A Dissertation on

"HISTOPATHOLOGICAL EVALUATION OF SUDDEN DEATH IN ADULTS WITH SPECIAL REFERENCE TO ANCILLARY STUDIES-PATHOLOGIST'S PERSPECTIVE"

Dissertation submitted to

THE TAMILNADU Dr.M.G.R MEDICAL UNIVERSITY

CHENNAI-600032

In Partial fulfillment of the regulations

Required for the award of

M.D.Degree in PATHOLOGY (BRANCH III)

DEPARTMENT OF PATHOLOGY

COIMBATORE MEDICAL COLLEGE

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DECLARATION

I hereby declare that the dissertation entitled "**HISTOPATHOLOGICAL EVALUATION OF SUDDEN DEATH IN ADULTS WITH SPECIAL REFERENCE TO ANCILLARY STUDIES- PATHOLOGIST'S PERSPECTIVE**" is a bonafide research work done by me in the Department of Pathology , Coimbatore Medical College during the period from **JANUARY 2018 TO JUNE 2019** under the guidance and supervision of **Dr. VINUTHA MALAICHAMY, MD.,** Senior Assistant Professor, Department of Pathology, Coimbatore Medical College, Coimbatore.

This dissertation is submitted to The Tamilnadu Dr.MGR Medical University, Chennai towards the partial fulfilment of the requirements for the award of M.D., Degree (Branch III) in Pathology. I have not submitted this dissertation on any previous occasion to any University for the award of any Degree.

Place: Coimbatore

Date:

Dr.S.SARANYA

Postgraduate student,
Department of Pathology,
Coimbatore Medical College,
Coimbatore

CERTIFICATE

This is to certify that the dissertation entitled "**HISTOPATHOLOGICAL EVALUATION OF SUDDEN DEATH IN ADULTS WITH SPECIAL REFERENCE TO ANCILLARY STUDIES-PATHOLOGIST'S PERSPECTIVE**" is a bonafide work done by **Dr.S.SARANYA,** a postgraduate student in the Department of Pathology, Coimbatore Medical College, Coimbatore under the guidance and supervision of **Dr.VINUTHA MALAICHAMY,MD.,** Senior Assistant Professor, Department of Pathology, Coimbatore Medical College and submitted in partial fulfilment of the regulations of The Tamilnadu Dr. MGR Medical University, Chennai towards the award of M.D. Degree (Branch III) in Pathology.

Guide

Dr.Vinuta Malaichamy M.D.,
Senior Assistant Professor
Department of Pathology,
Coimbatore Medical College,
Coimbatore.

Head of the Department

Dr.A.Dhanalakshmi MD.
Professor and Head
Department of Pathology,
Coimbatore Medical College,
Coimbatore.

Dean

Dr.B.ASOKAN,MS.,MCh.,
Coimbatore Medical College,
Coimbatore.

INSTITUTIONAL HUMAN ETHICS COMMITTEE
COIMBATORE MEDICAL COLLEGE, COIMBATOR – 14

EC Reg No. ECR/892/Inst/TN/2016
Telephone No: 0422 – 2574375/76
Fax : 0422 – 2574377

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To
Dr.Saranya S
Post Graduate,
Department of Pathology,
Coimbatore Medical College ,
Coimbatore -14.

Dear Dr.Saranya S

The Institutional Ethics Committee of Coimbatore Medical College, reviewed and discussed your application for approval of the proposal entitled "**Histopathological Evaluation of sudden Death in Adults with Special Reference to Ancillary Studies – Pathologist's Perspective.**"No.054/2017.

The following members of Ethics Committee were present in the meeting held on 24.11.2017.conducted at MM - II Seminar Hall, Coimbatore Medical College Hospital Coimbatore-18.

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This is to certify that this dissertation work titled "**HISTOPATHOLOGICAL EVALUATION OF SUDDEN DEATH IN ADULTS WITH SPECIAL REFERENCE TO ANCILLARY STUDIES- PATHOLOGIST'S PERSPECTIVE**" of the candidate **DR.S.SARANYA** with registration number **201713256** for the award of M.D degree in the branch of PATHOLOGY. I personally verified the urkund.com website for the purpose of plagiarism check I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **5 (Five)** percentage of plagiarism in the dissertation

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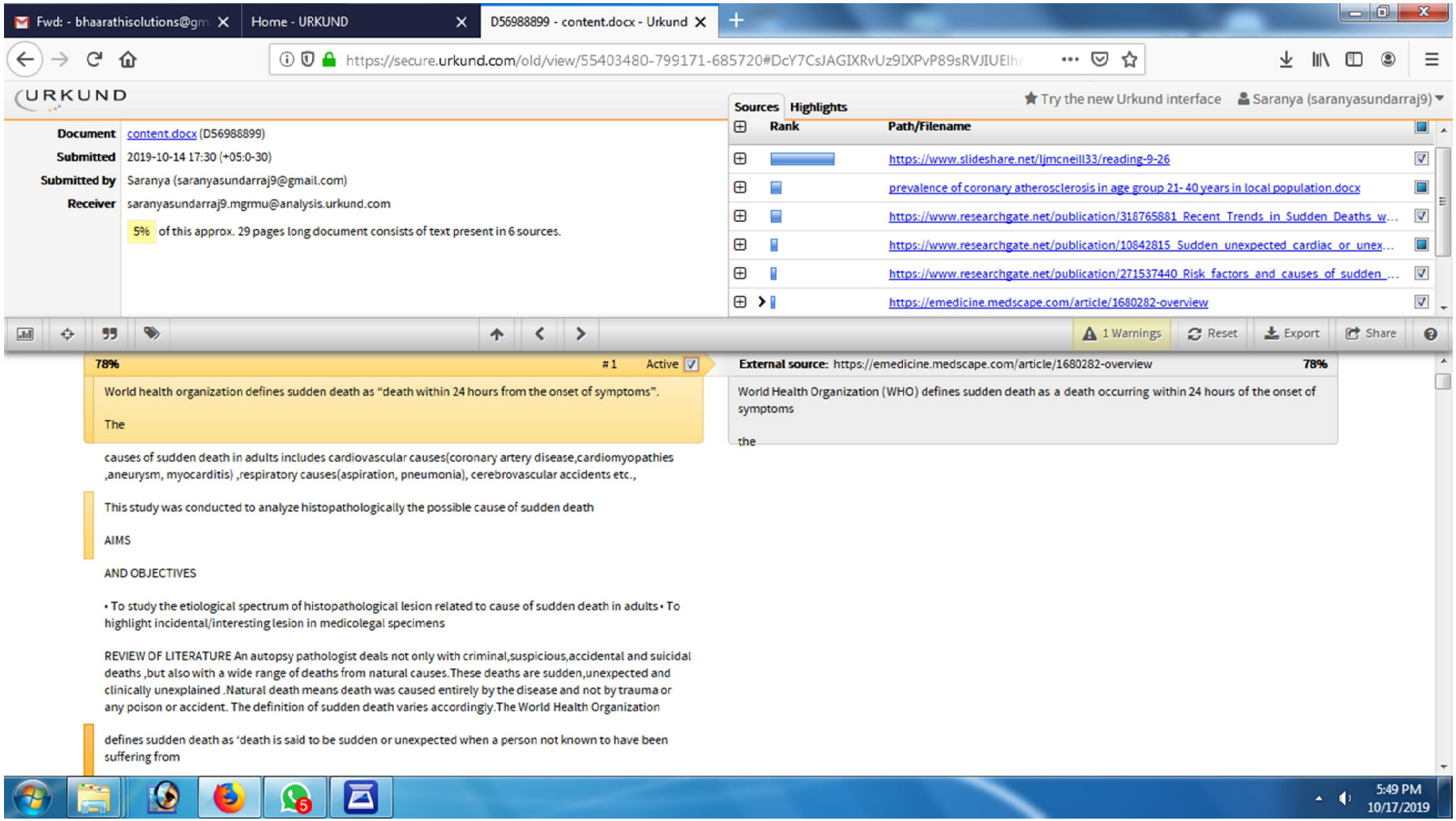
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World health organization defines sudden death as “death within 24 hours from the onset of symptoms”.
The
causes of sudden death in adults includes cardiovascular causes(coronary artery disease,cardiomyopathies ,aneurysm, myocarditis) ,respiratory causes(aspiration, pneumonia), cerebrovascular accidents etc.,
This study was conducted to analyze histopathologically the possible cause of sudden death
AIMS
AND OBJECTIVES
• To study the etiological spectrum of histopathological lesion related to cause of sudden death in adults • To highlight incidental/interesting lesion in medicolegal specimens
REVIEW OF LITERATURE An autopsy pathologist deals not only with criminal,suspicious,accidental and suicidal deaths ,but also with a wide range of deaths from natural causes.These deaths are sudden,unexpected and clinically unexplained .Natural death means death was caused entirely by the disease and not by trauma or any poison or accident. The definition of sudden death varies accordingly.The World Health Organization
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INTRODUCTION

INTRODUCTION

Sudden death in adults without any past history of chronic illness are increasing world over and is an issue of concern for medical professionals. Even in this modernized medical world, diagnostic tools lack precision to find the clinical cause of death in comparison to autopsy cause of death. The main aim of autopsy is to find out the most possible cause of death.

