clinical pathologic manifestations: fulminate, subacute, chronic active, and chronic persistent.

i. Fulminant myocarditis has a distinct onset of profound left ventricular dysfunction without dilatation. Biopsy shows multiple foci of active inflammation and necrosis. Patients usually show complete histologic and functional recovery, or die within 2 weeks.

ii. Subacute myocarditis has an indistinct onset. Histologically, there is active to borderline inflammation. While there is typically complete histologic resolution with time, patients often progress to dilated cardiomyopathy.

iii. Chronic active myocarditis also has an indistinct onset with moderate ventricular dysfunction and active or borderline biopsy findings. Ongoing inflammation and fibrosis may result in the development of restrictive cardiomyopathy within 2 to 4 years after presentation.

iv. Chronic persistent myocarditis usually has an indistinct onset without left ventricular dysfunction. Active to borderline inflammation is present, which persists over time. Patients generally continue to have normal left ventricular function.

B. Eosinophilic Myocarditis

can be attributed to eosinophilic syndromes or allergic reactions that result in left ventricular compromise. Eosinophils and myocyte damage are present in the biopsy . The differential diagnosis of eosinophilia in the myocardium also includes parasitic infection and hematologic malignancies; in an immunosuppressed patient, cytomegalovirus infection should enter the differential diagnosis.

C. Idiopathic Giant Cell Myocarditis

traditionally known as Fiedler myocarditis, is associated with autoimmune diseases (e.g., inflammatory bowel disease, hypothyroidism) and is rapidly fatal if untreated. It typically occurs in young, healthy, white adults and presents as congestive heart failure. Diffuse, geographic myocardial necrosis with a mixed inflammatory infiltrate including eosinophils and multinucleated giant cells in the absence of granulomas is typical . The giant cells have the immunohistochemical profile of histiocytes

D. Chagas Disease

Most form of common protozoal myocarditis, is caused by the hemoflagellate Trypanosoma cruzi and is uncommon in the United States. However, in endemic regions of South and Central America it accounts for 25% of all deaths of 25to 40 year olds. Up to 80% of patients with Chagas disease develop myocarditis. Histologically, myofibers contain parasites with an associated mild chronic inflammatory infiltrate. In the acute phase, dense inflammation with myocyte necrosis and trypanosome amastigotes in myocytes is characteristic, whereas the chronic phase shows interstitial and perivascular lymphoplasmacytic infiltrate without fibrosis.

E. Secondary Myocarditis

Secondary Myocarditis can occur in the setting of collagen vascular diseases, rheumatic fever (RF), drugs, heat stroke, and radiation.

F. Granulomatous Myocarditis

Granulomatous myocarditis can be seen in tuberculosis or sarcoidosis. Cardiac sarcoidosis shows no necrotizing granulomas in a background of fibrosis and necrosis. Cardiac involvement, though present in 25% of systemic cases of sarcoidosis, is usually patchy and therefore a single negative endomyocardial biopsy does not exclude the disease. The differential diagnosis in cases of suspected cardiac sarcoidosis includes idiopathic giant cell myocarditis, amyloid, Chagas disease, and Fabry disease.

2. Cardiomyopathy

A. Ischemic Cardiomyopathy

Ischemic Cardiomyopathy is usually secondary to severe coronary artery disease . Atherosclerotic cardiovascular disease is by far the most common cause of ischemic cardiomyopathy

B. Hypertrophic Cardiomyopathy

The criteria for hypertrophic cardiomyopathy included a high degree of left ventricular hypertrophy with wall thickness >16 mm , an unusual distribution heterogeneous, asymmetric, or sparing the anterior septum, a left ventricular cavity of normal size < 45 mm , the presence of striking electrocardiographic abnormalities - a marked increase in voltages, prominent Q waves, and deep, negative T waves.(21) It is typically seen in healthy individuals less than 30 years old, but can be seen at almost any age. Microscopically, disarray of myofibers , myofiber hypertrophy, basophilic degeneration, and interstitial fibrosis are characteristic, although nonspecific.(13) The distinction between hypertrophic cardiomyopathy and athlete's heart was based on echocardiographic and clinical features, such as the magnitude and distribution of thickening of the left ventricular wall, the dimension of the left ventricular cavity, the presence or absence of electrocardiographic abnormalities, the type of sport played, and the results of deconditioning.(21)

C. Dilated Cardiomyopathy

Dilated cardiomyopathy also known as congestive cardiomyopathy, presents as cardiac failure due to progressive cardiac dilatation with systolic dysfunction. Hypertrophy (increased weight with normal or reduced wall thickness) and marked dilatation of all chambers is typical . Histologic examination shows nonspecific abnormalities; in about 50% of the cases, leukocytic infiltrates are present in endomyocardial biopsies. Dilated cardiomyopathy occurring in the peripartum period ,up to 6 months after delivery is known as peripartum cardiomyopathy

D. Restrictive (Obliterative) Cardiomyopathy

The exact prevalence of RCM is unknown but it is probably the least common type of CMP. The disease may be isolated or can manifest as a part of systemic disorders, such as amyloidosis, sarcoidosis, scleroderma, storage disease, anthracycline toxicity, and post irradiation therapy.(11) The ventricles are normal

or slightly enlarged and are not dilated; in contrast, the atria exhibit relative bilateral dilatation. Patchy or interstitial fibrosis is found histologically. The eosinophilic form shows an eosinophil-rich myocardial infiltrate, whereas the non eosinophilic form shows nonspecific findings. Restrictive cardiomyopathy is typically caused by endomyocardial fibrosis or hemochromatosis, but is often idiopathic.

F. Arrhythmogenic Right Ventricular Cardiomyopathy

Arrhythmogenic Right Ventricular Cardiomyopathy is also known as right ventricular dysplasia, parchment right ventricle, and Uhl anomaly. This uncommon variant of familial cardiomyopathy shows replacement of the myocardium by adipose and fibrous tissue, predominantly in the inferior and infundibular wall, without associated coronary artery sclerosis. Mutations in a number of different genes have been shown to underlie the disease and so genetic testing is likely to become part of the diagnostic workup.

G. Drug/Radiation-Induced Cardiomyopathy

Drug/Radiation-Induced Cardiomyopathy is caused by drugs such as Adriamycin and cyclophosphamide and shows primarily subcellular changes that are best seen by electron microscopy.

3. Myocardial Ischemia—Ischemic Heart Disease

IHD can declare itself through one or more of the following clinical presentations:

- Myocardial infarction (MI), in which ischemia causes frank cardiac necrosis
- Angina pectoris (literally "chest pain"), in which ischemia is not severe enough to cause infarction, but the symptoms nevertheless portend infarction risk
- Chronic IHD with heart failure
- Sudden cardiac death (SCD)

A) Myocardial Infarction (MI)

MI, also commonly referred to as "heart attack," is the death of cardiac muscle due to prolonged ischemia. The major underlying cause of IHD is atherosclerosis. Although MIs can occur at virtually any age, 10% of MIs occur in people younger than 40 years of age, & 45% occur in people younger than 65 years of age. Psychological stress, hopelessness, and depression can also be risk factors for

disastrous cardiovascular events such as stroke, coronary ischemia, and myocardial infarction.(22)

Time	Gross Features	Light Microscope
Reversible Injury		
0– 1/2 hour	None	None
Irreversible Injury		
½-4 hours	None	Usually none; variable waviness of fibres at border
4-12 hours	Dark mottling (occasional)	Early coagulative necrosis; oedema; hemorrhage
12-24 hours	Dark mottling	Ongoing coagulative necrosis; pyknosis of nuclei; myocyte hyper eosinophilia; marginal contraction band necrosis; early neutrophilic infiltrate
1-3 days	Mottling with yellow-tan infarct	Coagulative necrosis, with loss of nuclei & striations; brisk interstitial infiltrate of neutrophils
3-7 days	Hyperaemic border; central yellow-tan softening	Beginning disintegration of dead myofibers, with dying neutrophils; early phagocytosis of dead cells by macrophages at infarct border
7-10 days	Maximally yellow-tan and soft, with depressed red-tan margins	Well-developed phagocytosis of dead cells; granulation tissue at margins
10-14 days	Red-gray depressed infarct borders	Well-established granulation tissue with new blood vessels and collagen deposition
2-8 weeks	Gray-white scar, progressive from border toward core of infarct	Increased collagen deposition, with decreased cellularity
>2 months	Scarring complete	Dense collagenous scar

Table 1 : Evolution of Morphologic Changes in Myocardial Infarction

B. Chronic Ischemic Heart Disease

Chronic IHD , often called ischemic cardiomyopathy by clinicians is used here to describe progressive congestive heart failure as a consequence of accumulated ischemic myocardial damage and/or inadequate compensatory responses. In most instances, there has been a prior MI and sometimes previous coronary arterial interventions and/ or bypass surgery.

D. DISORDERS OF THE PERICARDIUM

1. Acute Pericarditis

Acute Pericarditis is idiopathic in 90% of cases, but can be caused by viruses - Coxsackie B, echoviruses, influenza, mumps, Epstein–Barr virus or bacteria - Staphylococcus aureus, Streptococci, or Haemophilus influenza.

Acute serous pericarditis can be secondary to acute rheumatic fever (RF), connective tissue disorders like systemic lupus erythematosus, uremia, metastatic malignancy, and renal transplantation.

In contrast, acute fibrinous or serofibrinous pericarditis can be secondary to myocardial infarction , uremia, chest radiotherapy, rheumatic fever (RF), systemic lupus erythematosus, cardiac surgery, pneumonia, pleural infection, and cardiac trauma.

Caseous pericarditis is usually due to M. tuberculosis infection. Healed acute pericarditis usually results in a focal pearly thickened epicardial plaque, also known as a “soldier’s plaque.

Tuberculous pericarditis is an infrequent but serious form of tuberculosis. Its diagnosis is difficult and often delayed or not even reached, which results in complications such as constrictive pericarditis with high mortality rates.(23)

2. Chronic Pericarditis

can lead to constrictive pericarditis where the heart is encased by a thick layer of fibrous tissue. Constrictive pericarditis can follow caseous pericarditis or radiotherapy, but is usually idiopathic.

3. Neoplasms.

Although primary neoplasms of the pericardium are very rare (including mesothelioma, germ cell tumors, and angiosarcoma), pericardial involvement is present in up to about 10% of patients with disseminated malignancy.

4. Pericardial Effusions.

Effusions can be as large as 500 mL in some settings, such as congestive heart failure and hypoproteinemia. However, in acute cardiac tamponade, rapid accumulation of as little as 200 to 300 mL can cause cardiac compression and death.

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

is a progressive degenerative inflammatory disease characterized by the accumulation of lipids (both intracellular and extracellular), macrophages, T cells, proteoglycans, collagen, and calcium in arterial vessels.

Major Risk Factors for Atherosclerosis

Nonmodifiable (Constitutional)	Modifiable
Genetic abnormalities	Hyperlipidemia
Family history	Hypertension
Increasing age	Cigarette smoking
Male gender	Diabetes
	Inflammation

Table 2 . Risk factors of atherosclerosis

Atherosclerosis is the leading cause of acute coronary artery syndromes (men more affected than premenopausal women; approximately one in three men will suffer a cardiac event secondary to atherosclerosis before the age of 60. Atherosclerosis is also responsible for significant disease in large vessels outside of the heart.

David Barker pioneered the idea that the 20th century epidemic of coronary heart disease in Western countries might have originated in fetal life. He postulated that impaired fetal growth might have pre-disposed the survivors to heart disease in

later life(24). Premature coronary artery disease is quite common in our young population. Smoking is the commonest risk factor followed by hypertension, dyslipidemia and obesity. Early coronary artery disease can be prevented by modifying our life style, dietary habits and regular exercise.(25).

1. CORONARY VESSELS

The American Heart Association (AHA) has described the microscopic features of atherosclerosis in detail. The AHA scheme is as follows:

- Grade 1 : isolated macrophages or foam cells
- Grade 2 : intracellular lipid accumulation
- Grade 3 : grade 2 lesions along with small extracellular lipid pools
- Grade 4 : grade 2 changes with a core of extracellular lipid
- Grade 5 : lipid core and fibrous cap, or multiple lipid cores in fibrous layers that are calcific or fibrotic
- Grade 6 : more common grade 4 or 5 lesions with a surface defect, and/or hematoma/hemorrhage, and/or thrombosis.

Atherosclerotic plaques with time can lead to significant cross-sectional luminal narrowing, traditionally classified as

- Grade 1: less than 25% cross-sectional luminal narrowing
- Grade 2: 25% to 50% luminal narrowing
- Grade 3: 50% to 75% luminal narrowing
- Grade 4: greater than 75% cross-sectional luminal narrowing

75% cross-sectional luminal narrowing is critical stenosis that has an impact on blood flow. However, the most significant sequela of coronary atherosclerosis is plaque rupture with associated thrombosis which is often associated with sudden death . Of note, recently it has become clear that clonal hematopoiesis of indeterminate potential (CHIP) is a significant risk factor for coronary heart disease. Psychophysiological risk factors may also be associated with the development of atherosclerosis via interactions between the endothelial function and ANS regulation.(26)

MODIFIED AMERICAN HEART ASSOCIATION CRITERIA FOR GRADING ATHEROSCLEROTIC LESIONS

The AHA-recommended classification had been originally developed and used to convey the results of an inquiry into the compositions of atherosclerotic lesions as they silently develop over much of a lifetime in a population. (27)

AHA GRADE	HISTOPATHOLOGIC CHANGES
• **Grade 1**	Isolated intimal foamy cells (minimal change)
• **Grade 2**	numerous intimal foamy cells often in layers (fatty streaks)
• **Grade 3**	pools of extra cellular lipid without a well-defined core (intermediate lesion or pre-atheroma)
• **Grade 4**	well defined lipid core with luminal surface covered by normal intima (atheroma or fibro plaque)
• **Grade 5**	lipid core with a fibrous cap with or without calcification (fibroatheroma)
• **Grade 6**	fibro-atheroma with cap defect such as haemorrhage and thrombosis
• **Grade 7**	calcification prominent
• **Grade 8**	fibrous tissue change prominent

Table 3. Modified AHA grading of coronary atherosclerosis

2. AORTA.

Atherosclerotic disease involving the aorta features chronic inflammation with formation of atherosclerotic plaques. However, atherosclerosis in the aorta is complicated by the formation of aneurysms, in which by definition the vessel has at least a 50% greater than normal dilatation. In the aorta, as well as other large arteries, early lesions show a thickened intima with foam cells and scattered lymphocytes in a fatty streak. It is debatable whether the presence of fatty streaks in individuals 15 to 34 years of age has pathogenetic importance for the development of atherosclerosis(28).Atheromatous plaque progression is characterized by collection of extracellular lipid with inflammation, but without significant fibrosis and without

significant changes in the media. The advanced lesions that result in abdominal aortic aneurysms show a constellation of findings including severe atherosclerosis, degeneration of the media, adventitial inflammation, fibrosis of the vessel wall, dystrophic calcification, and nonorganized mural thrombus.