World health organization defines sudden death as "death within 24 hours from the onset of symptoms". The causes of sudden death in adults includes cardiovascular causes (coronary artery disease, cardiomyopathies, aneurysm, myocarditis), respiratory causes (aspiration, pneumonia), cerebrovascular accidents etc., This study was conducted to analyze histopathologically the possible cause of sudden death.

AIM & OBJECTIVES

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- To study the etiological spectrum of histopathological lesion related to cause of sudden death in adults.
- To highlight incidental/interesting lesion in medicolegal specimens.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

An autopsy pathologist deals not only with criminal, suspicious, accidental and suicidal deaths ,but also with a wide range of deaths from natural causes. These deaths are sudden, unexpected and clinically unexplained .Natural death means death was caused entirely by the disease and not by trauma or any poison or accident.

The definition of sudden death varies accordingly. The World Health Organization defines sudden death as ‘death is said to be sudden or unexpected when a person not known to have been suffering from any dangerous disease, injury or poisoning is found dead or dies within 24 hours after the onset of terminal illness’[1].Some limit sudden deaths as those occurring instantaneously or within one hour of onset of symptoms. There is more emphasis on the unexpected character rather than suddenness of death. The incidence of sudden death is approximately 10% of all deaths[2].

In sudden death , the immediate cause is always found in cardiovascular system. Other causes like cerebral hemorrhage, subarachnoid hemorrhage, pulmonary embolism, hemoptysis, haematemesis join with heart disease in being the reason for sudden unexpected death.

LIST OF NATURAL CAUSES OF SUDDEN DEATH:

CARDIOVASCULAR CAUSES:

- ISCHEMIC HEART DISEASE

  Atherosclerotic cardiovascular disease

  Myocardial infarction

- INFLAMMATORY HEART DISEASE

  Myocarditis

  Arteritis

- HYPERTROPHIED HEART

  Cardiomyopathy-hypertrophic, dilated, restrictive, Right ventricular dysplasia

  Systemic hypertension

- VALVULAR HEART DISEASE

  Aortic stenosis

  Mitral valve prolapse

  Mitral stenosis

  Infective endocarditis

- AORTIC ANEURYSM AND DISSECTION
- CONDUCTION SYSTEM ABNORMALITIES: Wolff Parkinson syndrome, Pre excitation syndrome, sick sinus syndrome, long QT syndrome, Brugada syndrome.
- NEOPLASTIC HEART DISEASE

PULMONARY CAUSES:

- Epiglottitis
- Pulmonary thromboembolism
- Pneumonia
- Tuberculosis
- Asthma
- Chronic obstructive lung disease
- Congestion
- Pulmonary edema
- Diffuse alveolar damage
- Chronic interstitial lung disease
- Pulmonary hypertension
- Tumours

GASTROINTESTINAL AND HEPATOBILIARY CAUSES:

- Gastritis
- Cirrhosis/esophageal varices
- Mallory weiss tear
- Strangulated hernia, intussusception, volvulus
- Hemochromatosis
- Pancreatitis

RETICULOENDOTHELIAL,HEMATOPOIETIC CAUSES:

- Hypersensitivity reactions
- Autoimmune disorders
- Immunodeficiency
- Leukemia/lymphoma
- Splenic rupture

GENITOURINARY CAUSES:

- Pyelonephritis
- Tumours

CENTRAL NERVOUS SYSTEM CAUSES:

- Infections(meningitis,encephalitis,brain abscess)
- Seizure disorder
- Cerebrovascular accident
- Hypertensive disease
- Spontaneous intraparenchymal hemorrhage
- Ruptured berry aneurysm
- Ruptured arteriovenous malformation
- Dural sinus thrombosis
- Tumours

MISCELLANEOUS CAUSES:

- Cerebral malaria
- Chronic alcoholism
- Amyloidosis
- Sickle cell disease
- Psychiatric disorders

CARDIOVASCULAR CAUSES:

The cardiovascular system is composed of the heart and the blood vessels. The most common cause of sudden natural death is due to cardiac causes[3].The mechanism of death in many heart diseases is related to arrhythmia. It is impossible for pathologists to diagnose an arrhythmia on autopsy[4]. There are a variety of diseases associated with an increased risk of arrhythmias and sudden death.

ISCHEMIC HEART DISEASE:

ATHEROSCLEROSIS:

Atherosclerosis is an arterial disease associated with arterial occlusions and aneurysms. It is the principal cause of myocardial infarction, stroke and gangrene of the extremities. It is the leading cause of death in the United States, Europe, and Japan[5]. They result from an inflammatory and proliferative response to injury of the endothelium and smooth muscle of the arterial wall[6]. The risk factors include family history, genetic abnormalities, increasing age, male gender, hyperlipidemia, hypertension,

cigarette smoking, diabetes and chronic inflammation[7].Factors included in pathogenesis are changes in lipid metabolism, increased endothelial permeability to serum lipoprotein complexes, endothelial activation due to flow turbulence at major bifurcations and activation of clotting cascade. Macrophages, growth factors and cytokines involve in this process. Histopathologically there is formation of intimal plaques, composed of lipid deposits and proliferation of fibroblasts and smooth muscle cells. There is reduplication and fragmentation of the internal elastic lamina with medial degeneration indicated by elastic tissue fragmentation and hyaline, collagenous and mucoid degeneration of smooth muscle and medial calcification. There is adventitial fibrosis and chronic inflammatory cell infiltrate[8].These plaques develop and grow slowly over decades. Stable plaques have dense fibrous cap, minimal lipid accumulation and little inflammation , whereas unstable plaques have thin caps, large lipid cores and dense inflammatory infiltrate. Stable plaques can cause narrowing of vessel lumens thereby producing symptoms related to chronic ischemia,whereas unstable plaques can cause fatal complications like acute plaque rupture, thrombosis or embolization.[7]

ISCHEMIC HEART DISEASE:

Ischemic heart disease is the leading cause of death in US and other developed nations. Myocardial ischemia results from an imbalance between coronary supply and myocardial demand. Left anterior

descending coronary artery(40 to 50%), right coronary artery(30 to 40%) left circumflex coronary artery (15 to 20%) are involved [7].It manifests as different, overlapping syndromes:

Angina pectoris is exertional chest pain and is due to transient myocardial ischemia that is inadequate to induce myocyte necrosis. It is due to atherosclerotic disease with greater than 75% stenosis(critical stenosis).

Unstable angina is due to small fissure or rupture of atherosclerotic plaque triggering platelet aggregation, vasoconstriction and formation of a nonocclusive mural thrombus.

Acute myocardial infarction results from acute thrombosis after plaque disruption; A majority occur in plaques without any features of critical stenosis.

Sudden cardiac death results from fatal arrhythmia without any significant acute myocardial damage.

Chronic ischemic heart disease is progressive heart failure due to ischemic injury, either from previous infarction or chronic ischemia.

MYOCARDIAL INFARCTION

Myocardial ischemia leads to loss of myocyte function within 1 to 2 minutes but causes necrosis only after 20 to 40 minutes. MI is diagnosed on the basis of symptoms, electrocardiographic changes and measurement of serum CK-MB and troponin levels. Gross and histologic changes of infarction require hours to days to develop. Grossly MI appears as mottled

areas with yellow tan infarct center. Gross histochemical stain TRIPHENYL TETRAZOLIUM CHLORIDE imparts red colour to noninfarcted myocardium where lactate dehydrogenase activity is preserved. Infarct area appears as unstained pale zone because dehydrogenase leaks out through the damaged red cell membrane.[7] Histopathologically, the appearance of MI is dependent on the age .The histologic changes include waviness of fibers (after 1 to 3 hours), progressing to coagulative necrosis with contraction bands (after 4 to 12 hours) and infiltration by neutrophils (after 2 to 24 hours),phagocytosis of dead cells with granulation tissue at margins(after 7 to 10 days) and dense collagenous scar(after 2 months). In cases of reperfusion, contraction band necrosis is noted after 18 to 24 hours since the cells begin to lose cross-striations and nuclear detail. Total coagulative necrosis can be seen by 24 to 72 hours. The Complications include ventricular rupture, papillary muscle rupture, aneurysm formation, mural thrombus, arrhythmia, pericarditis, and CHF.[9]

INFLAMMATORY HEART DISEASE:

MYOCARDITIS:

Myocarditis is myocardial damage(necrosis /degeneration) caused by inflammatory infiltrate secondary to infections or immune reactions (‘Dallas criteria’)[10].The infiltrate is usually of T lymphocytes and histiocytes.Immunohistochemical stains for CD3, CD4, CD20, CD45,

and CD45 should be performed.[11] The myocyte alterations include necrosis, vacuolization or disruption. The presence of edema is not a criteria for myocarditis.

Fenoglio et al[12] classified myocarditis into **acute, rapidly progressive** and **chronic.**

The etiology of myocarditis can be viral, bacterial, fungal, parasitic (particularly Chagas disease and toxoplasmosis), collagen–vascular disease (rheumatic fever), drug-induced, radiation-induced and Whipple disease and idiopathic causes.[13-14] Rare forms of granulomatous myocarditis include tuberculosis and sarcoidosis.[15]

The World Health Organization defines myocarditis as a minimum of 14 T cells per square millimetre with as many as four macrophages (Marburg criteria). The most common causative agents of viral myocarditis include enteroviruses (coxsackie A and B), adenovirus, echovirus, poliovirus, influenza viruses A and B and human immunodeficiency virus (HIV).

Fulminant myocarditis has onset within 2 weeks of presentation of profound left ventricular dysfunction without dilatation. Biopsy shows multiple foci of active inflammation and necrosis. Patients may show either complete recovery or may die within 2 weeks

Chronic active myocarditis has an indistinct onset with moderate ventricular dysfunction and active or borderline myocarditis. Ongoing

inflammation and fibrosis may result in the development of restrictive cardiomyopathy within 2 to 4 years.

Eosinophilic myocarditis (hypersensitivity myocarditis) is linked to treatment with methyldopa, antibiotics (penicillin, sulfonamides, streptomycin), anticonvulsants and antidepressants and also shows eosinophils and occasional giant cells. The myocardium has little myocyte necrosis and the inflammatory infiltrate is lymphohistiocytic and predominantly perivascular[16] .The differential diagnosis of eosinophilia in the myocardium includes parasitic infection, allergy, a hypereosinophilic syndrome and hematologic malignancies and Cytomegalovirus infection.

Idiopathic giant cell myocarditis (**Fiedler's myocarditis**) is characterized by destruction of the cardiac myocytes by cytotoxic T cells and the multinucleated cells.[17]Immunohistochemically they are positive for histiocyte markers.It is associated with autoimmune diseases like inflammatory bowel disease and hypothyroidism and is fatal if left untreated. It occurs in young 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 [18].

Other organisms associated with myocarditis include bacteria, fungi, spiro-chetes (especially Borrelia burgdorferi), Rickettsiae,

Chlamydia, parasites (Toxoplasma gondii in immunocompromised patients) and helminths (trichinosis).

Chagas disease(protozoal myocarditis) is caused by the hemoflagellate Trypanosoma cruzi. 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.

Secondary myocarditis can occur in collagen vascular diseases, Rheumatoid factor, drugs, heat stroke and radiation. Granulomatous myocarditis can be seen in tuberculosis or sarcoidosis.

CARDIAC SARCOIDOSIS:

Cardiac involvement in sarcoidosis is very rare. It manifests as ventricular arrhythmias ,conduction disturbances with high degrees of AV block and complete bundle branch block, sudden death,[19] congestive heart failure, papillary muscle dysfunction, acute myocardial infarction, ventricular aneurysm, or recurring pericardial effusions. Left-sided heart failure and syncope were the most common symptoms during hospital presentation. Histopathologically, many patterns like noncaseating granulomatous inflammation, lymphocytic myocarditis, DCM are observed. The classic granulomatous pattern is characterized by firm, white nodules in the interventricular septum, left ventricle or papillary

muscle which are confused as metastatic deposits or fibrous tumors. Noncaseating well-formed granulomas composed of epithelioid histiocytes and multinucleated giant cells arranged in aggregates are seen. Endocardial and pericardial involvement is observed in some cases. Lymphocytes are seen scattered around and within the granulomas. Fibrosis is present surrounding the granulomas, but myocyte necrosis is uncommon. Immunohistochemically, the epithelioid histiocytes express CD68 and the lymphocytes are CD4 T cells.[20]The differential diagnosis includes granulomatous and giant-cell lesions of the heart(Giant cell myocarditis and hypersensitivity myocarditis)

ARTERITIS:

Coronary arteritis due to long term systemic illness leads to thromboembolism or vessel narrowing thereby leading to sudden death[3]

HYPERTROPHIED HEART:

CARDIOMYOPATHY:

Cardiomyopathies are a heterogeneous group of myocardial diseases which exhibit ventricular dilatation or hypertrophy.It can be primary(due to genetic causes) or secondary (due to a systemic disorder).

DILATED CARDIOMYOPATHY:

It is characterized by cardiac dilatation and systolic dysfunction with concomitant hypertrophy.[21,22]The causes include genetic causes (mutation in gene encoding titin,oxidative phosphorylation,mitochondrial

defects and muscular dystrophies) [23], alcoholism, myocarditis, hemochromatosis, peripartum cardiomyopathy, chronic anemia, doxorubicin (adriamycin) toxicity and sarcoidosis. It can progress into heart failure, sudden death, atrial fibrillation and stroke. Grossly the heart is enlarged, heavy and flabby due to dilatation of all the chambers of the heart. Mural thrombi is seen. Histologic features are nonspecific. There is hypertrophy of muscle cells with enlarged nuclei .Interstitial and endocardial fibrosis is seen. **Takotsubo cardiomyopathy** is characterized by left ventricular contractile dysfunction following extreme stress.

Arrhythmogenic right ventricular cardiomyopathy (**right ventricular dysplasia, parchment right ventricle, and Uhl's anomaly**) is a inherited autosomal dominant disease causing right ventricular failure and ventricular tachycardia and fibrillation. It shows replacement of the myocardium of right ventricle by adipose and fibrous tissue, predominantly in the inferior and infundibular wall[24].**Naxos syndrome** is characterized by arrhythmogenic right ventricular cardiomyopathy and hyperkeratosis of palmar and plantar skin surface.

HYPERTROPHIC CARDIOMYOPATHY. It is genetically heterogeneous condition characterized by left ventricular hypertrophy without chamber dilation in the absence of an identifiable systemic or cardiac cause due to abnormal diastolic filling.[25,26] It is seen in healthy individuals younger than 30 years It is caused by germline mutation in

one of the many sarcomeric protein genes(beta myosin heavy chain, cardiac TnT,alpha tropomyosin,myosin binding protein C genes).[27] Affected individuals suffer from angina, exertional dyspnea or sudden cardiac death. Grossly the heart is thick walled, heavy and hypercontracting. There is disproportionate thickening of the ventricular septum to left ventricular free wall (asymmetric septal hypertrophy). The main microscopic changes are myofiber disarray , hypertrophy, exaggerated myocyte branching and interstitial fibrosis.[28-30] Another nonspecific change is basophilic degeneration of myocardium which appears as basophilic, finely granular material in the cytoplasm of myocardial fibers and consists of polyglucosan deposits.Septal vessels are thickened.

RESTRICTIVE CARDIOMYOPATHY:

It is characterized by decrease in ventricular compliance resulting in diastolic dysfunction. It may be idiopathic or associated with radiation fibrosis, amyloidosis, sarcoidosis and mestastatic tumours. Grossly the ventricles are normal or slightly enlarged but not dilated; in contrast, the atria exhibit relative bilateral dilatation. Patchy or interstitial fibrosis is found histologically. In the eosinophilic form (active stage) a myocarditis with a heavy component of eosinophils is present. In the noneosinophilic form (inactive stage) the biopsy findings are nonspecific.[31]

Other restrictive cardiomyopathy conditions include cardiac amyloidosis, hemochromatosis, endomyocardial fibrosis and loeffler's endomyocarditis

ENDOMYOCARDIAL FIBROSIS:

It occurs in children and young adults. It is characterized by fibrosis of endocardium extending from the apex upward including tricuspid and mitral valves.[32]

LOEFFLER'S ENDOMYOCARDITIS:

In addition to endomyocardial fibrosis there will be eosinophilia and eosinophilic infiltration of various organs. Major basic protein(toxic product of eosinophil) initiates endomyocardial necrosis, scarring and organization of the thrombus. These patients have myeloproliferative disorder with PDGFRA gene rearrangement.

HYPERTENSIVE CARDIOVASCULAR DISEASE:

Hypertensive cardiovascular disease is accompanied by atherosclerosis. There are many underlying causes of hypertension including adrenal gland tumors, kidney diseases, renal artery fibromuscular dysplasia and various endocrine disorders.Majority of cases are "essential" or "idiopathic" where an underlying cause cannot be determined. The major change is concentric left ventricular hypertrophy. Spontaneous brain hemorrhages, ruptured cerebral artery berry

aneurysms, lacunar infarcts and thoracic aorticaneurysms / dissections, nephrosclerosis are associated with hypertension

VALVULAR HEART DISEASE:

Aortic stenosis (**senile calcific aortic stenosis**) is a disorder of aging and is characterized by calcification with associated stenosis .Patients with congenitally bicuspid valves develop this disorder.

Mitral valve prolapse ("myxomatous degeneration of the mitral valve" or "floppy mitral valve syndrome" or barlow syndrome) is characterized by a floppy, rubbery mitral valve with redundant tissue.[33]Grossly the valve leaflets appear ballooned or prolapsed into the left atrium. The chordae tendinae are thinned and elongated in myxomatous degeneration. The disorder is an incidental autopsy finding. Sudden death can occur in patients with MVP. It is associated with Marfan syndrome.

Rheumatic heart disease (RHD) is a sequela of rheumatic fever (RF) caused by Streptococcus pyogenes (group A β-hemolytic streptococcus). RHD is the most common cause of mitral stenosis. Microscopically Aschoff nodules appear as interstitial collections of plump mononuclear cells with neutrophils arranged in a granuloma like formation. Aschoff giant cell has two or more nuclei with prominent nucleoli. Anitschkow cells are mononuclear histiocytes that are arranged in a palisade around the center of the granuloma. Progressive fibrosis leads to thickening of the

valve and chordae that eventually leads to fusion of the mitral leaflets at the commissures, producing the classic "fish mouth" appearance.