Sequence of evolution of atherosclerotic lesion

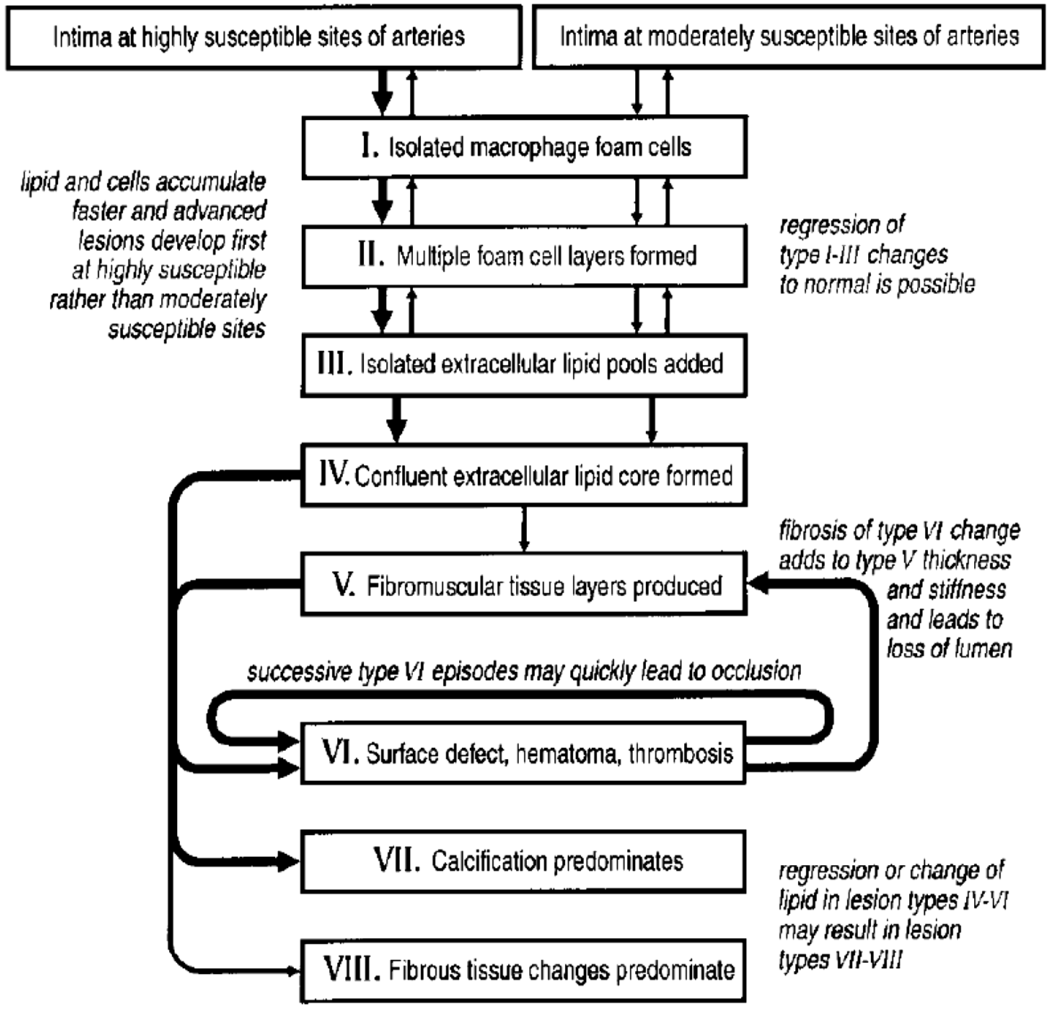


Figure 7.Outline of the sequence in the evolution of atherosclerotic lesions from type I to type IV and of the various possible subsequent pathways of progression to lesion types beyond type IV(27).

SARS-CoV-2 VIRUS INFECTION ASSOCIATED CARDIAC PATHOLOGY

Coronaviruses (CoVs) are single-stranded, enveloped RNA viruses that cause respiratory illnesses among humans and animals.(29) These ubiquitous viruses cause variably severe diseases that range from the common cold to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Pneumonia reported in Wuhan, China in late 2019 led to identification of a novel coronavirus, later designated as SARS coronavirus-2 (SARS-CoV-2), the etiologic agent of COVID-19(30) . Since that time, SARS-CoV-2 has spread rapidly across the world causing more than ten million infections and more than half a million deaths by early summer 2020 (31).

SARS-CoV-2 utilizes angiotensin-converting enzyme 2 (ACE2) for gaining entry into cells. Angiotensin-converting enzyme 2(ACE2) is expressed on vascular endothelial cells .(32)In some patients dying from COVID-19, SARS- CoV-2 has been shown to infect endothelial cells in the lungs, heart and other organs, with the endothelial cell infection being associated with thrombus in some cases (33)(34). Thrombus may also result in these patients from a generalized hyperinflammatory state, cytokine storm, with associated endothelial activation. COVID-19 is not typically associated with a generalized vasculitis.

Pre-existing cardiovascular comorbidities are prevalent among patients with COVID-19 and associated with a higher mortality rate(35). For example, in the study reported by the Chinese Centre for Disease Control and Prevention describing the early experience with the epidemic in the Hubie province, patients with cardiovascular comorbidities had a case fatality rate of 10.5% compared with an overall cohort fatality rate of 2.3% (36). There is also emerging robust evidence to suggest long-term cardiovascular sequalae after acute COVID-19 infection with an increased risk of incident conditions, including dysrhythmias, ischemic and nonischaemic heart disease, myocarditis, and thromboembolic disease, among different COVID- 19 disease severity groups compared with patients not infected with COVID-19 (37).

A study conducted by J D Haslbauer et al an increased severity of fibrin deposition, capillary dilatation, and microhaemorrhage was observed in RT-PCR-positive myocardium than in negatives and controls, with a positive correlation amongst these factors. Myocardial capillary dilatation, fibrin deposition, and microhaemorrhage may be the histomorphological correlate of COVID-19-associated coagulopathy. Increased cardio inflammation including one case of myocarditis was only detected in RT-PCR-negative hearts with significantly longer hospitalisation time. This may imply a secondary immunological response warranting further characterisation.(38)

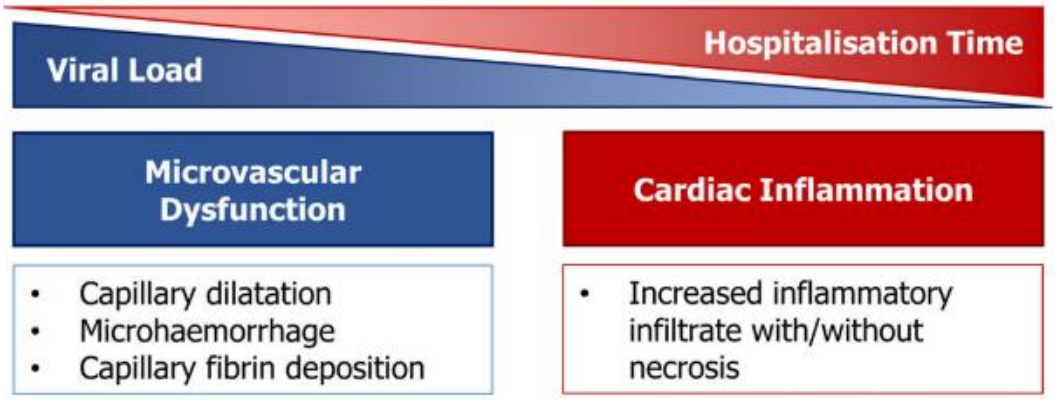


Figure 8. Temporal evolution of COVID-19-associated cardiopathy: early micro vasculopathy followed by secondary cardio inflammatory response**.**


RELEVANCE

RELEVANCE

Cardiovascular pathology is focused on diseases of the heart and blood vessels and is practiced as a subspecialty primarily in academic health centres and also in forensic pathology facilities. Autopsy continues to be a procedure of paramount importance in investigation of cardiovascular disease and sudden death.

Historically, autopsy contributed to our current knowledge of cardiovascular anatomy, physiology, and pathology. Major advances in the understanding of cardiovascular diseases, including atherosclerosis and coronary artery disease, congenital heart diseases, and cardiomyopathies, were possible through autopsy investigations and clinicopathological correlations.(8)The autopsy has been essential in the elucidation of the etiology and pathogenesis of many human diseases continuing to the present day with the COVID-19 pandemic.(39)

According to the Global Burden of Disease study age - standardized estimates, nearly a quarter of all deaths in India are attributable to cardiovascular diseases.Kerala is the most advanced Indian state in terms of epidemiological transition and has the highest prevalence of most of the non-communicable diseases (NCD) and risk factors.(14)This study was conducted with the objective to explore the vast spectrum of cardiac lesions in autopsy specimens & to identify coronary atherosclerotic changes according to age and gender in an tertiary care centre in kerala, which will aid in studying the epidemiology, pathophysiology and management modalities of these diseases.


METHODOLOGY

5.METHODOLOGY

RESEARCH QUESTION

What are the different histomorphological alterations in the heart, coronary vessels and aorta at autopsy in a tertiary care centre?

AIMS AND OBJECTIVES

1. To describe the histomorphological patterns of cardiac lesions in autopsy specimens in a tertiary care centre .

2. To identify Coronary Atherosclerotic changes related to age and gender in the study population.

STUDY DESIGN

Descriptive Cross-sectional Study

STUDY SETTING

Department of Pathology, Department of Forensic Medicine, Government Medical College, Ernakulum.

STUDY PERIOD

1 year from date of final approval by Institutional Ethics Committee & Institutional Review Board and clearance of study by the Kerala University of Health Sciences .

SAMPLE SIZE: 140

According to a study conducted by Marwah Nisha et al, proportion of cardiac pathology among autopsy specimens was 56 % .Based on this data and using sample size estimation formula, Sample size N= 4pq/d2

the minimum sample size required for the present study is found to be 140 (139.68). Where,

4 - Square of Z value of alpha error at 5% which is 1.96 approximated to 2.

P – Proportion from previous study (56%)

q – 100-p (44)

d – Relative precision of 15 % (8.4)

According to present statistics of our hospital, this sample size will be achieved by 1 year.

INCLUSION CRITERIA:

All autopsy heart specimens received at Pathology department from Jan 2021 – Dec 2021.

EXCLUSION CRITERIA:

1)Autolysed heart specimens 2) Foetal autopsy heart .

SAMPLING TECHNIQUE:

All consecutive autopsy heart specimens received in Department of Pathology will be included till the sample size is achieved.

STUDY TOOLS

1. Structured proforma for collecting basic details (age, gender) and histopathological findings in the heart, coronaries and aorta

2. Formalin fixed specimen processed by paraffin wax embedding.

3. Clean, dry microscopic slides.

4. Haematoxylin & eosin stain, special stains where ever indicated.

5. Microscope.

SAMPLING PROCEDURE:

The details of the autopsy were collected from the Department of Forensic Medicine , Government Medical College, Ernakulam and from the requisition forms received in the Department of Pathology. Formalin fixed specimens were inspected externally, dissected by in inflow outflow method, emptied of post-mortem clot & weighed. Whenever required, short axis method was followed. Measurement of thickness of right ventricular wall, left ventricular wall and interventricular septum was done. The valves were examined for stenosis and calcification. Areas of myocardial ischaemia whether recent or old was noted , and their location & sizes were recorded. All the three major coronary arteries i.e. right coronary artery, left anterior descending artery

and left circumflex coronary artery was examined using sections at regular intervals of 4-5mm and graded according to Modified American heart association (AHA) criteria for grading atherosclerotic lesions. The ascending aorta was checked for dilatation, thickening or atheromatous plaque. Sections were taken from right & left ventricular wall & three major coronaries and stump of aorta for microscopic examination. Additional sections will be taken wherever necessary.

Tissues were processed and subjected to paraffin section at 4 μm thickness, and then stained with routine haematoxylin and eosin staining method. Findings were noted in tabulated form and arranged according to their age group. The results was expressed as percentage of total value.

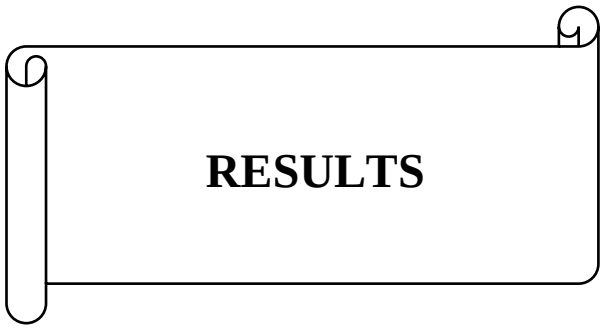
DATA MANAGEMENT AND STATISTICAL ANALYSIS

The data was numerically coded and entered in Microsoft excel spread sheet. Further statistical analysis will be done using SPSS software. Qualitative variables will be summarised using frequency and percentage. Quantitative data was summarised using mean and standard deviation. Association with qualitative variables will be done using Chi-Square test. A significant level will be fixed at a p value less than 0.05 .

BUDGET OF THE STUDY : Self Funded

ETHICAL CONSIDERATIONS:

The study protocol was submitted to the Scientific Research committee as well as Institutional Ethical committee of Government Medical College Ernakulam and clearance was obtained for conducting study. Confidentiality of the patient was ensured and maintained throughout the study.


RESULTS

RESULTS

A total of 140 autopsy specimens of heart received at the Dept. of Pathology GMC Ernakulam from 2021 to 2022 was included in the study. The histomorphological patterns of cardiac lesions were studied along with distribution of Atherosclerotic changes of coronaries and aorta according to age & gender .

1. Sex Distribution of cases in study

Out of the 140 cases 109 were (77.9 %) males & 31 (22.1%) were females with male to female ratio 3.5:1 .There was remarkable male dominance.

Gender	Number of Cases	Percentage
Female	31	22.1%
Male	109	77.9%
Total	**140**	**100%**

Table 4.Sex Distribution of cases in study(n=140)

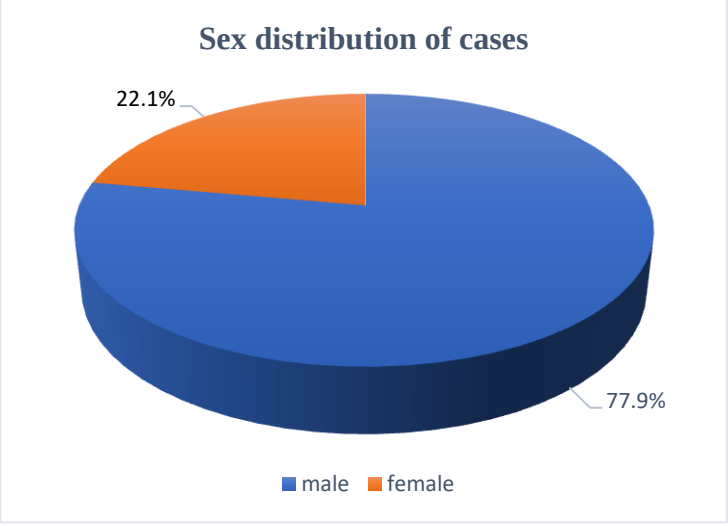


Figure 9. Pie chart of sex distribution

2.Age distribution of study population in different genders of study populatiom

The age of subjects ranged from 18years to 92 years. Maximum number of cases belonged to age group 41-50 yrs (26.4%) followed by 31-40 yrs (25%) with a mean age of 45.98 (Standard Deviation of 15.82)

Age Group	Number of Cases		Total (Percentage%)
	Females	Males	
< 20	1	3	4(2.9%)
21-30	3	18	21(15%)
31-40	10	25	35(25%)
41-50	8	29	37(26.4%)
51-60	2	18	20(14.3%)
61-70	0	11	11(7.9%)
71-80	3	3	6(4.3%)
81-90	2	2	4(2.9%)
91-100	2	0	2(1.4%)
Total	**31**	**109**	**140(100%)**

Table 5. Age distribution of study population(n=140)

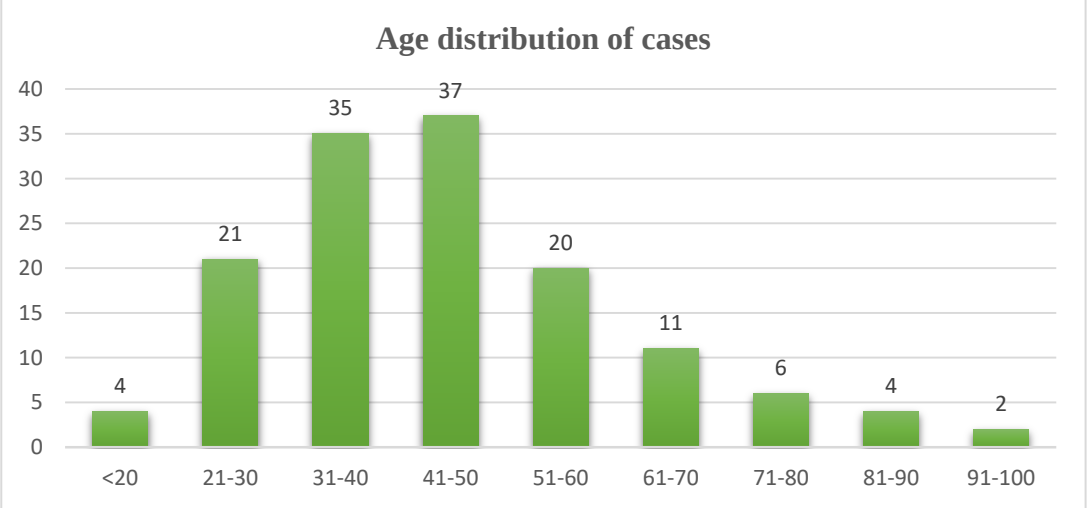


Figure 10. Bar Chart of age distribution in study population

3.Cause of death in study population

The alleged cause of death mentioned in most cases were sudden collapse 117 cases (83.6%).Other causes included 2.9% each of RTA & Assault ,2.1% each of hanging, drowning & electric shock followed by snake bite, carcinoma & burns.