INFECTIVE ENDOCARDITIS :

It is characterized by bacterial colonization of the valves, chordal attachments and mural endocardium [34]. Left-sided valves are more affected than right-sided valves (aortic mitral tricuspid pulmonic) .Valves with regurgitant alterations ,prosthetic valves and pacemaker/ intracardiac cardioverter-defibrillator wires, immunosuppressed patients and intravenous drug abusers are at great risk. It forms vegetations that are friable, red, irregular, and composed of granulation tissue and thrombus. It has the propensity to cause septic embolization. It can extend from the site of initiation at the cusp apposition line (atrial surface of AV valves and ventricular surface of semilunar valves) and can proceed to the leaflets, chordae, and annular regions to form abscesses.[35]The myocardium is not involved. Staphylococcus aureus produces acute endocarditis, whereas Streptococcus viridans produces subacute endocarditis. The commensals found in the oral cavity are also causative [Gram-negative HACEK organisms (Hemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingii)].Staphylococcus epidermidis causes infective endocarditis in the setting of prosthetic valves. Healed

infective endocarditis leaves residual valve damage and adjacent endocardial fibrosis.

Nonbacterial thrombotic endocarditis (marantic endocarditis) produces small pink, bland and sterile vegetations attached to the valve surface at the lines of closure .It occurs in hypercoagulable state (Trousseau syndrome)[36].

Libman–Sacks endocarditis is seen in cases of systemic lupus erythematosus.It is characterized by flat, pale tan, spreading bands of vegetations located on both surfaces of the valves or chordae tendinae.The valves affected are the tricuspid, mitral, pulmonic and aortic valves.

AORTIC ANEURYSMS (ABDOMINAL AND THORACIC)

Aneurysms are congenital or acquired dilations of the heart or blood vessels which involve the entire thickness of the wall. When it involves an attenuated but intact arterial or ventricular wall of the heart , it is known as ‘true aneurysm’. Examples of true aneurysm includes atherosclerotic, syphilitic, congenital vascular aneurysm and ventricular aneurysm. False aneurysm is a defect in the vascular wall leading to extravascular hematoma which communicates with intravascular space. Examples include ventricular rupture after myocardial infarction. Aortic Dissection occurs when blood enters through a defect in the arterial wall and tunnels between its layers [37]

Based on size and shape , aneursyms are classified as saccular and fusiform aneurysm. Saccular aneurysms are spherical outpouchings which involves a portion of the vessel wall. Fusiform aneurysms are diffuse circumferential dilations of a long vascular segment. Aneurysms occur when the connective tissue within the vessel wall is compromised in disorders like Marfan's syndrome , Loeys –Dietz syndrome, Ehlers Danlos syndrome. It also occurs as a result of structural weakness of the vessel wall caused by loss of smooth muscle cells or insufficient extracellular matrix which occurs because of ischemia and defective matrix remodelling.[38]Tertiary syphilis is another cause of aortic aneurysm. The most important causes are hypertension and atherosclerosis.

There are two types of aortic aneurysms, abdominal aortic aneurysm and thoracic aortic aneurysm.

Abdominal aortic aneurysm is a manifestation of atherosclerosis. It occurs in men and in smokers. Histologically there is destruction and thinning of the aortic media .Aneursym contains extensive thrombus within the lumen. As these becomes larger, the risk for rupture increases. Sudden death occurs when the aneurysm ruptures. The typical autopsy finding is massive hemoperitoneum and retroperitoneal hemorrhage .The variants include inflammatory, IgG4 related disease and mycotic aneurysm.

Thoracic aortic aneurysm is associated with hypertension, marfan's syndrome and loey dietz syndrome .It is a disorder of the connective tissue, so the aortic wall is susceptible to dissection and rupture.

In tertiary syphilis, the thoracic aorta becomes inflamed, thickened and dilated. Microscopically, there is aortitis, obliterative endarteritis and perivascular plasma cell inflammation .

CONDUCTION SYSTEM ABNORMALITIES:

These are characterized by abnormality in the electrical activity of the heart. Examples include Wolff–Parkinson–White syndrome, the long QT syndrome, pre excitation syndrome, sick sinus syndrome and Brugada syndrome. At autopsy, there is usually no detectable anatomic/morphologic abnormality present either grossly or microscopically. Specialized molecular tests to identify genetic mutations may allow pathologists to make postmortem diagnoses in the future.

NEOPLASTIC HEART DISEASE:

Tumors of the heart are rare and associated with sudden death through their mass effect or through induction of an arrhythmia. The primary heart tumours include atrial myxomas and papillary fibroelastomas of the valves. Rarely AV nodal tumor, "cystic tumor of the AV node" or "mesothelioma" can result in conduction system disturbances and sudden death.

Luke et al (1968) in their study found that out of 275 sudden deaths ,105 were due to cardiac causes,50 due to respiratory causes,37 due to gastrointestinal and hepatobiliary causes and 58 due to central nervous system causes[39].

Farb A(1995) in his study found that out of ninety cases (72 men and 18 women mean age-51±10 years) acute myocardial infarction observed in 19,healed myocardial infarction in 37 and no myocardial infarction in 34. Active coronary lesions like plaque disruption and luminal thrombosis were identified in 51.[40]

Kasthuri et al (2002) studied coronary artery disease (76.93%) – triple vessel disease contributes to maximum number of cases of sudden death.[41]

Doolan et al (2004)[42] in their study found that sudden death occurs in people aged less than or equal to 35 years in which cause was not established in 31% and was presumed to be due to primary arrhythmogenic disorders.

A study conducted by Ladich et al (2006)[43] highlights three general categories of cardiac disease not related to atherosclerosis : cardiomyopathy, inflammatory myocardial diseases and ion channel disorders.

Fabre et al (2006) in their study found that out of 453 sudden deaths, 267 hearts were structurally normal and the other 186 deaths were due to

non atherosclerotic causes like cardiomyopathy, inflammatory disorders (lymphocytic myocarditis & cardiac sarcoidosis), non atherosclerotic abnormalities of coronary arteries, valve diseases & miscellaneous causes.[44]

Robert (2011) in his study found that the incidence of fatal atherosclerotic coronary artery disease was 0.7 per 100000 person years for those less than 35 years of age and 13.7 per 100000 person years for those more than 35 years of age.[45]

A study conducted by Sree lakshmi et al (2014) showed 89.77% male deaths.75% of deaths were seen in less than 40 years of age.The maximum number of cases (39.77%) were seen in second decade followed by third decade (26.13%).Cardiac cause of sudden death accounted to 69.13% of cause, non cardiac cause contributed 11.36% of cases and in 19.31% cases even after detailed histopathologic examination cause of death could not be concluded.[46]

Pandian et al(2015) studied that sudden deaths are found in adults aged 31-35 years and males are more affected than females and most of them are due to cardiac cause like coronary artery disease (55.83%)[47]

Sushil et al(2017) in their study found that out of 124 cases,109 cases (87.9%) showed pathology in heart and aorta. Atherosclerotic coronary heart disease was the most common cause of death (72.58%) followed by hypertensive heart disease(4.83%),hypertrophic

cardiomyopathy (3.22%),myocarditis (3.22%),infective endocarditis (1.61%),rheumatic heart disease (0.8%),aortic dissection (0.8%) and syphilitic aortitis (0.8%).[48]

Chaturvedi et al (2019) in their study found that non cardiac causes like infections, cerebrovascular accidents (73.4%) predominated over cardiac causes of sudden death.[49]

PULMONARY CAUSES:

The respiratory causes ranked second among the causes of sudden death.[3]

EPIGLOTTITIS*:*

Epiglottitis is the inflammation of epiglottis due to infections like Hemophilus Influenza and Streptococcus Pyogenes .It can cause narrowing of the airway resulting in an asphyxial death .Microscopically there will be vascular congestion,stromal edema and acute inflammation of the epiglottis and aryepiglottic fold.[50]

PULMONARY EMBOLISM:

The pulmonary artery thrombi are embolic in origin arising from the deep veins of the lower leg. The risk factors include prolonged bedrest, leg surgery, severe trauma, congestive heart failure, use of oral contraceptives (estrogen), disseminated cancer, and genetic causes of hypercoagulability (factor V mutation)[51].The main consequences are increase in pulmonary arterial pressure and ischemia of the pulmonary

parenchyma. The saddle emboli is a large emboli embedded in main pulmonary artery or its branches. These affect the lower lobes and are wedge shaped red infarct. Microscopically there will be coagulative necrosis of the lung parenchyma and hemorrhage. The majority of emboli are clinically silent, a minority cause acute cor pulmonale, shock or death and pulmonary infarction. The risk of recurrence is usually high.

PNEUMONIA:

When a lung becomes infected with microbes it is known as "pneumonia." It may be community acquired or hospital acquired or chronic pneumonia .The community acquired pneumonia is lung infection in healthy individuals acquired from environment. These are due to streptococcus pneumonia ,hemophilus influenza,moraxella catarrhalis and staphylococcus,pseudomonas,.respiratory syncytial virus and metapneumovirus[52]. The hospital-acquired pneumonias are defined as pulmonary infections acquired during hospital stay. Chronic pneumonia is due to mycobacterium tuberculosis, histoplasma capsulatum and blastomyces dermatidis. There are two types based on anatomic distribution: lobar (in which an entire lung lobe is affected) and bronchopneumonia (patchy consolidation of the lung).Grossly the lungs are heavy, boggy and red. Microscopically four stages are idenitified:1.**congestion**-characterized by vascular engorgement, intra alveolar fluid with neutrophils and bacteria.2.**stage of red hepatisation**-

massive exudation by neutrophils,red cells and fibrin 3.**stage of grey hepatisation**-disintegration of red cells and persistence of exudates.4.**resolution**-exudates broken down by enzymatic digestion to produce debri which are ingested by macrophages and organized by fibroblasts. Viral pneumonias usually have interstitial inflammation. Sometimes bacterial pneumonia can be superimposed on the viral pneumonia referred as "superinfection."The complications include abscess formation, empyema and bacteremic dissemination causing endocarditis, meningitis and arthritis. Pneumocystis carinii pneumonia is a opportunistic infection seen in chronically debilitated and immunosuppressed individuals. Microscopically it is characterized by a foamy intra-alveolar exudate with lymphoplasmacytic interstitial infiltrate.[53]

ASPIRATION PNEUMONIA:

It is a condition where gastric contents are inhaled and inflammation and gastric acid damage ensues. It occurs in patients with neuromuscular disorders and chronically debilitated persons. Microscopically pathologists are usually able to identify food particles and acid damage.[54,55]

TUBERCULOSIS:

Tuberculosis is a chronic granulomatous airborne disease caused by M.tuberculosis usually affecting the lungs .Initial exposure to

mycobacteria results in development of delayed hypersensitivity (as determined by a positive result on the tuberculin skin test). CD4+ T cells of the TH1 subset have a role in cell mediated immunity against mycobacteria by the stimulation of macrophages. The mediators of inflammation include IFN-γ, TNF, and nitric oxide. Grossly it appears as grey white consolidation involving lower part of upper lobe or upper part of lower lobe (Ghon's focus).The **Ghon complex** is the combination of parenchymal lung lesion and nodal involvement. The histopathologic hallmark is the presence of granulomas (epithelioid histiocytes) usually with central caseating necrosis and multinucleated giant cells.[56,57]. Secondary (reactivation) tuberculosis arises in previously exposed persons when host immune defenses are compromised and manifests as cavitary lesions in the lung apices. Special stains like AFB will be done to detect bacilli. Both primary progressive tuberculosis and secondary tuberculosis can result in miliary tuberculosis and tuberculous meningitis. HIV-seropositive status is a risk factor for recrudescence of active tuberculosis.

ATYPICAL MYCOBACTERIOSIS :

Atypical mycobacteriosis includes infection by M. avium, M. kansasii and M. malmoense.[58] It occurs in immunocompromised hosts and in patients with preexisting lung disease.

CHRONIC OBSTRUCTIVE LUNG DISEASE(COPD):

COPD encompasses asthma, emphysema, chronic bronchitis and bronchiectasis.It affects older individuals. COPD can cause death in many ways, including chronic hypoxia, right-sided heart failure, superimposed infection, rupture of an air pocket with pneumothorax, or rupture of a blood vessel (with associated hemoptysis).

ASTHMA:

Asthma is characterized by reversible bronchoconstriction caused by airway hyperresponsiveness to a variety of stimuli.[59]It is categorized as atopic(evidence of allergen sensitization, immune activation in a patient with allergic rhinitis or eczema) and non atopic asthma (no evidence of allergen sensitization). Atopic asthma is caused by a TH2 and IgE-mediated immunologic reaction to environmental allergens and is characterized by acute-phase (immediate) and late-phase reactions[60]. The TH2 cytokines IL-4, IL-5 and IL-13 are important mediators. Triggers for nonatopic asthma include viral infections and inhaled air pollutants. Grossly lungs are overdistended. Eosinophils are found in almost all subtypes of asthma. Eosinophil products such as major basic protein are responsible for airway damage. Microscopically airway remodeling features like thickening of airway wall, sub-basement membrane fibrosis, increased vascularity and hypertrophy of bronchial glands and smooth muscle are noted. Patients present with chest tightness, dyspnea, wheezing

and cough. Sputum or bronchoalveolar specimens show curschmann spirals and charcot leyden crystals.

EMPHYSEMA:

Emphysema is characterized by permanent enlargement of air spaces distal to terminal bronchioles accompanied by destruction of their walls without any fibrosis.The subtypes include centriacinar (most common smoking related affects central parts of the acini),panacinar (acini are uniformly enlarged and seen in patients with α1-antitrypsin deficiency), distal acinar(distal acini is involved) and irregular emphysema (associated with scarring).Smoking and inhaled pollutants causes accumulation of inflammatory cells, releasing elastases and oxidants which destroy the alveolar walls without adequate mesenchymal repair response. Patients present with dyspnea, cough and wheezing. Patients with emphysema are characterized as "pink puffers." Emphysema usually coexists with chronic bronchitis. Microscopically there will be destruction of alveolar walls without fibrosis, leading to enlarged air spaces.

CHRONIC BRONCHITIS:

Chronic bronchitis is defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years. Cigarette smoking and air pollutants are the risk factors. Chronic obstructive component results from small airway disease (chronic bronchiolitis) and

coexistent emphysema. Histologic examination demonstrates enlargement of mucus-secreting glands, goblet cell metaplasia and bronchiolar wall fibrosis. Patients present with hypercapnia, hypoxemia and cyanosis (blue bloaters).

BRONCHIECTASIS:

It is the permanent dilation of bronchi and bronchioles caused by destruction of the muscle and the elastic tissue, resulting from necrotizing infections with staphylococcus aureus and klebsiella. The conditions predisposing to bronchiectasis include Bronchial obstruction, Congenital or hereditary conditions like cystic fibrosis and Kartagener syndrome or immotile cilia syndrome (primary ciliary dyskinesia)[61] and young's syndrome. It may be obstructive or non obstructive[62]. It affects the lower lobes bilaterally. Grossly the airways are dilated almost upto the pleural spaces. It is classified into saccular, cystic and cylindric types based on the shape of bronchial dilatation. Microscopically there will be acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles and the desquamation of lining epithelium with ulceration. The Complications of bronchiectasis are bronchopleural fistula with empyema, brain abscess and amyloidosis.

CONGESTION:

Congestion is a passive process resulting from impaired venous outflow. Acute pulmonary congestion has engorged alveolar capillaries ,alveolar septal edema and intra-alveolar hemorrhage. In chronic pulmonary congestion**,** the septa become thickened and fibrotic and the alveolar spaces contain hemosiderin laden macrophages ("heart failure cells"). In acute hepatic congestion**,** the central vein and sinusoids are distended with blood and central hepatocyte dropout due to necrosis. The periportal hepatocytes shows less damage because of their proximity to hepatic arterioles. The chronic passive congestion of the liver grossly has red brown depressed central regions surrounded by uncongested tan fatty liver **(nutmeg liver).** Microscopic findings include centrilobular hepatocyte necrosis, hemorrhage and hemosiderin-laden macrophages.

PULMONARY EDEMA:

Pulmonary edema is due to hemodynamic disturbances or local microvascular injury. Congestive heart failure raises hydrostatic pressure. Microvascular injury causes leakage of fluids and proteins into interstitial space and into alveoli also. Grossly lungs are wet and heavy in lower lobes. Microscopically the alveoli are filled with pink floccular material .Congested capillaries and hemosiderin laden macrophages are seen. Later there will be fibrosis and thickening of alveolar walls (**brown induration of lungs**).

DIFFUSE ALVEOLAR DAMAGE:

It is diffuse and bilateral. It may be caused by infectious agents (viruses), inhalants ,drugs (chemotherapeutic agents and amiodarone), ingestants (kerosene or paraquat), shock, sepsis and radiation. It is otherwise known as **adult respiratory distress syndrome**. The earliest stages consist of edema, intra-alveolar hemorrhage and fibrin deposition. This is followed by hyaline membrane formation (prominent after 3–7 days), a sparse interstitial inflammatory infiltrate, fibrin thrombi and hyperplasia of the type II pneumocytes which may exhibit atypia, mitotic activity, intracytoplasmic lipid accumulation and cytoplasmic hyaline (Mallory) bodies.[63] The combination of squamous metaplasia and cytologic atypia may mimic a squamous cell carcinoma.[64] In a later (organizing) stage, there is interstitial and intraluminal fibroblastic proliferation along with hyperplastic lining cells.

INTERSTITIAL / RESTRICTIVE LUNG DISEASES:

Chronic interstitial lung diseases are heterogeneous group of disorders characterized predominantly by bilateral patchy involvement of the pulmonary connective tissue and interstitium in the alveolar walls. It usually affects older individuals. The hallmark feature is reduced compliance, which necessitates increased effort of breathing (dyspnea). Chest radiographs show groundglass opacities. The patients can develop respiratory failure, pulmonary hypertension and cor pulmonale. Advanced

cases result in scarring and destruction of the lung referred as honeycomb lung. The pathogenetic factor is injury to the alveoli with activation of macrophages and release of fibrogenic cytokines such as TGF-β.