Cause Of Death	No. of Cases	Percentage
Sudden Collapse	117	83.6%
RTA	4	2.9%
Hanging	3	2.1%
Snake Bite	2	1.4%
Burns	1	0.7%
Drowing	3	2.1%
Electric Shock	3	2.1%
Seizure	1	0.7%
Carcinoma	2	1.4%
Assault	4	2.9%
TOTAL	**140**	**100%**

Table 6.Cause of death in study population

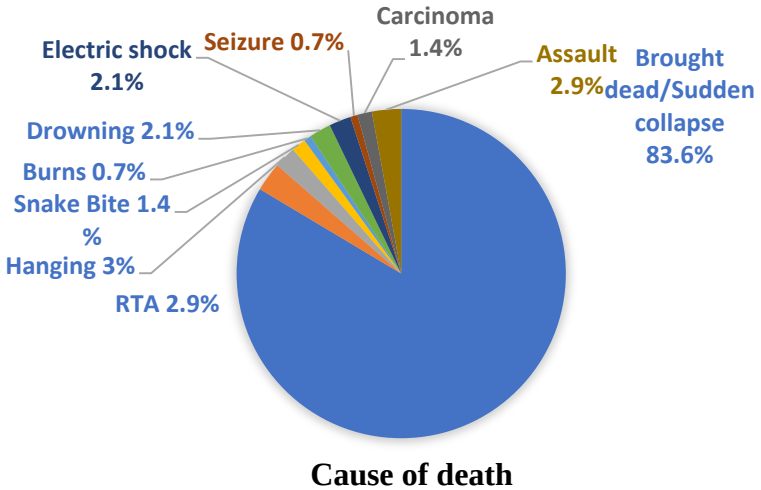


Figure 11. Pie chart of cause of death in study population

4.Comorbidites

Out of the 140 cases ,15 cases (10.7%) had RT-PCR confirmed SARS-CoV-2 virus infection of which 11(73.33%) cases showed cardiac pathology.

Valvular heart disease was seen in 4 cases (2.95). DM & HTN was recorded in 3(2.1%) & 4(2.9%) cases respectively. Both DM & HTN was seen in 2 cases (1.4%).

Comorbidities	No.of Cases	Percentage
Diabetes Mellitus	3	2.1%
Hypertension	4	2.9%
Diabetes mellitus &Hypertension	2	1.4%
Dyslipidemia & Hypertension	1	0.7%
Valvular Heart Disease	4	2.9%
SARS-CoV-2 virus infection	15	10.7%
Heart Disease	4	2.9%
Others-Renal, Hepatic, Respiratory illness	18	12.9%
Not Documented	89	63.6%
Total	**140**	**100%**

Table 7. Comorbidities in study population

5.Weight of heart

Post fixation heart weight recorded ranged from a minimum of 125g to a maximum heart weight of 625g with a mean weight of 327g and standard deviation of 95.29.

Heart weight was within normal range in 27 cases (87.1 %) of females & 89 cases (81.65%) of males . Out of the 31 females , 4 (12.90%) showed increased heart weight. 20(18.35%) out of 109 males showed increased heart weight.

There was significant difference in weight in males & females (p values <0.05)

Gender	Normal Heart Weight	Weight > 350gm in females > 400gm in males	Total
Female	27(87.1%)	4(12.90%)	31
Male	89(81.65%)	20(18.35%)	109
Total	116(82.85%)	24(17.14%)	140

Table 8. Gender wise distribution of weight of heart

6. Right Ventricular wall thickness

Right ventricular thickness was found to be in the normal range in 22(71%) females and 69(63.3 %)males. Out of 140 cases, 40(36.7%) males and 9 (29%) females showed increased RV wall thickness, which was not statistically significant . The mean RV wall thickness was 0.503cm with a standard deviation of 0.144

Gender	Normal RV Thickness	RV wall thickness >0.6cm	Total
Female	22(71%)	9(29%)	31(100%)
Male	69(63.3%)	40(36.7%)	109(100%)
Total	91(65%)	49(35%)	140(100%)

Table 9. Gender wise distribution of Right ventricular wall thickness

Increased Right ventricular wall thickness was found in 31(38.75%) cases above 40 years where as 18(30%) cases below and equal to 40 years showed increased Right ventricular wall thickness.

Age	Normal RV Thickness	RV Thickness > 0.6cm	Total
</=4o Years	42(70%)	18(30%)	60(42.86%)
>40 Yrs	49(61.25%)	31(38.75%)	80(57.14%)
Total	91(65%)	49(35%)	140(100%)

Table 10. Distribution of Right ventricular wall thickness before &after the 4th decade

7.Left Ventricular wall thickness

The mean Left ventricular thickness was found to be 1.466 cm with a standard deviation of 0.269. Out of the 140 cases 40(28.58%) cases showed increased LV wall thickness , which included 3(9.7%)females and 37(33.94%) males. This was not statistically significant.

Gender	Normal LV Thickness	LV Thickness > 1.6cm	Total
Female	28(90.3%)	3(9.7%)	31(100%)
Male	72(66.06%)	37(33.94%)	109(100%)
Total	100(71.42%)	40(28.58%)	140(100%)

Table 11. Gender wise distribution of Left ventricular wall thickness

Increased Left ventricular was thickness was found in 29 (36.25%) cases in the 4th decade and above where as 14(23.33%) cases below and equal to 40 years showed increased Left Ventricular wall thickness

Age	Normal LV Thickness	LV Thickness >1.6cm	Total
</=4o Years	46(76.67%)	14(23.33%)	60(42.86%)
>40 Years	51(63.75%)	29(36.25%)	80(57.14%)
Total	97(69.29%)	43(30.71%)	140(100%)

Table 12. Distribution of Left ventricular wall thickness before &after the 4th decade

8.Histomorphological spectrum of cardiac changes

A wide spectrum of histomorphological findings were observed, the most common being Coronary atherosclerosis (80.7%) followed by Ischemic heart disease (IHD)(44.28%).There were 16(11.42%) cases of myocarditis which included lymphocytic (2.8%) & eosinophilic (0.71%) myocarditis. One case of vaso-occlusive crisis of sickle cell disease(0.71%), cardiac amyloidosis(0.71%) & infective endocarditis(0.71%) was noted .Twenty seven(19.3%) cases revealed no significant changes in the heart .

Histopathological Findings	No.of Cases	Percentage
Coronary Atherosclerosis	113	80.7%
Ischemic Heart Disease	62	44.28%
Myocardial Hypertrophy	14	10%
Myocarditis	16	11.42%
Eosinophilic Myocarditis	1	0.71%
Lymphocytic Myocarditis	4	2.8%
Pericarditis	5	3.57%
Infective Endocarditis	1	0.71%
Infection -Tuberculosis	2	1.42%
Vaso-Occlusive Crisis-Sickle Cell Disease	1	0.71%
Cardiac Amyloidosis	1	0.71%
No Significant Pathology	27	19.3%

Table13.Histomorphological spectrum of cardiac changes

Cases of Ischemic heart disease (IHD) included chronic IHD (27.86%), acute myocardial infarction (MI) (10.71%) and acute on chronic IHD (5.71%).

	Percentage of ischemic heart disease		
	Acute MI	Chronic IHD	Acute on chronic IHD
Percentage %	10.71%	27.86%	5.71%
No. of cases	15	39	8

Table 14. Frequencies of acute MI, chronic IHD and acute on chronic IHD

9.Age and gender distribution of coronary atherosclerosis

In the study there is a male preponderance of coronary atherosclerosis with 92 cases (84.4%) compared to females with 21 cases (67.74%).Frequency of coronary atherosclerosis is higher in age group above 40 years with 72 cases (51.43%) of which males are more frequently involved than females with 59 (54.13%) cases & 13 (41.94%) cases respectively

	Coronary atherosclerosis present		Coronary atherosclerosis absent		Total
	</=40 years	>40 years	</= 40 years	>40 years	
Females	**8 (25.8%)**	**13 (41.94%)**	**6 (19.35%)**	**4 (12.9%)**	**31 (100%)**
Males	**33 (30.28%)**	**59 (54.13%)**	**13 (11.93%)**	**4 (3.67%)**	**109 (100%)**
Total	**41 (29.29%)**	**72 (51.43%)**	**19 (13.57%)**	**8 (5.71%)**	**140 (100%)**

Table 15. Age and gender distribution of coronary atherosclerosis

10.Distribution of number of coronary vessels involved by coronary atherosclerosis

Amongst the 140 cases studied,113cases (80.7%) showed atherosclerotic changes in coronary vessels out of which, all the three coronary arteries were involved in cases 60(42.80%) followed by double vessel involvement in 39 cases(27.9%) and single vessel involvement in cases 14(10%).No significant /mild atherosclerosis was found in 27(19.3%)of cases.

Number Of Coronary Vessels Involved By Coronary Atherosclerosis	Number of Cases	Percentage
Single vessel	14	10%
Double vessel	39	27.9%
Triple vessel	60	42.9%
No significant/mild atherosclerosis	27	19.3%
Total	140	100%

Table 16. Frequency of number of coronary vessels involved by coronary atherosclerosis

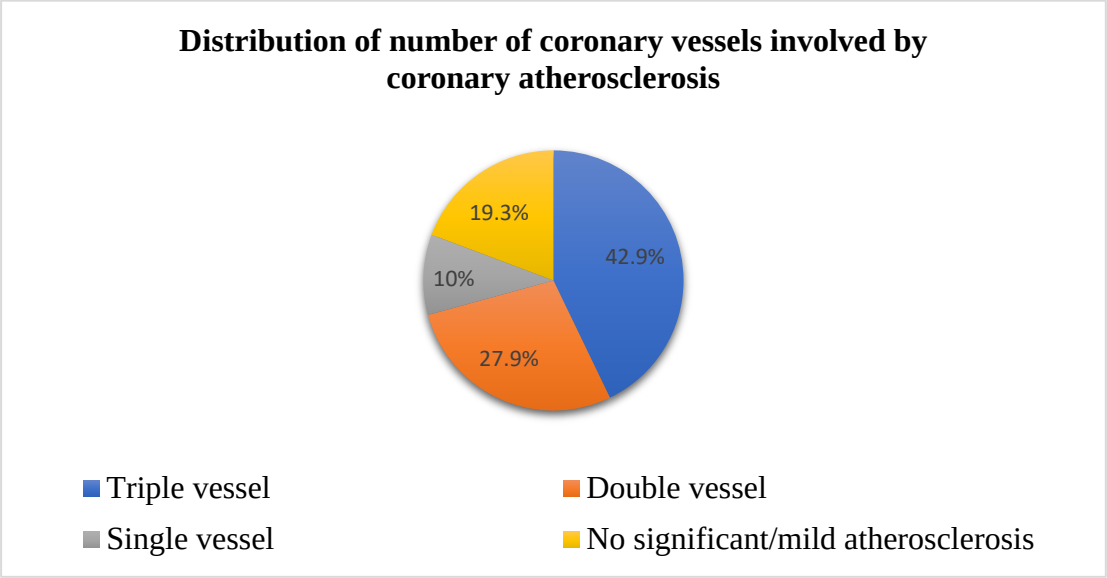


Figure 12. Pie chart of distribution of number of coronaries involved by coronary atherosclerosis

10.Frequency of coronary atherosclerosis in 3 major coronaries

Three major coronaries of the autopsy cases were graded on the basis of percentage occlusion. Left Anterior descending Artery was the most common coronary involved in 101cases (72.14%) followed by Right Coronary Artery in 92(65.71%)cases and Left Circumflex Artery in 80 (57.14%) cases.

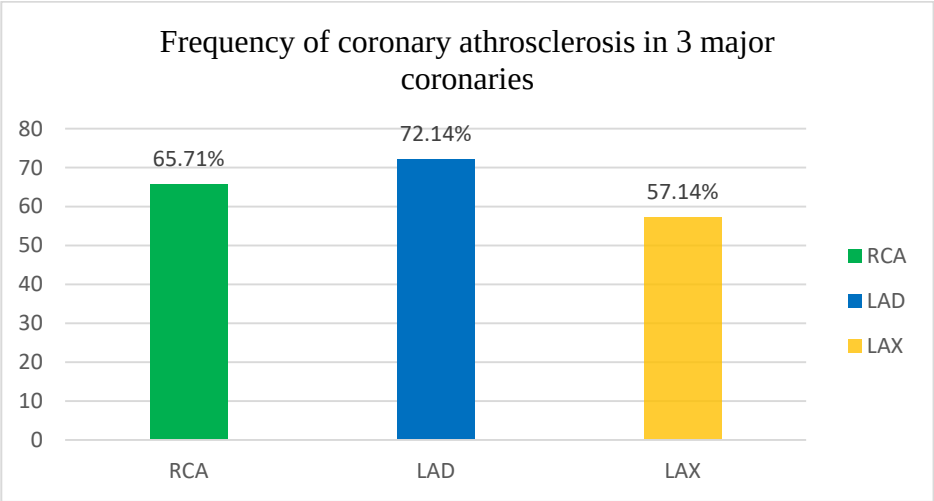


Figure 13. Bar diagram showing frequency of coronary atherosclerosis in 3 major coronaries.

11.Age wise distribution of coronary atherosclerosis in major coronaries

The frequency of coronary atherosclerosis in all three coronary vessels were higher after the age of 40 years, especially in Left Anterior Descending artery in 66 cases (82.5%)

Age group	</= 40years			>40years		
Vessels	**RCA**	**LAD**	**LCX**	**RCA**	**LAD**	**LCX**
Vessel occlusion present	**33 (55%)**	**35 (58.33%)**	**28 (46.67%)**	**59 (73.75%)**	**66 (82.5%)**	**52 (65%)**
Vessel occlusion absent	**27 (45%)**	**25 (41.67%)**	**32 (53.33%)**	**21 (26.25%)**	**14 (17.5%)**	**28 (35%)**
Total	**60(100%)**			**80(100%)**		

Table 17. Age wise distribution of coronary atherosclerosis in major coronaries

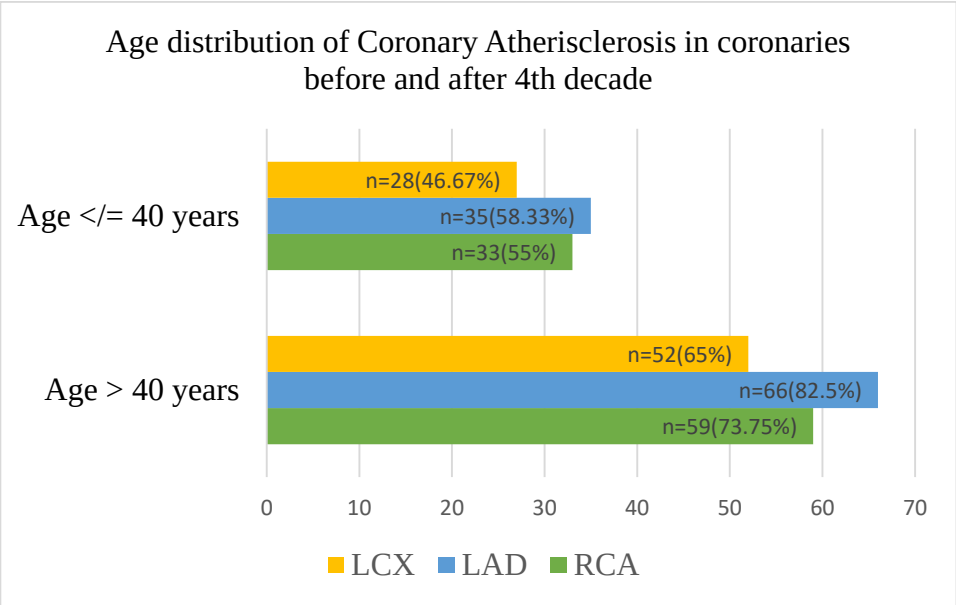


Figure 14. Clustered Bar diagram -age distribution of coronary atherosclerosis in 3 major coronaries before and after 40 years

12.Gender wise distribution of coronary atherosclerosis in Major coronaries

In our study the incidence of coronary atherosclerosis was more in males compared to females, with Left Anterior Descending artery involvement seen in 84 (77.06%)males and 17 (54.84%) females. Right coronary artery involvement was observed in 75 (68.81%) and 17 (54.84%) males and females respectively. Left circumflex artery involvement seen in 66 (60.55%) males and 14(45.16%)females.