Idiopathic pulmonary fibrosis is characterized by patchy interstitial fibrosis, fibroblastic foci and formation of cystic spaces (honeycomb lung)[65]. This is otherwise known as **usual interstitial pneumonia** (UIP).

Nonspecific interstitial pneumonia is a chronic bilateral interstitial lung disease of unknown etiology and carries a much better prognosis.Microscopically two patterns were recognized. The cellular pattern shows mild-to-moderate chronic interstitial inflammation in a uniform or patchy distribution. The fibrosing pattern consists of diffuse or patchy interstitial fibrosis.

Cryptogenic organizing pneumonia or Bronchiolitis obliterans–organizing pneumonia (BOOP) may be associated with infections, inhalants (silo-filler lung), drugs and collagen-vascular diseases but mostly it is idiopathic.[66] The onset is acute and characterized by cough, dyspnea, fever and malaise.[67] The prognosis is generally excellent.Morphologically, the hallmark of the disease is fibroblastic plugs (‘Masson bodies’) which are elongated to serpiginous in shape and are formed by spindle to stellate fibroblasts embedded in a pale-staining matrix. Other changes include foamy macrophages, neutrophils and thickening of the alveolar septa.

Desquamative interstitial pneumonia (DIP) is characterized by a filling of the alveolar spaces by large mononuclear cells.Ultrastructurally, the desquamated cells have features of macrophages. Necrosis, hyaline membranes and fibrin are absent.

Respiratory bronchiolitis-associated interstitial lung disease : It is a common incidental finding in heavy smokers.Histologically there will be alveolar macrophages within respiratory bronchioles spilling into neighboring alveoli.[68]

Lymphoid interstitial pneumonia is characterized by a lymphocytic infiltrate admixed with histiocytes and plasma cells, occupying the lung interstitium.[69] Serum immunoglobulin abnormalities may be present. It has been associated with Sjogren syndrome and IgG4 related diseases.

PNEUMOCONIOSES:

Pneumoconioses consists of a group of chronic fibrosing diseases of the lung due to exposure to organic and inorganic particulates like mineral dust(coal,silica and asbestos). Particles that are 1 to 5 μm in diameter get lodged at the bifurcation of the distal airways. Smoking worsens the effects of all inhaled mineral dusts.Pulmonary alveolar macrophages play a role by promoting inflammation and producing reactive oxygen species and fibrogenic cytokines.

Coal workers pneumoconioses varies from asymptomatic anthracosis to simple coal worker's pneumoconiosis (coal macules or nodules, and

centrilobular emphysema) to progressive massive fibrosis (PMF)[70] manifested by increasing pulmonary dysfunction, pulmonary hypertension and cor pulmonale.

The **Silicosis** is the most common pneumoconiosis in the world and crystalline silica (e.g., quartz) is the main culprit. It manifests from asymptomatic silicotic nodules to progressive massive fibrosis. Persons with silicosis have an increased susceptibility to tuberculosis.

Asbestosis: Asbestos exposure leads to 1) parenchymal interstitial fibrosis (asbestosis) (2) localized fibrous plaques (3) pleural effusions (4) lung carcinomas (5) malignant pleural and peritoneal mesotheliomas and (6) laryngeal carcinoma. There are two forms of asbestos: serpentine and amphibole. Microscopically Asbestosis is characterized by diffuse pulmonary interstitial fibrosis and **asbestos bodies** which consist of asbestos fibers coated with an iron-containing proteinaceous material. Asbestosis begins in the lower lobes and subpleurally.[71]

Pleural plaques are well-circumscribed plaques of dense collagen containing calcium. They develop on the anterior and posterolateral aspects of the parietal pleura **.**They do not contain asbestos bodies.

PULMONARY HYPERTENSION:

Pulmonary hypertension refers to a condition where the blood pressure within the pulmonary arteries is elevated. The chronic lung diseases like asthma, COPD, chronic interstitial diseases, etc., can cause

pulmonary hypertension. Primary pulmonary hypertension is more common in young women[72,73]. Pulmonary hypertension results in right ventricular hypertrophy and right-sided heart failure. Deaths can result from arrhythmias, heart failure or the underlying lung pathology.

NEOPLASIA:

Benign lung tumors are rare. Malignant lung tumours are either primary or secondary (due to metastasis).Primary lung tumours are adenocarcinoma, squamous cell carcinoma, small cell carcinoma and large cell carcinoma. In majority of cases, lung cancer is diagnosed before death occurs. Occasionally cases are diagnosed at autopsy.

Prateek rastogi (2011) in his study found that out of 274 sudden death , 81 (29.56%) were due to respiratory causes and were seen mostly in the age group 40 to 60 years.Males were mostly affected (88.88%).Various causes includes pulmonary tuberculosis (43.2%), pneumonia (28.39%) and upper respiratory diseases with other extra pulmonary causes(23.45%).[74]

A study conducted by Cheng et al (2001) in 14 patients aged less than 30 years died with the history of asthma revealed bronchial infiltration of eosinophils (100%),thickened basement membrane of the bronchial mucosa (85.7%),proliferative mucous gland (64.3%) and mucous plug in bronchiole (57.1%).[75]

Ansari et al (2002) analyzed 128 cases which includes HIV positive and negative patients and found that 11% of sudden deaths can be attributed to pneumocystis jirovecii.[76]

Vaideeswar et al (2004) in their study found that among 20475 autopsies done over 12 years period, 0.19% of cases (n=39) had invasive aspergillosis.[77]

Renee et al(2005) in their study found that among 24708 cases during the study period of April 1991 to February 2002 , 56% were due to natural causes. There were 167 cases of lung cancer (0.7%) amongst individuals who died naturally.[78]

Chia-yu Chang (2016) in his study found that 1.3% of patients died due to aspiration pneumonia out of 42732 autopsies and most of them had stroke as a cause for aspiration.[55]

GASTROINTESTINAL AND HEPATOBILIARY CAUSES:

GASTRITIS:

Gastritis means inflammation of the stomach lining including the mucosa and the deeper parts. The causative agents include alcohol consumption, drugs ,stress and trauma. It is a frequent finding on autopsy.[79] The spectrum of acute gastritis ranges from asymptomatic disease to mild epigastric pain, nausea and vomiting. It is characterized by superficial (shallow) mucosal erosions that are pinpoint to several millimeters in size. Curling ulcers is seen in burn Patients and Cushing

ulcers is seen in persons with increased intracranial pressure and Wischnewsky ulcers is seen in cases of hypothermia. The chronic gastritis is caused by H. Pylori Infection. H. pylori gastritis affects the antrum and is associated with increased gastric acid production. The induced mucosa-associated lymphoid tissue can transform into MALT lymphoma. Autoimmune gastritis causes atrophy of the gastric body oxyntic glands, which results in decreased gastric acid production, Antral G cell hyperplasia, achlorhydria and vitamin B12 deficiency. Anti-parietal cell and anti–intrinsic factor antibodies are present. Intestinal metaplasia is a risk factor for development of gastric adenocarcinoma.

CIRRHOSIS/ESOPHAGEAL VARICES:

The three main characteristics of cirrhosis are (1) involvement of most or all of the liver, (2) bridging fibrous septa and (3) parenchymal nodules containing both senescent and replicating (stem/progenitor cell) hepatocytes. The most frequent causes are chronic hepatitis B and C and alcoholic and nonalcoholic steatohepatitis. Less frequent causes are autoimmune and biliary diseases and metabolic conditions such as hemochromatosis. The main complications are decreased liver function, portal hypertension, and increased risk for development of hepatocellular carcinoma. Portal hypertension in cirrhosis results from increased resistance to portal flow at the level of the sinusoids[80] .With the rise in portal venous pressure, shunts develop. The principal sites of shunt

formation are seen around the veins within the rectum (manifest as hemorrhoids), the cardioesophageal junction (producing esophagogastric varices), the retroperitoneum and the falciform ligament of the liver. Abdominal wall collaterals appear as dilated subcutaneous veins extending outward from the umbilicus (caput medusae).Patients with esophageal varices present with massive hematemesis.[81]

Rosmorduc et al (1992) [82] in their study found that massive microvesicular and macrovesicular steatosis constituted of mainly triglycerides involving 100% of hepatocytes was the cause of death in 4 patients who died suddenly.

Chejfec G (2001)[83] in his study found that enlarged fatty livers were the only abnormality noted in 11 patients with chronic alcoholism who died suddenly.

INFECTIONS:

Several Bacterial(staphylococcus aureus,salmonella typhi, treponema pallidum), fungal (histoplasma) and parasitic (schistosomiasis, fasciola hepatica, Clonorchis sinensis, echinococcus) infections can infect liver and rarely cause sudden death.

MALLORY–WEISS TEAR:

Following binge drinking, the junction between esophagus and stomach is more prone for tearing because of repeated retching.

STRANGULATED HERNIA, INTUSSUCEPTION AND VOLVULUS:

The acute inflammation of a portion of the GI tract or appendix or meckel's diverticulum with subsequent perforation, rupture, bleeding or peritonitis can lead to death. The strangulated hernias, infarcted bowel segments, intussusception or volvulus bowel segments and areas containing a tumor can also lead to sudden death.

HEMOCHROMATOSIS:

Hemochromatosis is excessive accumulation of iron in the liver, pancreas and heart. It may be primary (genetic abnormality) or secondary due to multiple blood transfusions, blood and bone marrow disorders, chronic liver diseases. The primary hemochromatosis is an autosomal recessive disorder caused by a mutation of the HFE gene, which normally regulates intestinal absorption of iron. The clinical manifestations include cirrhosis, diabetes mellitus, and skin pigmentation. Special stains like Prussian blue can be used to demonstrate iron.

ACUTE PANCREATITIS:

Acute pancreatitis is a reversible pancreatic parenchymal injury with inflammation[7].The annual incidence is 10 to 20 cases per 100000 people. The major etiologic factors include high alcohol consumption and biliary tract disease (calculi) ,genetic defects (PRSS1,SPINK1),ischemia, systemic shock, various drugs (e.g., estrogens, corticosteroids,

immunosuppressives), pancreatic trauma, hypercalcemia, hyperlipidemia, infections (HIV) and pregnancy[84]. These factors promote the inappropriate activation of digestive enzymes which destruct the pancreatic tissue and elicit an inflammatory reaction. Diagnostic studies include serum amylase ,lipase and trypsinogens. Imaging modalities include (endoscopic ultrasonography [EUS], dynamic contrast enhanced CT, and magnetic resonance cholangiopancreatography). Grossly pancreas appears to be swollen, wet, firm to hemorrhagic and / or necrotic. Fat necrosis appears as grayish-yellow plaques and nodules in pancreatic adipose tissue. The Atlanta Classification classifies acute pancreatitis into mild (edematous) and severe (necrotizing). In mild pancreatitis (acute interstitial pancreatitis), the histologic features are mild inflammation, interstitial edema, focal fat necrosis in the pancreatic parenchyma and peripancreatic fat. Pancreatic parenchyma is almost preserved. Fat necrosis is due to the activity of lipase. The resultant fatty acids combine with calcium forming salts which imparts blue colour to the fat cells. In severe pancreatitis (acute necrotizing pancreatitis), there will be panlobular coagulative necrosis and extensive fat necrosis of peripancreatic tissues . Neutrophils are seen in the region between the normal tissues and the necrosis. Thrombi are common in capillaries and venules. Some intact pancreatic acini are dilated and contains inspissated secretions. In acute hemorrhagic pancreatitis ,necrosis is accompanied by

hemorrhage within the substance of the gland[85].The complications of acute pancreatitis include pancreatic pseudocysts ,pancreatic abscess , pancreatic necrosis and chronic pancreatitis. Mortality is high (up to 8%) due to the released inflammatory mediators which lead to multiorgan dysfunction and sepsis .

Tsokos et al (2007) [86]in his study found that among 6178 autopsies there were 27 cases of acute pancreatitis which presented as sudden unexpected death.

RETICULOENDOTHELIAL AND IMMUNE CAUSES:

The reticuloendothelial system includes the bone marrow, the spleen, the lymph nodes and the thymus. It is involved with the immune system and blood cell production (bone marrow). The immune system is involved in the recognition and elimination of harmful substances including micro-organisms, foreign substances and malignant cells. Immune disorders like hypersensitivity reactions,autoimmune diseases ,immunodeficiency disorders(HIV) play a role in death. They have nonspecific morphologic findings.

GENITOURINARY CAUSES:

The genitourinary system includes the kidneys, ureters, bladder, urethra , testis, uterus, ovaries and prostate. Nephrosclerosis is the presence of glomerulosclerosis , interstitial fibrosis,tubular atrophy, arteriosclerosis and arteriolosclerosis and it is associated with

hypertension. There will be luminal reduction of the renal vessels. Malignant nephrosclerosis is associated with malignant hypertension (BP>200/100 mm/Hg) which manifests as fibrinoid necrosis of arterioles and hyperplastic arteriolosclerosis. Pyelonephritis is the suppurative inflammation of the kidney caused by infection via ascending or hematogeneous route or by obstructive lesions of the bladder and vesicoureteric reflux.. Acute pyelonephritis has prominent neutrophilic infiltrate or granulomatous inflammation. The complications are papillary necrosis, pyonephrosis and perinephric abscess. Chronic pyelonephritis leads to irregular scarring which is more prominent at the upper and lower poles. Pyelonephritis can lead to sepsis and death. Kidney tumours(Wilms tumor in children; renal cell carcinoma in adults) can rarely cause death. The malignant tumours of testes ,prostate, uterus, cervix and ovaries can lead to death. The prostatic hyperplasia causes the veins around it to become dilated leading to thromboembolism.

CENTRAL NERVOUS SYSTEM CAUSES:

INFECTION:

Infectious agents(bacteria, virus and parasites) reach the central nervous system through the hematogeneous route, direct implantation, local extension and through the peripheral nerves.

MENINGITIS:

Meningitis is the inflammatory condition involving the leptomeninges. It can be divided into acute pyogenic (bacterial), aseptic (viral), and chronic meningitis (tuberculous, spirochetal).The patient presents with headache ,fever, rigidity and neck stiffness.

ACUTE PYOGENIC MENINGITIS:

The microorganisms vary with age. Escherichia coli and the group B Streptococci in neonates, Neisseria Meningitidis in adolescents and in young adults and Streptococcus pneumoniae and Listeria monocytogenes in older individuals. CSF examination shows abundant neutrophils, elevated protein and reduced glucose. Grossly meninges show purulent and hemorrhagic material. Microscopically neutrophils fill the entire subarachnoid space around the leptomeningeal blood vessels. Gram stain reveals the causative organism.

ASEPTIC MENINGITIS:

It is less fulminant than pyogenic meningitis. CSF examination shows lymphocytosis, moderate protein elevation and a normal glucose level. Microscopically there will be a mild to moderate leptomeningeal lymphocytic infiltrate.

CHRONIC MENINGITIS:

It may be due to mycobacterial or spirochetal infections.

Tuberculous meningitis show a mixture of polymorphonuclear and mononuclear cells with elevated protein level and reduced glucose levels on CSF examination.Grossly the subarachnoid space and leptomeninges contains a gelatinous or fibrinous exudates. Microscopically there are mixtures of lymphocytes, plasma cells and macrophages, well-formed granulomas with caseous necrosis and giant cells.

Neurosyphilis occurs in tertiary stage of syphilis in about 10% of persons infected with treponema pallidum. It produces chronic meningitis with an obliterative endarteritis rich in plasma cells and lymphocytes. Neuroborreliosis is caused by Borrelia burgdorferi, the pathogen of Lyme disease[87].

BRAIN ABSCESS:

Brain abscesses are caused by bacterial infections.. They occur due to sepsis, bacterial endocarditis, mastoiditis, sinusitis and bronchiectasis. Grossly there will be necrotic centre surrounded by fibrous capsule .Microscopically the necrotic center is surrounded by edema and granulation tissue and reactive gliosis.

VIRAL ENCEPHALITIS:

They are caused by viruses that are transmitted by mosquitoes and ticks. Examples include Eastern equine encephalitis, Western equine encephalitis, St. Louis encephalitis, and West Nile viral encephalitis. Microscopically there will be intense perivascular lymphocytic

inflammation. Blood and tissue samples can be sent to the Centers for Disease Control (CDC) for definitive diagnosis. Herpes and CMV can infect fetuses or immunocompromised persons. Progressive multifocal leukoencephalopathy (PML) is caused by JC virus, a polyomavirus which infects oligodendrocytes. Rabies is transmitted to humans via the bite of a rabid animal (dogs and bat). It has a long incubation period and is considered fatal. Specimens have to be handled with special care while grossing. Fungal and parasitic infections occurs in immunocompromised patients (AIDS). Examples include Cryptococcus, toxoplasmosis, and aspergillosis ,cysticercosis and naegleria fowleri infections.

Cysticercosis is caused by the tapeworm Tenia solium.When ingested the larval forms enter into the gastrointestinal tract, where they develop into mature tapeworms and encyst. Cysts are common in the brain and subarachnoid space and disseminates to heart ,muscle, eyes and skin[88].It manifests as a mass lesion and can cause seizures and sudden death.Microscopically the cysts are ovoid and white to opalescent contain invaginated scolex with hooklets that are bathed in clear cystic fluid.

Naegleria fowleri which lives in stagnant water enter the sinuses and invade the brain when the person swims in that water and cause death.

PRION DISEASES :

Prion disease is characterised by the conversion of normal cellular protein (PrP^{C}) into an abnormal conformation ($PrP^{SC)}$ with special

characteristics like resistance to protease digestion and self propagation.[89]Prion diseases may be sporadic, familial or transmissible.Familial forms have PRP gene mutation or polymorphism at codon 129 that encodes methionine or valine. Disease phenotypes include kuru, Creutzfeldt–Jakob disease (CJD), 'variant' CJD (linked to exposure of bovine spongiform encephalopathy), Gerstmann–Straussler–Scheinker disease and fatal familial insomnia.

CREUTZFELDT-JACOB DISEASE :

CJD is transmitted via contaminated neurosurgical instruments, corneal transplantation and human growth hormone supplements. These involve middle-aged or older adults . There is cognitive decline with profound dementia and generalized myoclonus. Western blotting of tissue extracts after proteinase K digestion is diagnostic. The disease is fatal and the average survival is 7 months after the symptom onset. Histologically there is spongiform transformation of the cerebral cortex, caudate and putamen ; this multifocal process results in formation of uneven vacuoles within neurophil and in the perikaryon of neurons. There is neuronal loss ,reactive gliosis and cyst formation in advanced cases. Inflammation is absent. The diagnostic feature of prion-associated diseases evident in only 5% of cases is the deposition of amyloid ('spiked ball' plaques or kuru plaques) that display radiate, spicular contours and are strongly PAS and congo red positive.