	Vessel Occlusion present			Vessel occlusion absent		
Sex	**RCA**	**LAD**	**LCX**	**RCA**	**LAD**	**LCX**
Females	**17 (54.84%)**	**17 (54.84%)**	**14 (45.16%)**	**14 (45.16%)**	**14 (45.16%)**	**17- (54.84%)**
Males	**75 (68.81%)**	**84 (77.06%)**	**66 (60.55%)**	**34 (31.19%)**	**25 (22.94%**	**43**

Table 18. Gender wise distribution of coronary atherosclerosis in Major coronaries

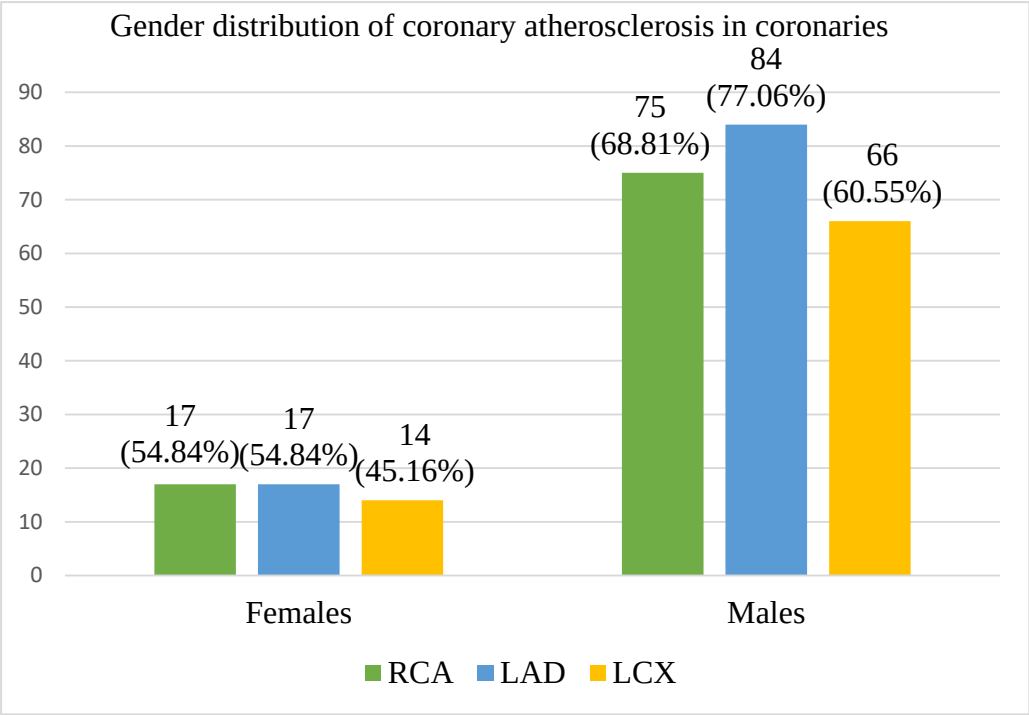


Figure 15. Bar diagram-gender distribution of coronary atherosclerosis in major coronaries

13.Severity grading of Coronary Atherosclerosis based on % of occlusion:

Left Anterior Descending artery was the most commonly involved artery with 30 cases (21.43%)showing 50-75% occlusion, followed by involvement of Right Coronary Artery and Left Circumflex artery .

% Of Occlusion	RCA	LAD	LCX
0-25%	89(63.57%)	73(52.14%)	97(69.29%)
25-50%	20(14.29%)	16(11.43%)	12(8.57%)
50-75%	18(12.86%)	30(21.43%)	19(13.57%)
75-100%	13(9.29%)	21(15%)	12(8.57%)
Total	140(100%)	140(100%)	140(100%)

Table 19. Severity grading of Coronary Atherosclerosis based on % of occlusion:

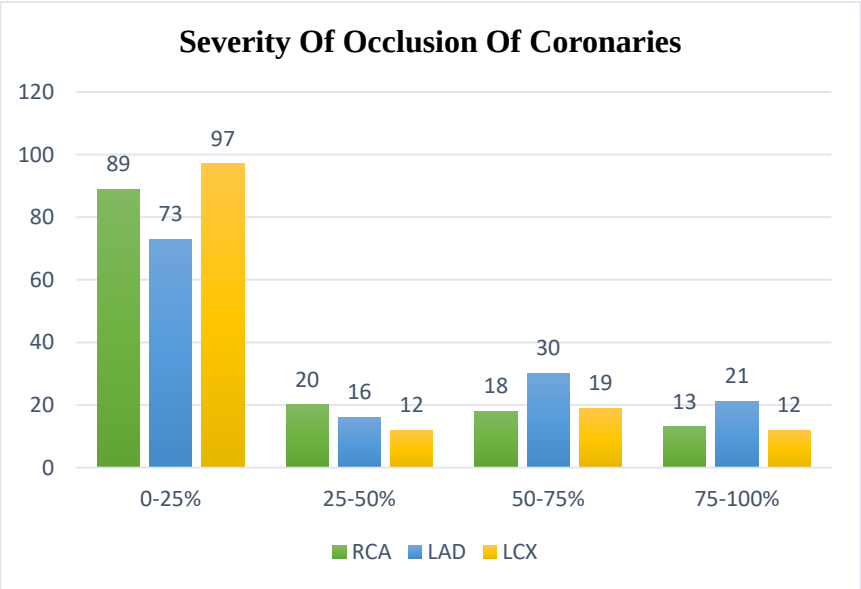


Figure 16. Bar diagram -Severity grading of Coronary Atherosclerosis based on % of occlusion:

14.Severity grading of Coronary Atherosclerosis based on Modified AHA criteria

The three major coronary arteries were graded in 1-8 grades as per Modified AHA criteria. It was seen that in majority of autopsy cases coronaries were involved to some extent . But Left Anterior Descending is the most common coronary artery involved with grade 7 occlusion in majority of cases (20%) followed by Right Coronary Artery and Left Circumflex artery.

Modified AHA Grading	RCA	LAD	LCX
Normal	21(15%)	17(12.1%)	33(23.6%)
Grade I	27(19.3%)	22(15.7%)	27(19.3%)
Grade II	18(12.9%)	15(10.7%)	24(17.1%
Grade III	17(12.1%)	15(10.7%)	8(5.7%)
Grade IV	24(17.1%)	18(12.9%)	11(7.9%)
Grade V	7(5%)	14(10%)	7(5%)
Grade VI	5(3.6%)	10(7.1%)	12(8.6%)
Grade VII	20(14.3%)	28(20%)	16(11.4%)
Grade VIII	1(0.7%)	1(0.7%)	2(1.4%)

Table 20. Severity grading of Coronary Atherosclerosis based on Modified AHA criteria

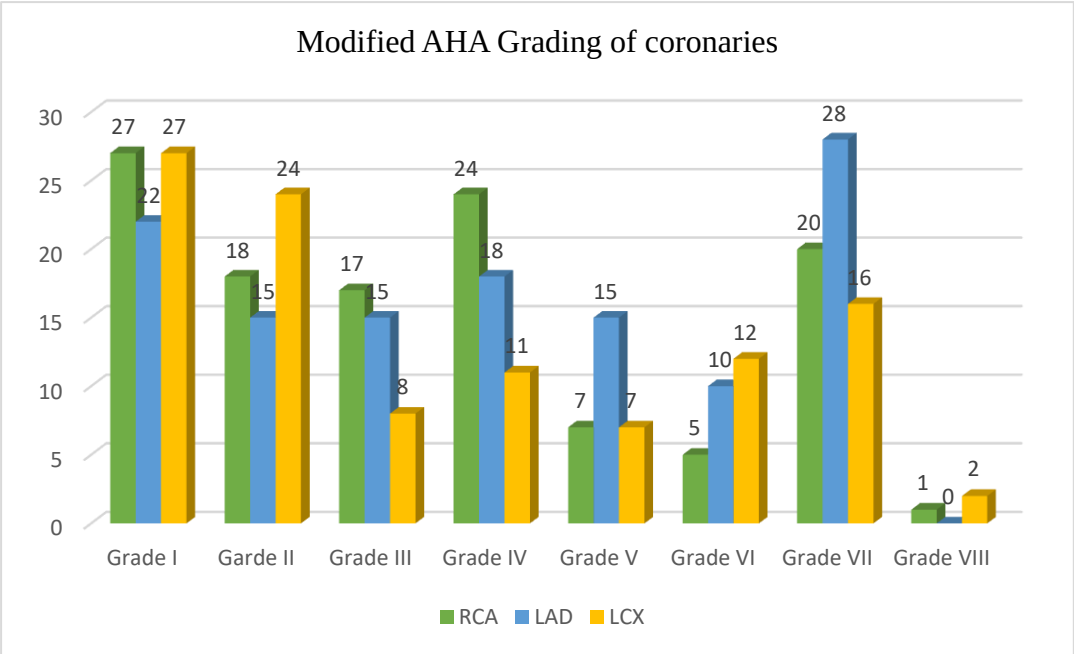


Figure 17. Bar diagram- Severity grading of Coronary Atherosclerosis based on Modified AHA criteria

15.Age wise distribution of Atherosclerosis of aorta before and after 4th decade

Among the 80 cases who were above 40 years of age,77(96.25 %) showed changes of atherosclerosis in aorta. Among the 60 cases who were below 40 years of age, 45(75%) showed aortic atherosclerosis. Aortic atherosclerosis was more in the older age group above 40 years, but not statistically significant.

Age	Atherosclerosis Aorta Present	Atherosclerosis Aorta Absent	Total
</=4o Years	45(75%)	15(25%)	60(100%)
>40 Years	77(96.25%)	3(3.75%)	80(100%)
Total	122(87.14%)	18(12.85%)	140

Table 21. Age wise distribution of Atherosclerosis of aorta before and after 4th decade

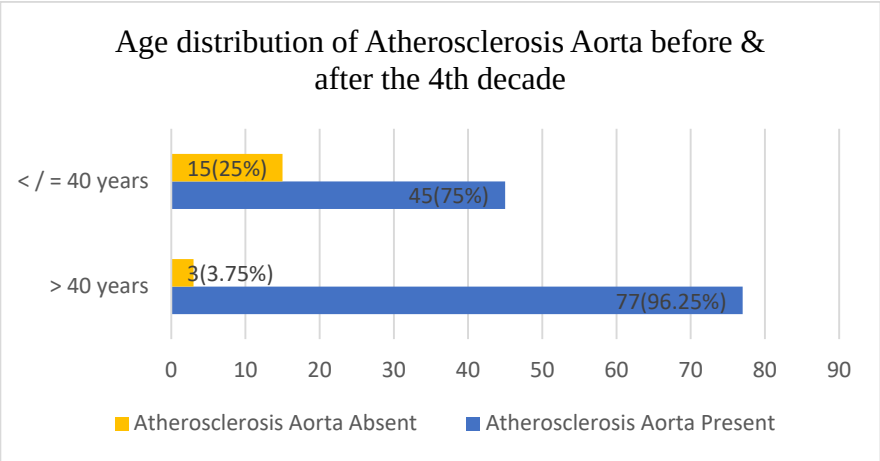


Figure 18.Age wise distribution of Atherosclerosis of aorta before and after 4th decade

16.Gender wise distribution of Atherosclerosis of Aorta before & after 4th decade

Males were more affected by Aortic atherosclerosis than females with 96(88.07%) cases and 26 (83.87%)cases respectively.

Age	Atherosclerosis Aorta Present	Atherosclerosis Aorta Absent	Total
Females	26(83.87%)	5(16.13%)	31(100%)
Males	96(88.07%)	13(11.93%)	109(100%)
Total	122(87.14%)	18(12.86%)	140(100%)

Table 22. Gender wise distribution of Atherosclerosis of Aorta before & after 4th decade

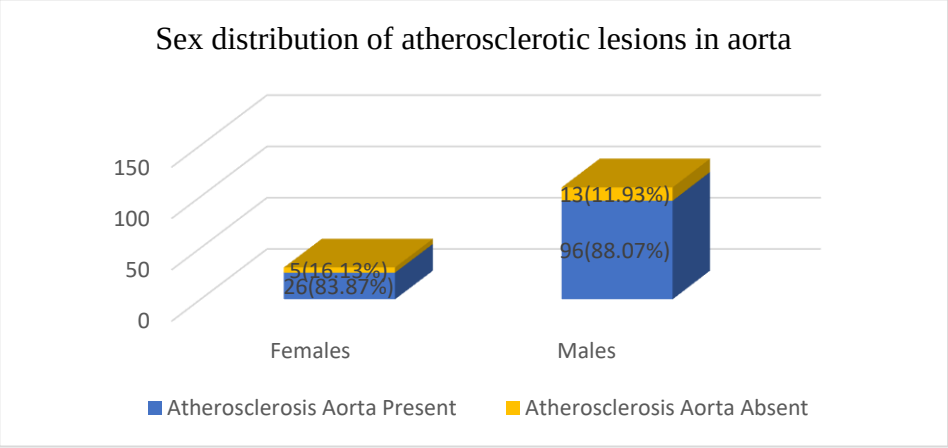


Figure 19. Gender wise distribution of Atherosclerosis of Aorta before & after 4th decade

17.Spectrum of cardiac pathology in SARS-CoV-2 virus infection

As our study was conducted during the COVID -19 pandemic, we received 15 cases (10.7%) of RT-PCR confirmed SARS-CoV-2 virus infection of which most of the cases (10 cases,66.66%) were males. Out of the 15 cases , 11(73.33%) cases showed coronary atherosclerosis which was the most frequent histomorphological finding. 8 (53.33%) cases showed myocardial pathology which included 2 (13.33%) cases of myocarditis ,3(20%) cases of chronic ischemic heart disease & 3(20%) cases of acute myocardial infarction. One case of pericarditis (6.66%)was seen. Three (20%) cases showed LV hypertrophy (LVwall thickness >1.5cm) . Our results indicate a modest involvement of the heart in SARS -CoV-2 virus infection.

Histopathlogical findings in Myocardium in SARS-CoV-2 infection.	Present study (n=15)
Interstitial fibrosis	9(60%)
Ischemic necrosis	3(20%)
Capillary dilatation	12(80%)
Microhaemorrhage	4(26.67%)
Focal Capillary fibrin	3(20%)
Interstitial edema	12(80%)
Inflammatory infiltrate without necrosis	4(26.67%)
Myocarditis	2(13.33%)

Table 23. Spectrum of histopathological findings in myocardium of cases with SARS-CoV-2 infection.

Histological evaluation of the cases of SARS-CoV-2 virus infection showed capillary dilatation and interstitial oedema in 12(80%)cases, interstitial fibrosis in 9(60%)cases, microhaemorrhage & inflammatory infiltrate without necrosis in 4(26.67%)cases each.3 cases(20%) of ischemic necrosis & 2 cases of myocarditis was seen.3 cases (20%) showed focal capillary fibrin.

PHOTOGRAPHS

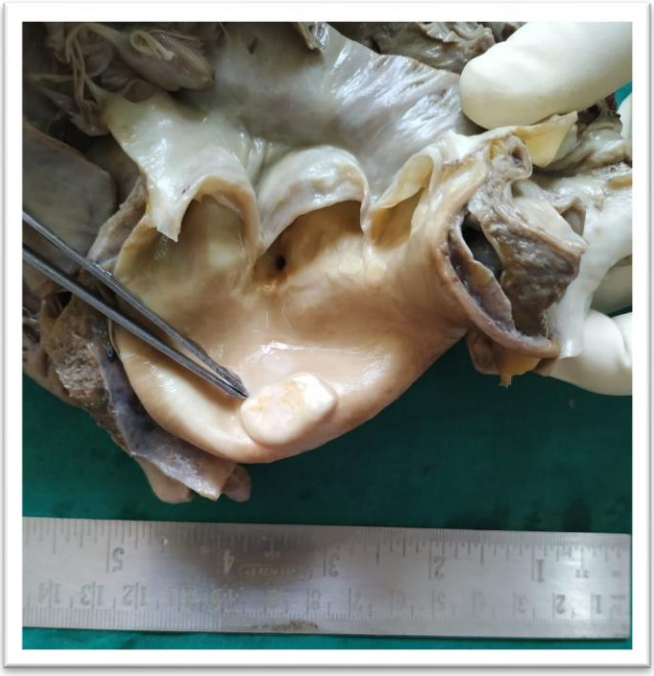


Figure 20. Atheroma Aorta

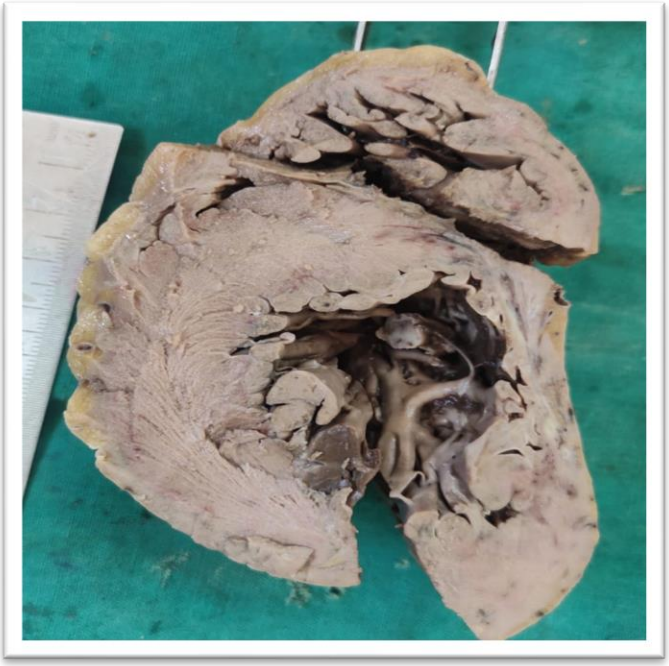


Figure 21. Gross image of Left Ventricular Hypertrophy

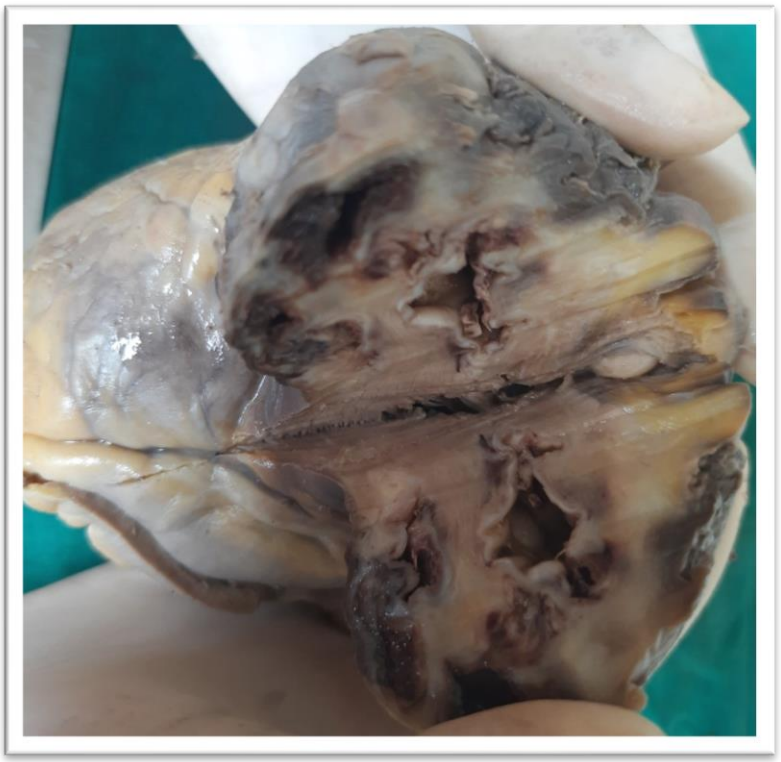


Figure 22. Gross image of Tuberculosis of Heart

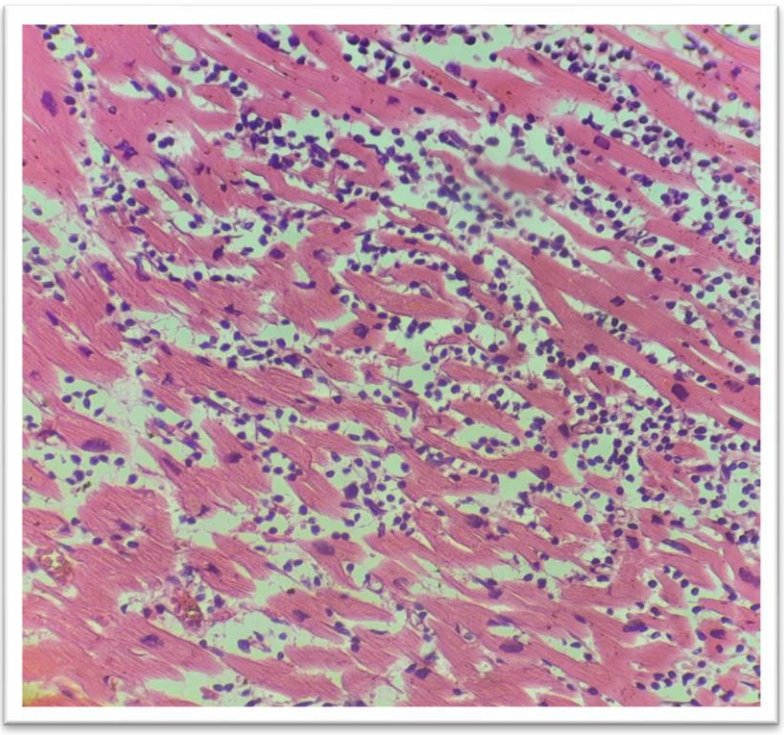


Figure 23. Photomicrograph of lymphocytic Myocarditis (H & E ,40X)

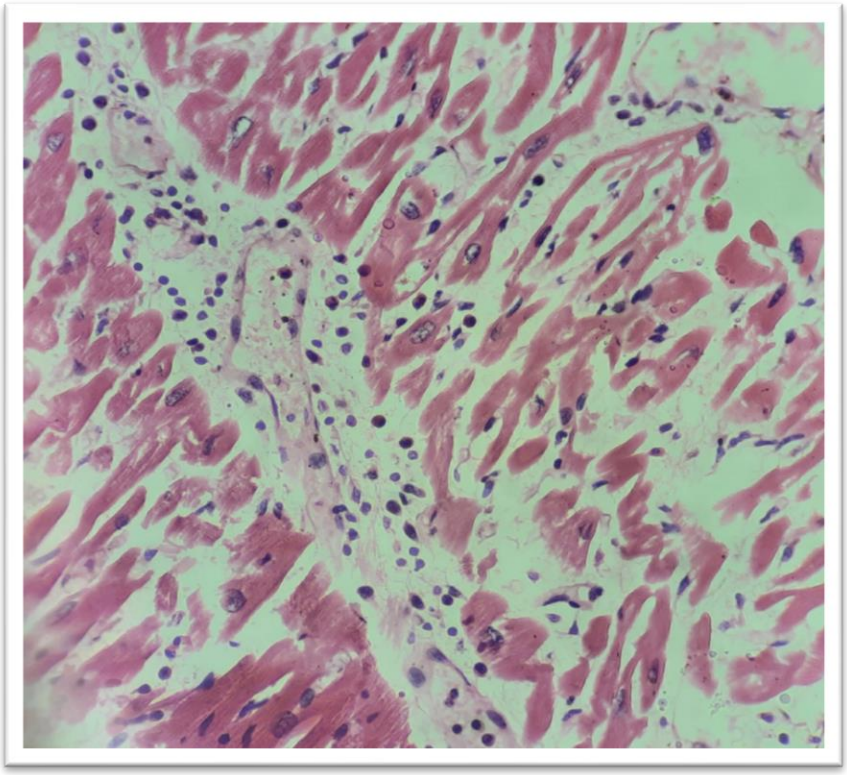


Figure 24.Photomicrograph of Eosinophilic Myocarditis (H & E ,40X)

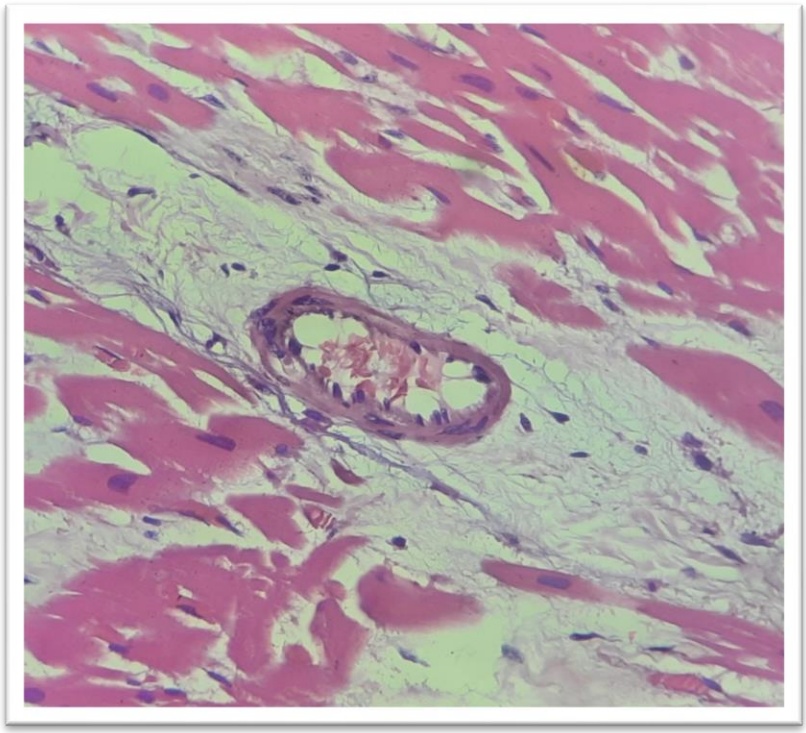


Figure 25. Photomicrograph of Vaso-occlusive Crisis- Arteries Clogged By Sickle Cells (H &E , 40 X)

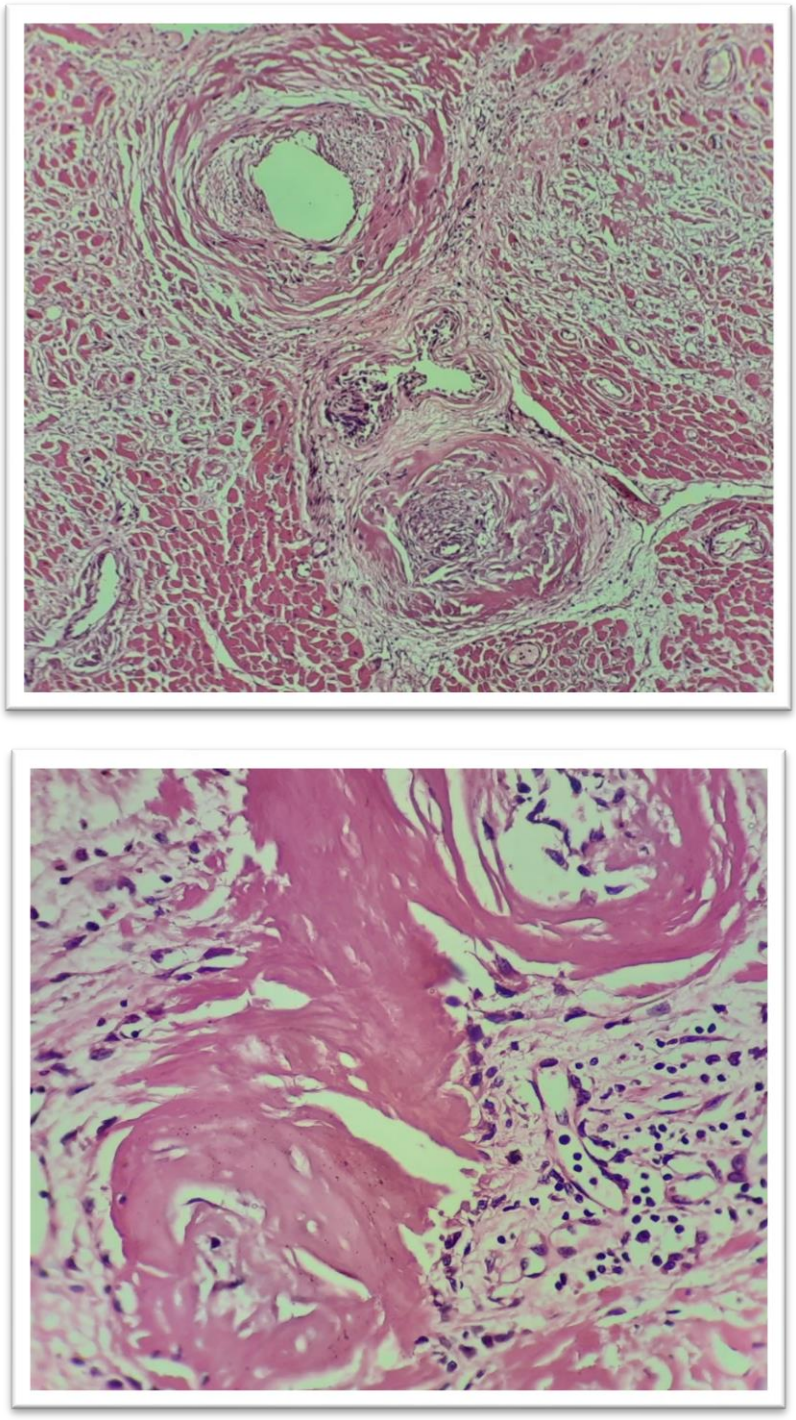


Figure 26. Photomicrograph of Amyloid deposition in the wall of coronary arterioles with atrophic myocytes (H & E ,10X & 40X)

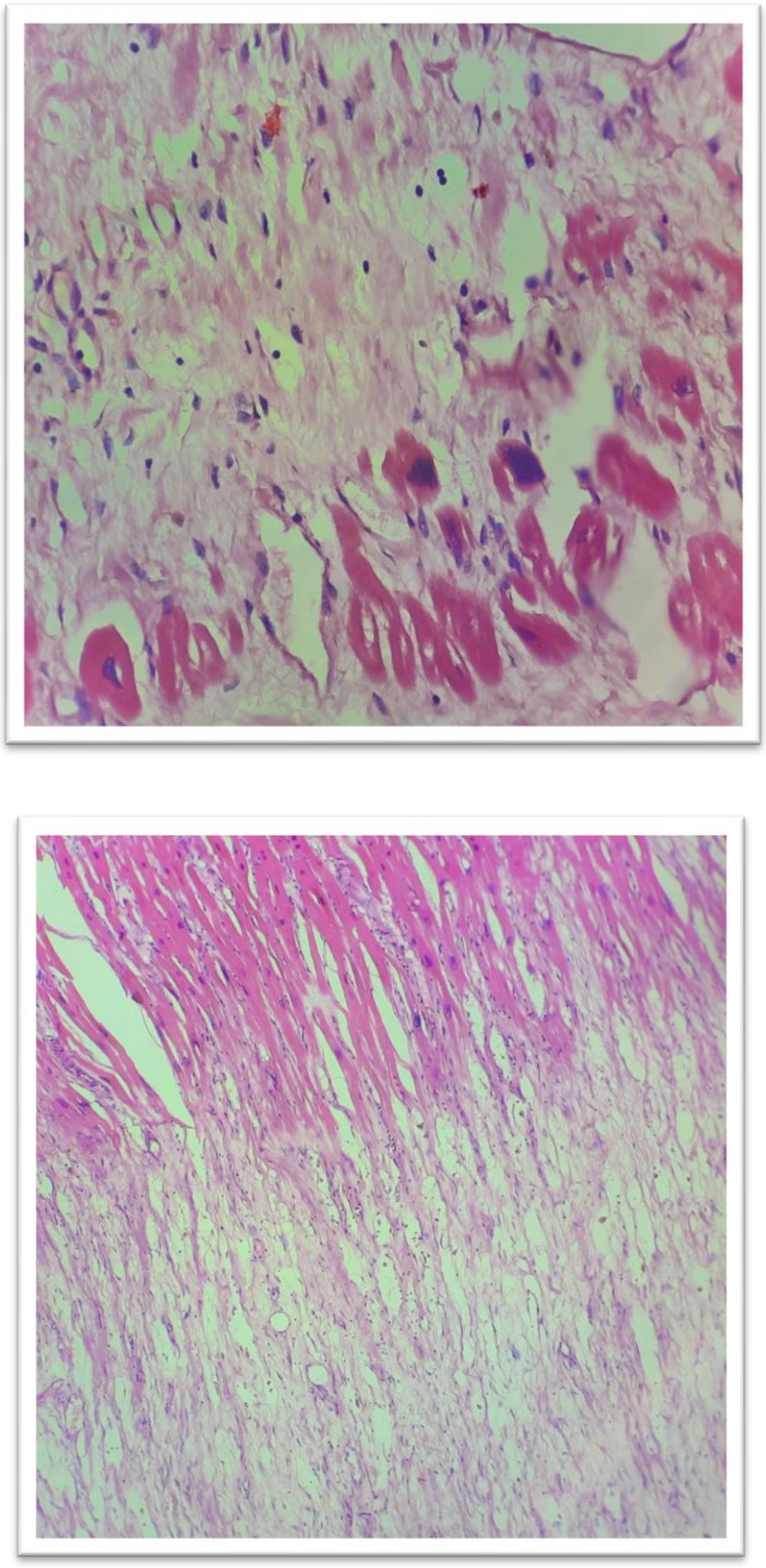


Figure 27. Photomicrograph of Myocardial Infarction – Necrosed myocardial fibers with acute inflammatory infiltrate (H& E 10X & 40 X)

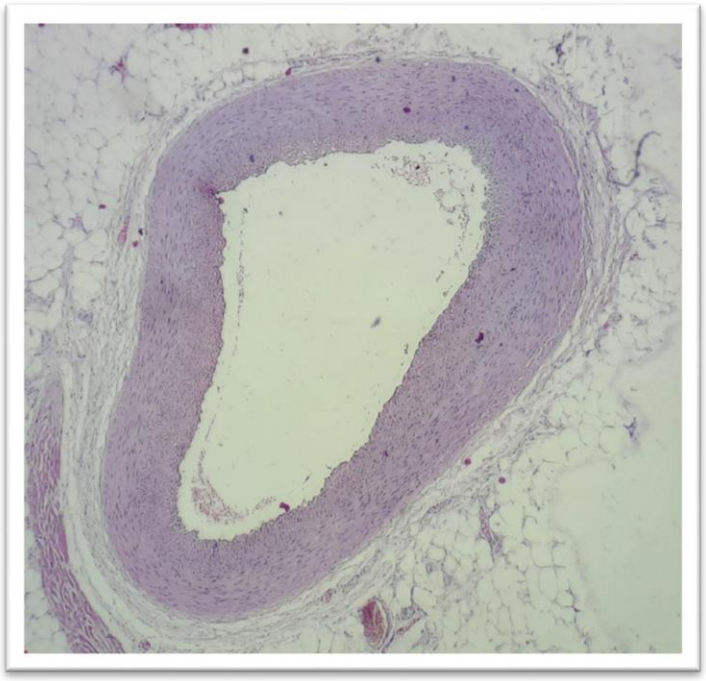


Figure 28. Photomicrograph of Grade I coronary atherosclerosis (H & E ,40X)

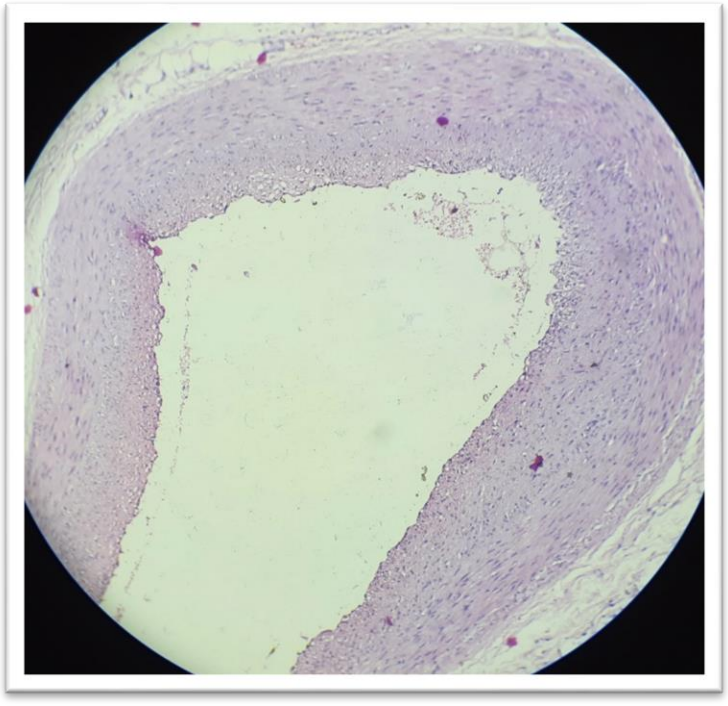


Figure 29. Photomicrograph of Grade II coronary atherosclerosis (H & E ,40X)

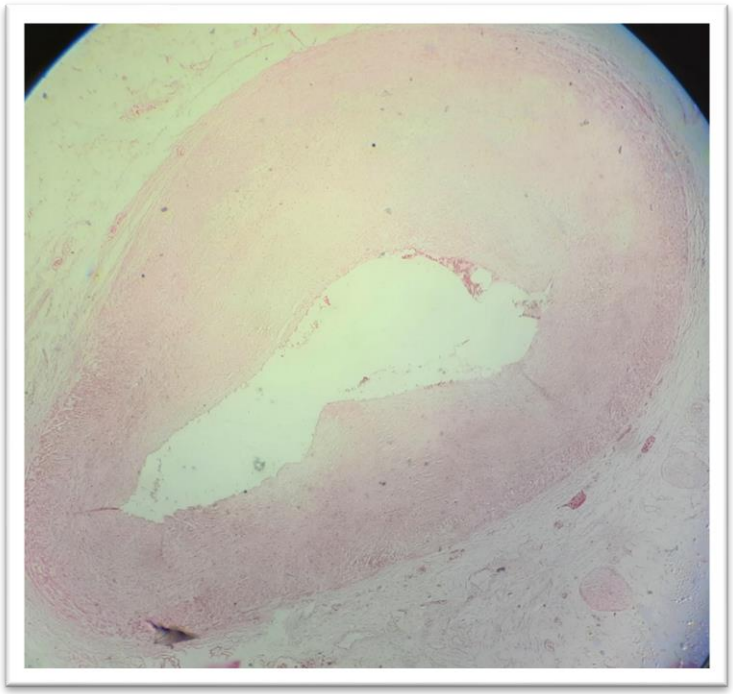


Figure 30. Photomicrograph of Grade III coronary atherosclerosis (H & E ,40X)

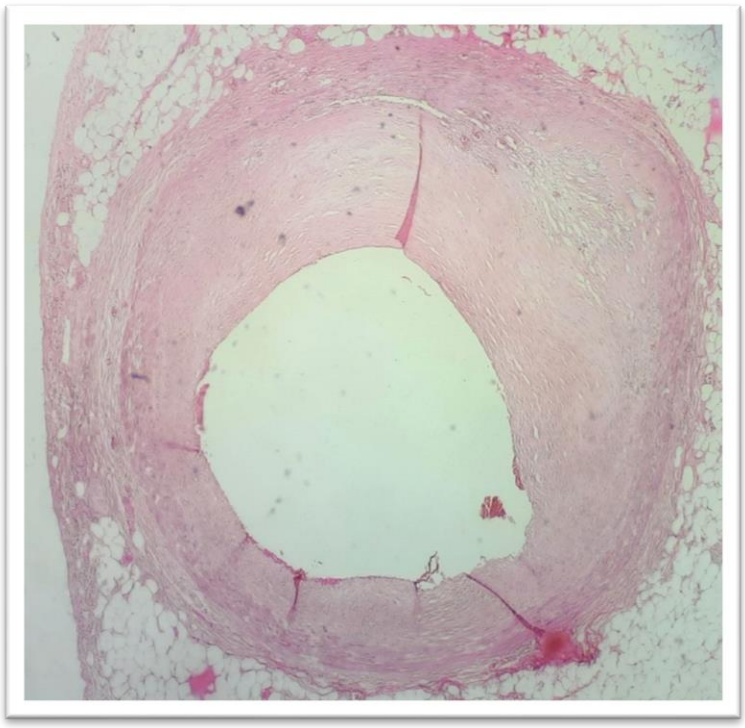


Figure 31. Photomicrograph of Grade IV coronary atherosclerosis (H & E ,40X)

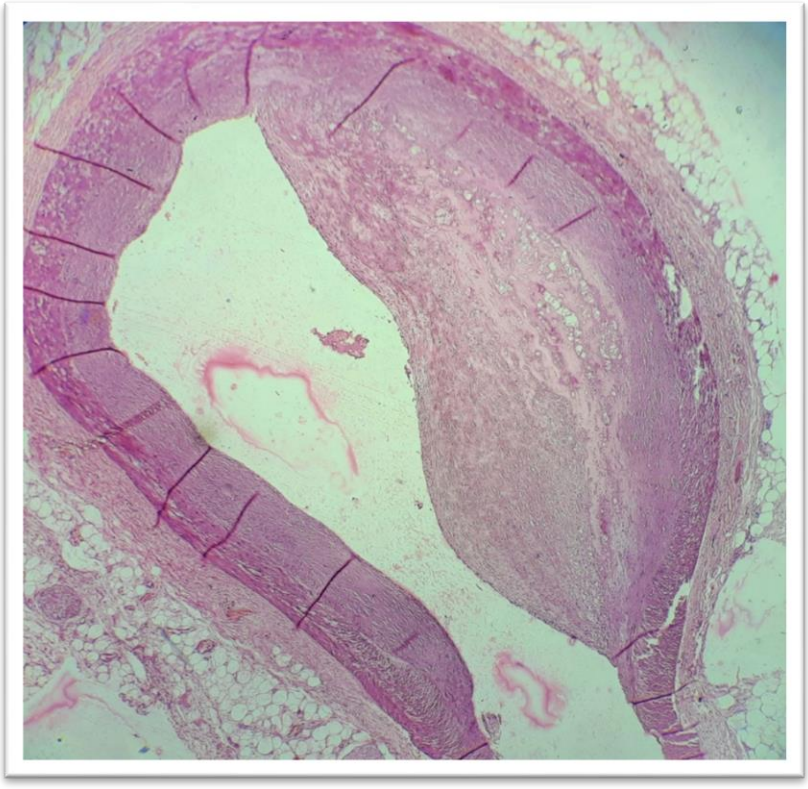


Figure 32. Photomicrograph of Grade V coronary atherosclerosis(H & E ,40X)

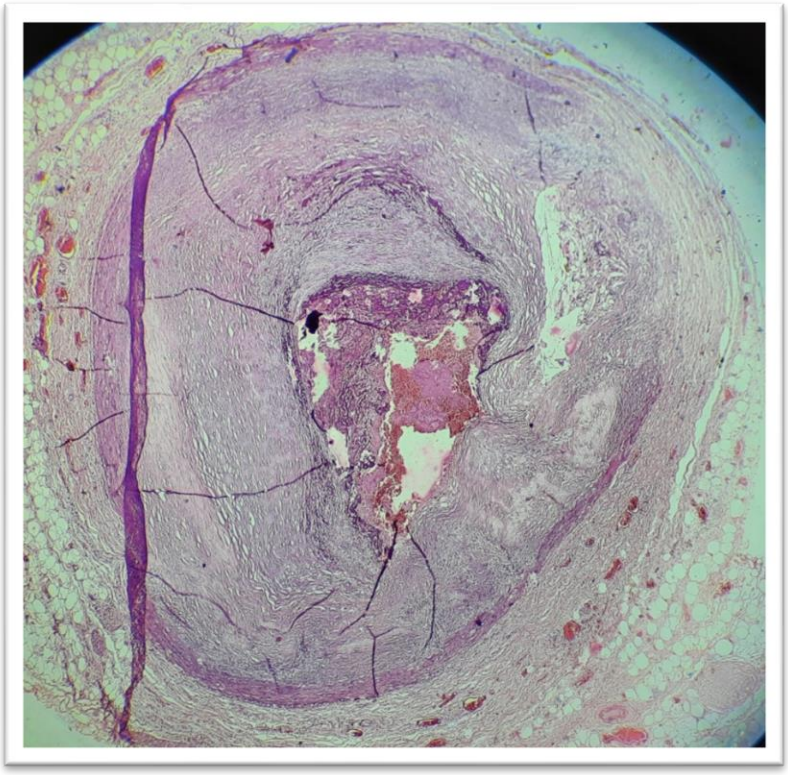


Figure 33. Photomicrograph of Grade VI coronary atherosclerosis(H & E ,40X)

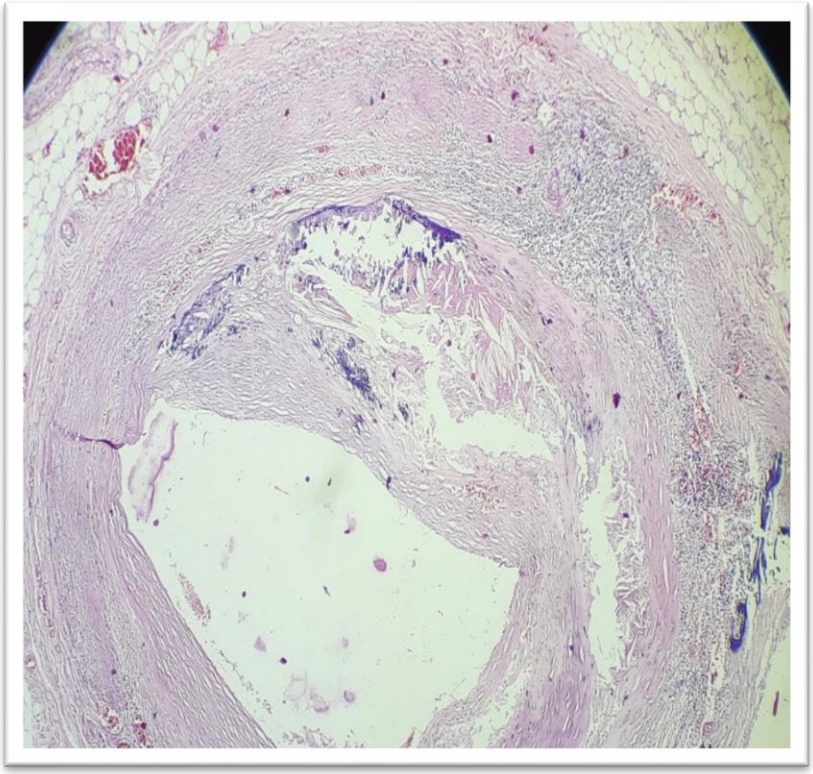


Figure 34. Photomicrograph of Grade VII coronary atherosclerosis(H & E ,40X)

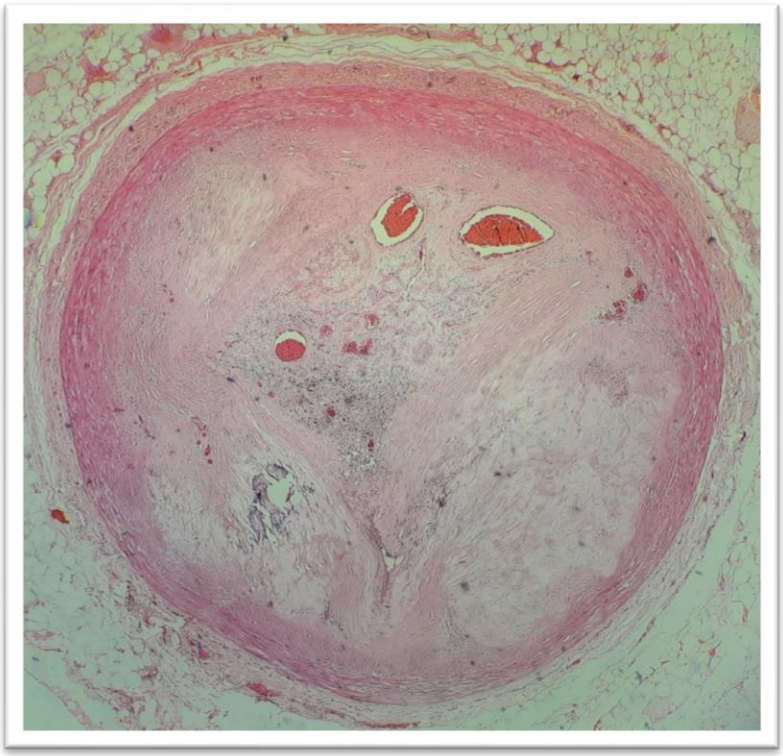


Figure 35. Photomicrograph of Grade VIII coronary atherosclerosis(H & E ,40X)


DISCUSSION

DISCUSSION

Cardiovascular disease (CVD) is a major health burden worldwide leading to deaths. Advances in treatment & effective secondary prevention, has improved life expectancy.Autopsy study for assessing atherosclerosis is proved as a great method, since this study is invasive, expensive & difficult in living population. Autopsy findings reveal, majority of sudden and unexpected deaths are squeal to coronary artery disease.

As study of atherosclerosis in the living population is difficult, invasive & expensive especially in developing countries like India . With the limited amount of resources available in rural and semi-urban population in India for studying atherosclerosis, an autopsy study gives a good measure of the prevalence, grading and distribution pattern of atherosclerotic lesions. Identifying the prevalence of sub-clinical atherosclerosis in a population helps the health administrators to plan preventive measures & strategy to prevent death in young age.(40)

In India, there is a wide variation of race, geographic factor, dietary habits, life style, tobacco & alcohol usage among population. So, epidemiological study of specific population is of great importance . Indian population affected atherosclerosis with more advanced lesion at younger age than in other ethnic group.

The aim of our study was to describe the spectrum of histomorphological patterns of cardiac lesions in a tertiary care center & to identify coronary atherosclerotic changes related to age and gender.

Comparison of mean age group in different studies

In the present study majority of cases belonged to age group 41-50 yrs (26.4%)**.** Ahmed et al concluded that 40-59 yrs is the most common age group for the heart diseases. Rao et al reported 50 -60 yrs as the commonest age group.

Comparison of male to female ratio in different studies

In the present study, it was observed that 109 cases (77.9%) were males and 31(22.1%) were females ,with male to female ratio of 3.5:1.Various studies conducted by Joseph et al,(41) Ekta Rani et al(40) Rao et al(41) and others also revealed increased proportion in males indicating that sudden natural death from all causes (cardiac and non cardiac) was more common in men. Unlike other studies , females outnumbered males in the study by Khiste et al.

Study	Male:Female ratio
Present study	3.5:1
Ekta Rani et al (42)	11:1
Rao et al (43)	10:1
Joseph et al(39)	6.9:1
Khiste et al(44)	1:1.16

Table 24. Comparison of male:female ratio in different studies

Comparison of frequency of coronary atherosclerosis in different studies

Out of 140 autopsied hearts, 113 (80.7%) revealed coronary artery atherosclerosis in one or more vessels. This was similar to studies conducted by Ahmed et al (79%) in Pakistan. Studies conducted by Farioli et (45) in USA and Kasthuri et al showed similar frequencies of coronary atherosclerosis.

Study	% of Coronary atherosclerosis
Present study – Kerala	80.7%
Kasthuri et al(60)- Banglore(2002)	76.92%
Shah et al (46) – Gujrat (2019	61.18%
Garg et al (47)– Haryana (2018)	55.3%
Chandrakala Joshi(48) – Raipur (2016)	64.34%
Sonawane et al(49)- Maharashtra (2017)	72.58%
Ahmed et al (61)- Pakistan(2005)	79%
Farioli et al(45) – USA (2015)	78%
Wang et al (62)- China(2014)	50.5 %
Santos et al(50) – Brazil (2014)	64.1%

Table 25. Comparison of frequencies of coronary atherosclerosis in different studies

In this modern globalized era, where human life style has become more and more complex and challenging. Various life stressors (anxiety, depression, etc.) along with a sedentary lifestyle and lack of exercise and poor dietary habits like intake of junk food and increased use of refined and processed food items in place of whole grains and fresh fruits and vegetables can be important factors for earlier initiation of development and progressive increase in atherosclerotic lesions in this young Indian population.

Comparison of Histopathological findings in heart & coronaries & their incidence

In the present study, atherosclerotic coronary heart disease was the principal cause of death (80.7%) followed by ischemic heart disease(44.28%),myocardial hypertrophy (10%), myocarditis (11.42%), infective endocarditis (0.71%),tuberculosis (1.42%). We received 1 case of cardiac amyloidosis (0.07%). Atherosclerotic coronary artery disease was the leading cause of death in all the studies however Garg et al, reported the lowest percentage (55.3%) of deaths due to atherosclerotic CAD.Our study showed I case (0.71%) of sickle cell disease .Study by Chandrakala joshi showed 5.21% of sickle cell disease which was not reported in other studies. Both myocarditis and hypertrophic cardiomyopathy as causes of death showed high degree of variation in different studies. Highest percentage of myocardial hypertrophy was reported by Chandrakala joshi(52.7%) ,while our study showed 10% & other studies showed lower percentage. Our study showed higher percentage of myocarditis (11.42%).Similar percentage was reported by Chandrakala Joshi(9.56%) where as other studies showed lower percentage.

HISTOPATHOLOGICAL FINDINGS	Present study	Marwa Nisha et al(51)	Farioli et al(45)	Garg et al(47)	Chadrakala Joshi(48)	Sonawane et al(49)
Coronary Atherosclerosis	80.7 %	71%	72.5%	55.3%	74%	72.5%
Ischemic Heart Disease	44.28%	35.9	-	14.1%	28.69%	-
C/C IHD	27.86%	25.5%	-	4.25%	-	-
A/C MI	10.71%	7%	-	9.92%	-	-
A/C On C/C IHD	5.71%	3.4%	-	-	-	-
Myocardial hypertrophy	10%	2.5%	3.22%	7.09%	52.17%	3.22%
Myocarditis	11.42%	1.5%	3.22%	3.5%	9.56%	3.22%
Pericarditis	3.57%	0.5%	-	2.8%	0.86%	-
Infective Endocarditis	0.71%	1.61%	-	0.07%	-	1.61%
Infection -Tuberculosis	1.42%	0.5%	-	-	-	-
Vaso-Occlusive Crisis-Sickle Cell Disease	0.71%	-	-	-	5.21%	-

Table 26. Comparison of incidence of histopathological findings in heart & coronaries in different studies

Comparison of frequencies of acute MI,chronic IHD & acute on chronic IHD

The frequency of different forms of IHD (acute MI, acute MI with underlined changes of healed MI, healed MI) and compared them with the extent of coronary artery atherosclerosis and observed that changes of healed MI and 3 vessel disease were most common, as in studies of Farb A, Friedman & Davies and others .Ahmad et al, classified MI into 2 categories - recent and old MI, reported old MI in 35.1% cases and recent MI in 20% cases respectively.

STUDY	MYOCARDIAL INFARCTION %		
	Acute MI	Chronic IHD	Acute on chronic IHD
Present study	10.71%	27.86%	5.71%
Marwa Nisha et al(51)	7%	25.5%	3.4%
Friedman et al(63)	12%	52%	NA
Baroldi et al(64)	17%	82%	NA
Davies et al(65)	40%	57%	NA
Farb et al(66)	10%	41%	11%

Table27. Comparison of frequencies of acute MI, chronic healed MI & acute on chronic MI in different studies

Comparison of frequencies of extent of coronary atherosclerosis

In our study, maximum cases (42.9%) had involvement of all the three vessels followed by two vessel (27.9%) and single vessel (10%) involvement. When compared with other studies there was no particular pattern of involvement of coronaries, but three vessel diseases was more common in all the studies including our study

Study	Coronary Atherosclerosis %			No significant /Mild atherosclerosis
	One Vessel	Two Vessel	Three Vessel	
Present study	10%	27.9%	42.9%	19.3%
Harveen B et al(52)	6.12%	16.3%	24.4%	NA
Marwa Nisha etal(51)	8.33%	27.77%	56.94%	6.94%
Yazdi et al(53)	23.6%	17.3%	26.5%	NA

Table 28. Comparison of frequencies of extent of vessel involvement in different studies

There was no specific cardiovascular pathology in 27 out of 140 (19.3%) cases in the present study.

Comparison of frequency of involvement of major coronaries by coronary atherosclrosis

In the Present study, the degree of involvement of atherosclerosis in LAD (72.14%) was more compared to LCX(57.14%) & RCA(65.71%). Our study is concordant with studies done by.Viral M et al(40) Lakshmi et al(54) &Thej et al(55) all of which showed involvement of LAD, followed by RCA and LCX. ,

To our finding Left Anterior Descending is the most common coronary artery involved with grade 7 occlusion according to modified AHA criteria in majority of cases (20%, n=28).In the study by Harveen et al, Left Anterior Descending artery is the most common coronary involved with grade 4-7 followed by Right Coronary Artery and Left Circumflex artery.

Comparison of spectrum of cardiac pathology in RT-PCR confirmed SARS-CoV-2 virus infection

In our study out of the 15 cases of RT -PCR confirmed SARS-CoV-2 virus infection ,11(73.33%) cases showed coronary atherosclerosis .This was comparable to the study conducted by Ferrer Gomez et al(20) which also showed Coronary atherosclerosis as the most frequent histopathological finding (8 patients, 26.7%).

We had 2 (13.33%) cases of myocarditis which was higher compared to Ferrer Gomez et at, where the study showed 2 cases of myocarditis (6.66%). 2 cases(4%) of myocarditis was also reported by C.J. Sang III, A. Burkett, B. Heindl et al.(56).In the study by Sharon E Fox et al cardiac findings were notable for absence of lymphocytic myocarditis.(57)

LV hypertrophy (LV wall thickness > 1.5cm) was seen in 3 (20%) cases in our study & in 4 cases (13.3%) in the study by Ferrer Gomez et al.

Acute myocardial ischemia was observed in eight (16.0%) cases by C.J. Sang III, A. Burkett, B. Heindl et al and in 5(17%) cases by Elsoukkary et al(58), where as

our study showed 3 cases(20%). R. Almamlouk et al(59) reported lesser percentage (11.8%) of cases with acute myocardial ischemia.

Histological findings in myocardium	Present study (n=15)	J D Haslbauer et al (n=23)
Interstitial fibrosis	9(60%)	12(52%)
Ischemic necrosis	3(20%)	7(30%)
Capillary dilatation	12(80%)	22(96%)
Microhemorrhage	4(26.67%)	13(57%)
Focal Capillary fibrin	3(20%)	8(35%)
Interstitial edema	11(73.33%)	15(65%)
Inflammatory infiltrate without necrosis	4(26.66%)	4(17%)
Lymphohisticytic myocarditis	2(13.33%)	1(4%)

Table 29. Comparison of histopathological spectrum of cardiac changes in RT-PCR confirmed SARS-CoV-2 virus infection

In our study, histomorphologic evaluation of myocardium in the cases of SARS-CoV-2 virus infection showed capillary dilatation & interstitial edema in 12(80%) & interstitial fibrosis in 9(60%)cases .This was comparable to the study conducted by J D Haslbauer et al(38) which reported capillary dilatation in 22(96%) cases ,interstitial oedema in 15(65%) cases, interstitial fibrosis in 12(52%)cases.

LIMITATIONS OF THE STUDY.

Information regarding the clinical details and risk factors contributing to cardiovascular diseases could not be obtained in all cases which were autopsied.

CONCLUSION

CONCLUSION

From the present study it was concluded that coronary atherosclerosis was the major pathology identified constituting 80.7% of the cases followed by ischemic heart disease in 44.28%of cases.

Ischemic heart disease may be the leading cause of death with coronary atherosclerosis being the most significant pathogenetic mechanism. Three-vessel disease the most common pattern of involvement(42.9%), same fact emphasized by other authors. Left anterior descending artery was most commoly involved by coronary atherosclerosis among the major coronaries(72.14%).The study showed high prevalence of atherosclerosis(80.7%) in Ernakulam, Kerala.There is a male preponderance (84.4%) of coronary atherosclerosis compared to females(67.74%). In the study frequency of coronary atherosclerosis is higher in age group above 40 years (51.43%) , of which males are more frequently involved (54.13%) than females.

The study of human atherosclerotic lesion is an extremely difficult task in a living subject and autopsy study is the best possible way to work on it. Our study highlights the increasing prevalence and severity of atherosclerotic lesions in Indian population. It also calls for institution of screening programs and preventive and control measures against atherosclerosis from an early age.

SARS-CoV-2 infection is commonly associated with myocardial injury and heart failure (56). In the present study Covid related cardiac changes seen were inflammatory changes, microvasculopathy associated changes and myocarditis. The pathophysiology behind this phenomenon remains unclear, with many diverse and multifaceted hypotheses. Though our study involved only a small number of cases we could contribute to this understanding . Continued autopsy studies are needed to further understand this disease process and to guide future therapeutic interventions.

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ANNEXURES

ANNEXURE I

PROFORMA

1) GENERAL INFORMATION:

Sl. No: PM No: Received on: / / Age: Gender:

Cause of death : Co-morbidities, if any:

2) GROSS FINDINGS OF HEART :

External appearance & Pericardial changes:

Weight (gm)

Wall thickness (cm) RV Wall: LV Wall:

Valves:

Coronary Arteries: Grade of occlusion (Grade I-IV)

RCA: LAD: LCX:

Aorta:

3) MICROSCOPY:

Myocardium:

Coronary Arteries : % Occlusion AHA Grade of occlusion(I-VII)

RCA:

LAD:

LCX:

Aorta:

4) DIAGNOSIS:

ANNEXURE II

AMERICAN HEART ASSOCIATION CRITERIA FOR GRADING ATHEROSCLEROTIC LESIONS

- Grade 1 - Isolated intimal foamy cells (minimal change)
- Grade 2 - Numerous intimal foamy cells often in layers (fatty streaks)
- Grade 3 - Pools of extra cellular lipid without a well-defined core (intermediate lesion /pre-atheroma)
- Grade 4 - Well defined lipid core with luminal surface covered by normal intima (atheroma or fibro plaque)
- Grade 5 - Lipid core with a fibrous cap with or without calcification (fibro atheroma)
- Grade 6 - Fibro-atheroma with cap defect such as haemorrhage and thrombosis
- Grade 7 - Calcification prominent
- Grade 8 - Fibrous tissue change prominent

ANNEXURE III

MASTER CHART 1

SL.NO	AGE	AGE GROUP	GENDER	CAUSE OF DEATH	CO-MORBIDITIES	WEIGHT	RV WALL THICKNESS	LV WALL THICKNESS	RCA % OF OCCLUSION	LAD % OF OCCLUSION	LCX % OF OCCLUISON	AORTA
1	30	3	2	1	0	350	0.4	1.5	2	1	1	1
2	48	5	2	1	0	450	0.5	2	1	2	1	1
3	84	9	2	1	1	250	0.3	1	2	1	1	1
4	44	5	1	1	5	350	0.5	1.6	2	1	1	1
5	45	5	2	1	0	325	0.7	1.6	4	4	1	1
6	33	4	2	1	0	300	0.7	1.7	3	2	1	1
7	44	5	2	1	2	300	0.3	1.3	2	2	1	1
8	49	5	2	1	0	375	0.5	2.2	2	4	4	0
9	47	5	2	1	0	375	0.6	2	3	4	4	1
10	54	6	2	1	0	350	0.6	1.6	1	1	4	1
11	73	8	2	10	5	275	0.4	1.6	1	1	1	1
12	41	5	1	1	0	275	0.5	1.1	1	1	1	1
13	40	4	1	1	0	125	0.4	1.2	1	1	1	0
14	50	5	2	1	7	375	0.5	1.5	1	3	1	1
15	75	8	1	9	7	275	0.6	1.5	1	3	1	1
16	36	4	1	1	0	250	0.5	1.5	1	3	1	1
17	38	4	2	1	0	375	0.5	1.7	1	4	3	0
18	56	6	2	1	2,3	275	0.4	1.5	1	1	1	1
19	32	4	2	1	0	250	0.5	1.3	1	3	1	1
20	18	2	1	3	0	150	0.6	1	1	1	1	0
21	39	4	2	1	0	250	0.5	1.6	3	1	1	1
22	27	3	2	1	5	250	0.6	1.4	1	4	1	1
23	37	4	2	3	0	250	0.6	1.2	1	1	1	0
24	19	2	2	1	0	260	0.5	1.3	1	1	1	0
25	59	6	2	1	0	370	0.3	1.5	2	2	1	1
26	44	5	2	1	4	400	0.5	1.7	2	4	3	1
27	38	4	2	1	7	250	0.6	1.4	1	2	1	1
28	46	5	2	1	0	600	0.8	1.9	2	1	2	1
29	48	5	2	2	0	550	0.7	2.1	2	4	3	1
30	39	4	2	1	4	575	0.5	2	1	1	1	1
31	51	6	2	1	4	575	0.6	1.5	1	4	1	1
32	24	3	2	1	0	250	0.5	1.2	1	1	1	1
33	36	4	1	1	0	240	0.5	1	1	1	1	1
34	30	3	2	1	0	250	0.4	1	1	1	1	1
35	30	3	2	1	0	275	0.5	1.3	1	1	1	1
36	60	6	1	4	5	375	0.5	1.5	1	1	1	1
37	27	3	2	1	7	375	0.8	1.5	1	1	1	1

38	57	6	2	1	4	375	0.7	1.5	3	4	5	1
39	38	4	2	1	0	250	0.6	1.4	1	1	1	1
40	50	5	1	1	2	250	0.6	1.2	4	4	1	1
41	39	4	2	1	0	270	0.4	1.1	3	2	1	1
42	75	8	1	5	6	375	0.3	1.3	3	3	1	1
43	66	7	2	6	5	420	0.6	1.5	1	1	1	1
44	36	4	1	8	0	250	0.4	1.2	2	1	1	1
45	26	3	2	6	0	375	0.3	1.1	1	1	1	0
46	40	4	2	1	0	325	0.8	1.7	1	4	2	1
47	24	3	2	1	0	250	0.4	1.3	1	1	1	1
48	65	7	2	1	0	350	0.6	1.3	4	2	1	1
49	36	4	2	4	0	250	0.4	1.2	2	1	1	1
50	44	5	2	1	0	425	0.5	1.5	2	1	3	1
51	37	4	1	1	0	275	0.4	1.3	1	3	1	1
52	54	6	2	10	0	300	0.6	1.3	4	1	1	1
53	84	9	1	1	7	375	0.7	1.6	1	1	1	1
54	30	3	2	1	0	225	0.5	1.5	1	1	1	1
55	25	3	2	1	0	275	0.5	1.5	1	1	1	0
56	68	7	2	10	5	250	0.6	1.7	2	1	2	1
57	53	6	2	1	0	300	0.6	1.5	4	3	3	1
58	36	4	2	3	0	275	0.5	1.3	1	2	2	1
59	55	6	2	1	5	300	0.4	1.4	1	1	1	1
60	50	5	2	1	0	250	0.4	1.2	1	1	1	1
61	34	4	2	1	1,2	350	0.4	1.4	4	3	3	1
62	92	10	1	1	7	225	0.5	1	1	3	3	1
63	40	4	2	1	0	350	0.6	1.6	2	4	2	1
64	32	4	2	1	0	300	0.4	1.5	1	1	1	0
65	35	4	1	1	0	250	0.3	1	1	3	1	0
66	55	6	1	1	0	325	0.7	1.6	3	3	3	1
67	27	3	2	1	0	300	0.4	1.3	1	1	1	1
68	57	6	2	7	0	375	0.5	1.8	1	2	1	1
69	53	6	2	1	7	225	0.6	1.5	3	3	1	1
70	46	5	2	1	1	350	0.8	1.9	2	3	3	1
71	74	8	2	9	6	175	0.05	1.3	2	5	1	1
72	48	5	2	1	5	300	0.6	1.5	4	3	4	1
73	65	7	2	1	0	275	0.4	1.2	1	3	2	1
74	21	3	2	1	0	250	0.6	1.5	1	1	1	0
75	29	3	1	1	0	175	0.4	1.1	1	1	1	1
76	25	3	2	1	0	300	0.6	1.5	1	3	1	0
77	43	5	2	1	6	350	0.6	1	1	3	1	0
78	67	7	2	1	7	530	1	2	4	4	1	1
79	44	5	2	1	7	350	0.5	1.5	1	1	1	1
80	62	7	2	2	5	275	0.3	1	1	2	1	1
81	47	5	2	1	0	300	0.4	1.3	1	1	1	1
82	52	6	2	1	7	325	0.4	1.3	4	3	3	1

83	46	5	2	1	0	350	1	1.6	1	4	1	1
84	32	4	2	1	0	325	0.5	1.3	3	3	1	1
85	34	4	2	1	0	275	0.4	1.3	1	1	1	1
86	38	4	2	1	0	300	0.5	1	1	3	4	1
87	39	4	2	1	0	625	0.6	1.8	1	1	1	1
88	86	9	1	1	7	250	0.3	1.4	3	3	3	1
89	38	4	1	1	0	200	0.3	1.3	1	1	1	1
90	70	7	2	7	5	425	0.5	1.2	1	3	2	1
91	50	5	2	1	0	250	0.5	1.5	1	1	1	1
92	92	10	1	1	7	425	0.6	1.2	1	1	1	1
93	51	6	2	1	0	500	0.6	2	1	2	3	1
94	28	3	2	1	0	625	0.7	2.3	3	1	1	1
95	45	5	2	1	0	300	0.5	1.3	1	1	1	1
96	44	5	2	1	0	375	0.6	1.7	3	1	4	1
97	40	4	2	1	6	550	0.4	1.8	1	2	1	1
98	24	3	1	1	5	250	0.4	1	1	1	1	1
99	41	5	2	1	7	450	0.6	1.5	1	3	1	0
100	19	2	2	1	7	325	0.5	1.7	1	1	1	1
101	20	2	2	1	0	275	0.4	1.4	1	1	1	0
102	50	5	2	1	7	425	0.5	1.4	1	1	1	1
103	21	3	1	1	5	225	0.4	1.3	1	1	1	0
104	72	8	2	1	7	500	0.6	2	4	4	1	1
105	48	5	2	1	0	275	0.4	1.3	2	4	1	1
106	30	3	2	7	0	225	0.8	1.4	1	1	1	1
107	36	4	2	1	0	375	0.5	1.9	3	3	3	1
108	38	4	2	1	0	335	0.3	1.4	1	1	1	0
109	68	7	2	1	0	500	0.3	1.5	1	1	1	1
110	38	4	1	1	0	325	0.4	1.5	1	1	1	1
111	44	5	1	1	5	290	0.5	1.3	1	1	1	1
112	29	3	2	1	0	300	0.6	1.5	1	1	1	1
113	47	5	2	1	0	325	0.5	1.7	3	3	3	1
114	46	5	1	6	0	300	0.5	1.5	1	1	1	1
115	39	4	2	1	7	350	0.4	1.3	1	3	4	1
116	51	6	2	2	0	375	0.7	1.7	4	1	3	1
117	29	3	2	1	0	300	0.4	1.1	1	2	2	1
118	50	5	1	1	0	275	0.8	1.5	1	1	1	1
119	49	5	1	1	2	250	0.5	1.2	1	1	1	1
120	33	4	1	1	0	200	0.6	1.3	1	3	1	0
121	55	6	2	1	0	250	0.4	1.9	3	2	2	1
122	36	4	2	1	0	375	0.6	1.6	1	1	2	1
123	50	5	2	1	7	375	0.4	1.8	1	3	2	1
124	62	7	2	10	0	350	0.6	1.4	3	4	4	1
125	49	5	2	1	5	375	0.4	1.3	1	1	1	1
126	53	6	2	1	0	250	0.3	1.3	3	2	2	1
127	62	7	2	1	0	325	0.3	1.5	3	3	3	1

128	66	7	2	1	0	325	0.5	1.7	1	3	3	1
129	49	5	1	2	0	275	0.3	1.4	1	1	1	1
130	57	6	2	1	1	275	0.3	1.6	4	4	4	1
131	85	9	2	1	0	500	0.4	1.7	1	1	3	1
132	72	8	1	1	0	275	0.7	1.5	1	1	1	1
133	29	3	2	1	0	350	0.6	1.6	1	1	1	1
134	47	5	2	1	5	275	0.3	1.5	1	1	1	1
135	52	6	2	1	1,2	575	0.4	1.7	1	1	1	1
136	39	4	1	1	0	300	0.4	1.5	4	4	4	1
137	49	5	2	1	0	300	0.5	1.5	2	1	1	1
138	48	5	2	1	2	425	0.4	1.9	2	2	4	1
139	57	6	2	1	0	325	0.4	1.2	1	1	1	1
140	40	4	2	1	0	375	0.5	1.6	2	4	3	1

MASTER CHART 2

SL.NO	HISTOMORPHOLOGICAL FINDINGS IN HEART	MODIFIED AHA GRADING OF RCA	MODIFIED AHA GRADING OF LAD	MODIFIED AHA GRADING OF LCX	CORONARY ATHEROSCLEROSIS	NUMBER OF VESSELS INVOLVED
1	0	3	1	0	1	1
2	4	3	3	3	1	3
3	1	7	0	7	1	2
4	5	4	1	2	1	2
5	0	4	8	3	1	3
6	7	4	4	4	1	3
7	1	7	7	3	1	3
8	4	7	7	6	1	3
9	2,4	4	6	8	1	3
10	1	1	1	8	1	1
11	0	4	4	3	1	3
12	0	1	2	1	1	1
13	0	0	0	0	0	0
14	0	3	6	3	1	3
15	6	0	7	4	1	2
16	0	2	4	2	1	3
17	1	7	7	7	1	3
18	0	3	3	1	1	2

19	0	1	4	2	1	2
20	0	0	0	0	0	0
21	4	2	0	1	1	1
22	2	0	4	2	1	2
23	0	1	1	0	0	0
24	0	1	1	1	0	0
25	1	4	7	0	1	2
26	1	4	7	4	1	3
27	0	1	1	0	0	0
28	4,10	7	7	7	1	3
29	1,4	4	7	7	1	3
30	4	3	3	2	1	3
31	1,8	0	7	0	1	1
32	0	1	1	1	0	0
33	3	1	0	2	1	1
34	0	2	2	2	1	3
35	0	0	1	1	0	0
36	0	0	0	1	0	0
37	6	1	2	1	1	1
38	1	4	6	1	1	2
39	0	1	1	1	0	0
40	1	4	4	4	1	3
41	0	7	5	6	1	3
42	0	7	7	0	1	2
43	1	3	3	2	1	3
44	3	4	2	2	1	3
45	0	2	0	2	1	2
46	3,4	7	5	5	1	3
47	5	0	1	1	0	0
48	1	6	7	2	1	3
49	0	5	6	0	1	2
50	1,8	3	3	5	1	3
51	0	2	2	2	1	3
52	0	4	3	1	1	2
53	4,6	2	0	0	1	1
54	2	2	4	0	1	2
55	5	1	1	0	0	0
56	1	3	2	1	1	2
57	5	7	7	6	1	3
58	0	4	6	4	1	3
59	1	4	3	0	1	2
60	0	1	0	1	0	0
61	1	6	7	6	1	3
62	1	3	7	7	1	3
63	2	6	6	6	1	3

64	0	2	0	2	1	2
65	5	2	4	0	1	2
66	2	7	7	7	1	3
67	0	3	3	0	1	2
68	0	4	4	4	1	3
69	0	4	5	4	1	3
70	2	5	7	7	1	3
71	1	5	0	2	1	2
72	2	7	7	6	1	3
73	5	0	6	5	1	2
74	1	1	2	2	1	2
75	5	2	0	0	1	1
76	0	0	5	0	1	1
77	5	0	3	2	1	2
78	3,4	7	7	3	1	3
79	0	4	4	4	1	3
80	0	2	5	0	1	2
81	0	1	2	0	1	1
82	1	4	4	1	1	2
83	0	2	7	1	1	2
84	1	7	7	1	1	2
85	5	1	1	1	0	0
86	2	4	6	7	1	3
87	4	3	3	4	1	3
88	3	7	7	7	1	3
89	2	0	1	1	0	0
90	6	2	7	7	1	2
91	0	1	1	1	0	0
92	1	3	5	2	1	3
93	5	3	5	5	1	3
94	1	5	3	2	1	3
95	3	1	2	2	1	2
96	1	5	2	7	1	3
97	4	2	2	1	1	2
98	0	1	1	0	0	0
99	1	3	7	1	1	2
100	9	1	0	0	0	0
101	5	1	0	0	0	0
102	5	0	2	2	1	2
103	0	0	0	0	0	0
104	1,4	7	7	5	1	3
105	0	5	5	2	1	3
106	0	1	1	0	0	0
107	0	7	5	3	1	3
108	1	3	4	0	1	2

109	1,6	1	3	2	1	2
110	5	0	1	1	0	0
111	0	2	2	3	1	3
112	0	0	1	0	0	0
113	0	5	5	6	1	3
114	0	1	2	0	1	1
115	1	1	3	6	1	2
116	5	8	4	7	1	3
117	2	2	5	6	1	3
118	5	0	0	0	0	0
119	0	4	4	0	1	2
120	1	3	4	2	1	3
121	1	6	7	4	1	3
122	3	0	5	2	1	2
123	1	4	4	4	1	3
124	3	7	7	6	1	3
125	5	0	4	1	1	1
126	1	4	4	7	1	3
127	1	6	5	6	1	3
128	2	2	6	6	1	3
129	2	0	1	0	0	0
130	2	7	7	7	1	3
131	1	0	0	7	1	1
132	0	1	1	0	0	0
133	0	3	3	0	1	2
134	2	1	1	1	0	0
135	4	2	3	1	1	2
136	1	7	6	5	1	3
137	1	4	2	1	1	2
138	2	4	5	7	1	3
139	1	1	1	0	0	0
140	1	7	7	5	1	3

MASTER CHART 3

RT-PCR confirmed SARS CoV-2 cases

SL.NO	AGE	GENDER	INTERSTITIAL FIBROSIS	ISCHEIMIC NECROSIS	CAPILLARY DILATION	MICRO HEMORRHAGE	FOCAL CAPILLARY FIBRIN	INTERSTITIAL EDEMA	INFLAMMATORY INFILTRATE WITHOUT NECROSIS	MYOCARDITIS
4	44	1	0	0	0	0	0	1	0	1
11	73	2	0	0	0	0	0	1	0	0
22	27	2	1	1	1	1	0	1	0	0
36	60	1	1	0	1	0	0	1	0	0
43	66	2	1	0	1	0	0	0	1	0
56	68	2	1	0	1	0	0	0	1	0
59	55	2	1	0	1	1	1	0	0	0
72	48	2	1	1	0	1	0	1	0	0
80	62	2	1	0	1	0	0	1	1	0
90	70	2	0	0	1	0	0	1	0	0
98	24	1	0	0	1	0	0	1	0	0
103	21	1	0	0	1	0	0	1	1	0
111	44	1	1	0	1	0	0	1	0	0
125	49	2	1	0	1	0	1	1	0	1
134	47	2	0	1	1	1	1	1	0	0

KEY TO MASTER CHART

1)Age Group

1	**0-10**
2	11-20
3	21-30
4	31-40
5	41-50
6	51-60
7	61-70
8	71-80
9	81-90
10	91-100

2)Gender

1	**Female**
2	Male

3)Cause of death

1	Sudden collapse
2	RTA
3	Hanging
4	Snake bite
5	Burns
6	Drowning
7	Electric shock
8	Seizure
9	Carcinoma
10	Assault

4)Comorbidities

0	Not documented
1	DM
2	HTN
3	DLP
4	Valvular Heart Disease
5	COVID
6	Heart disease
7	Others-Renal ,Hepatic, Respiratory illness

5) Histopathological findings in heart

0	No Significant pathology
1	Chronic MI
2	Acute MI
3	Acute on chronic MI
4	Cardiac Hypertrophy
5	Myocarditis
6	Pericarditis
7	Infective endocarditis
8	Infection -tuberculosis
9	Vasso occlusive crisis-sickle cell anemia
10	Amyloidosis

6) Coronary Atherosclerosis

0	**Absent**
1	Present

7) Severity Of Coronary Atherosclerosis Based On % Of Occlusion:

RCA, LAD & LCX

1	**Grade I :0-25%**
2	Grade II:25-50%
3	Grade III:50-75%
4	Grade IV:75-100%

8)Modified AHA Grading Coronary Atherosclerosis:

RCA, LAD &LCX

0	Unremarkable
1	Grade I
2	Grade II
3	Grade III
4	Grade IV
5	Grade V
6	Grade VI
7	Grade VII
8	Grade VIII

9)Atherosclerosis Aorta

0	**Absent**
1	Present

10)Histopathological spectrum of cardiac changes in SARS-CoV 2 cases-

- **Interstitial fibrosis**
- **Ischemic necrosis**
- **Capillary dilatation**
- **Microhaemorrhage**
- **Focal Capillary Fibrin**
- **Interstitial Oedema**
- **Inflammatory infiltrate without necrosis**
- **Myocarditis**

0	**Absent**
1	Present

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Date :

Place: *Dr Mary Diana Vincent*

LIST OF ABBREVIATIONS USED

1. ACS- Acute Coronary Syndrome
2. AMI- Acute Myocardial Infarction
3. AV- Atrio Ventricular
4. CVD- Cardio Vascular Disease
5. DALY- Disability Adjusted Life Years
6. DLP-Dyslipidema
7. DM-Diabetes Mellitus
8. HTN-Hypertension
9. LAD- Left Anterior Descending
10. LCX- Left Circumflex
11. LV-Left Ventricular
12. MI-Myocardial Infarction
13. RCA- Right Coronary Artery
14. RF – Rheumatic fever
15. RV-Right Ventricular
16. SARS-CoV -2 -Severe acute respiratory syndrome coronavirus 2