Formalinized and paraffin-embedded specimens retains transmissibility.So biopsy material requires special handling. Fixation protocols (formic acid immersion following initial formalinization) have been developed that eliminate infectivity.[90] Usually these specimens are sent in formalin to the National Prion Disease Pathology Surveillance Center of the United States where they can assess specimens for *PrP* gene mutations and PrP deposition.

SEIZURE DISORDERS:

Seizures represent abnormal electrical activity within the CNS. The grand mal seizure is the most common which manifests as generalized body convulsions. Trauma, tumors, strokes, infections, etc. can induce seizures. Idiopathic seizure disorders have no underlying CNS disorder. Persons with a chronic seizure disorder are at risk for sudden, unexpected death due to cardiac dysrhythmia. It is impossible for pathologists to identify underlying microscopic cause for seizures.

CEREBROVASCULAR DISEASE:

Cerebrovascular disease or stroke is an acute-onset neurologic deficit resulting from hemorrhagic or obstructive vascular lesions. They are due to loss of blood supply. They can be widespread or focal and affect regions with the least vascular supply like area between anterior and middle cerebral artery distributions (border zone or watershed infarcts).Global cerebral ischemia or diffuse ischemic or hypoxic

encephalopathy occurs due to cardiac arrest, shock and hypotension. They affect neurons of hippocampus, cerebellar purkinje cells and cerebral cortex. Grossly brain becomes edematous with widening of gyri and narrowing of sulci. Microscopically in acute changes there will be microvacuolization of neurons with cytoplasmic eosinophilia and nuclear pyknosis and karyorrhexis and neutrophilic infiltrate. Subacute changes include tissue necrosis, influx of macrophages, vascular proliferation and reactive gliosis. Repair after 2 weeks is characterized by removal of necrotic tissue, loss of CNS architecture and gliosis. Focal cerebral infarcts are most commonly embolic or thrombotic. Here a initial nonhemorrhagic infarct can become hemorrhagic.

HYPERTENSIVE DISEASE:

SPONTANEOUS INTRAPARENCHYMAL HEMORRHAGE:

Spontaneous intraparenchymal hemorrhage occur in the deep cerebrum like basal ganglia or thalamus,the cerebellum or the pons. Charcot bouchard aneursyms are minute aneursyms associated with hypertension. Microscopically there will be extravasation of blood with compressed adjacent brain parenchyma showing anoxic neuronal and glial changes and edema.

RUPTURED BERRY ANEURYSM:

A berry or saccular aneurysm is a localized out-pouching of the wall of a cerebral artery that is at risk for rupture.It is the most frequent

cause of subarachnoid hemorrhage.Other aneursyms affecting CNS includes atherosclerotic, mycotic aneurysm,traumatic and dissecting aneurysm. They are found near the major branching points along arteries. These are due to structural abnormality of vessel wall,polycystic kidney disease, Ehler Danlos syndrome,fibromuscular dysplasia and coarctation of aorta[91].Rupture of a cerebral artery berry aneurysm is accompanied by "the worst headache" the person has ever experienced. Microscopically there will be absence of smooth muscle and internal elastic lamina with hyalinised intima.

ARTERIOVENOUS MALFORMATION (AVM):

Arteriovenous malformation is characterized by complex network of intercommunicating arterial and venous structures[92]. They affect both males and females and manifest between the ages of 10 and 30 years with seizures, intracerebral hemorrhage or subarachnoid hemorrhage.Multiple AVMs occurs in hereditary hemorrhagic telangiectasia.

DURAL SINUS THROMBOSIS:

Dural venous thrombosis is a rare condition that can cause headache, stroke and even sudden death. The condition is common in women in third decade .The risk factors include deep venous thrombosis.

TUMOURS:

Brain tumors occurs in benign and malignant forms.Benign tumors can result in death due to their mass effect or because of obstruction of

CSF flow. Colloid cyst are benign unilocular cyst lined by mucinous epithelium occurring usually in adults. They are found in the anterior third ventricle near foramen of monro. Patient presents with headache due to obstruction of CSF flow. Malignant tumors can lead to death by invasion of vital structures, hemorrhage or metastasis. The most common malignant brain tumor is glioblastoma multiforme .

M Black et al (2002)[93] in their study found that the causes of sudden death caused by intracranial pathology were due to sudden unexplained death in epilepsy[SUDEP],intracranial hemorrhage,purulent meningitis or brain abscess or due to brain tumours.

MISCELLANEOUS CAUSES:

CEREBRAL MALARIA:

Plasmodium falciparum ,the cause of severe cerebral malaria and four other species (plasmodium vivax, ovale, malariae, knowlesi) that infect humans are transmitted by female anopheles mosquito. Plasmodium falciparum infection is associated with high levels of parsitemia, that lead to severe anemia, cerebral symptoms, renal failure, pulmonary edema and death. Plasmodium faciparum infects all types of red cells while other species infect young or old red cells.Plasmodium falciparum infected red cells form rosette and release proteins like PfEMP1 which bind to endothelial cell ligands like CD36,VCAM1 and E selectin. This causes ischemia which is the main cause of cerebral malaria.

Microscopically in cerebral malaria, brain vessels are plugged with parasitized red cells forming ring haemorrhages called **durck granuloma**.

CHRONIC ALCOHOLISM:

Chronic alcoholism affects numerous organ and can result in death. Brain damage includes central pontine myelinosis, cerebellar vermis atrophy and mamillary body atrophy / necrosis (Wernicke–Korsakoff syndrome in association with thiamine deficiency)[94] . It is frequent to identify remote (old) brain contusions in alcoholics. Ethanol-induced dilated cardiomyopathy is a frequent finding in chronic alcoholics which is at risk for fatal arrhythmias[95]. Pulmonary infections like pneumonia, aspiration pneumonia, and abscesses are common in alcoholics. Ethanol-related liver disease includes steatosis, alcoholic hepatitis, cirrhosis, portal hypertension and esophageal varices . Gastritis and peptic ulcer disease are more common in alcoholics. Spontaneous bacterial peritonitis is most common in chronic alcoholics.

AMYLOIDOSIS:

Amyloidosis is characterized by the extracellular deposition of misfolded proteins that aggregate to form insoluble fibrils called amyloid which causes tissue injury and impair normal function by pressure atrophy on cells. Congo Red stain shows apple green birefringence when observed by polarizing microscopy. It may be localized or systemic. It is associated with monoclonal B cell proliferations (amyloid deposits are

immunoglobulin light chains), rheumatoid arthritis (deposits are amyloid A protein),alzheimer's disease(amyloid B protein),familial amyloid polyneuropathies(transthyretin) and with dialysis (beta 2 microglobulin). It affects various organs like heart (arrhythmia,cardiomyopathy),kidney (nephrotic syndrome, renal failure), spleen (sago spleen and lardaceous spleen) and gastrointestinal system.

SICKLE CELL DISEASE:

Sickle cell disease is an autosomal recessive inherited hemoglobinopathy characterized by replacement of aminoacid glutamic acid by valine in 6^{th} position of beta globin chain resulting in HbS molecule. On deoxygenation or dehydration, the HbS molecules can aggregate and polymerize resulting in a rigid sickle shape of the red blood cells. These sickled red cells cause microvascular occlusion and anemia .Clinically, patients presents with anemia, excess bilirubin,gallstones and hepatosplenomegaly. The complications are pain or vaso occlusive crisis,aplastic crisis(due to parvo virus B19 infection), acute chest syndrome, salmonella osteomyelitis, priaprism ,dactylitis (painful swollen toes and fingers) and infarction of various organs (spleen, bone, brain) and stroke. Persons who have one defective gene and one normal gene are said to have "sickle cell trait" or "carriers." They are usually aymptomatic. In persons suspected of having sickle cell disease or trait at autopsy, pathologists can send blood samples for a haemoglobin electrophoresis test which will allow for a postmortem diagnosis.

MATERIALS & METHODS

MATERIALS AND METHODS:

STUDY DESIGN:

Prospective and descriptive study

PLACE OF STUDY:

Department of pathology, Coimbatore Medical college Hospital, Coimbatore.

STUDY PERIOD:

January 2018 to June 2019

INCLUSION CRITERIA:

- Autopsy specimens of adults aged 15-45 years who has died suddenly

EXCLUSION CRITERIA:

- Autopsy specimens of age less than 15 years and more than 45 years
- Unnatural death(accident, suicide, homicide, pregnancy related deaths)
- Autolysed specimens

Autopsy specimens of adults who has died suddenly were received from forensic department in 10% buffered formalin .Detailed gross examination findings were noted in all the organs. Representative areas

were taken from the specimen with 4mm thickness. Tissues were processed and subjected to paraffin section at 4 micron thickness and then stained with hematoxylin and eosin staining method. Special staining and immunohistochemical studies were done wherever feasible. The results were tabulated and analyzed.

RESULTS

OBSERVATION AND RESULTS

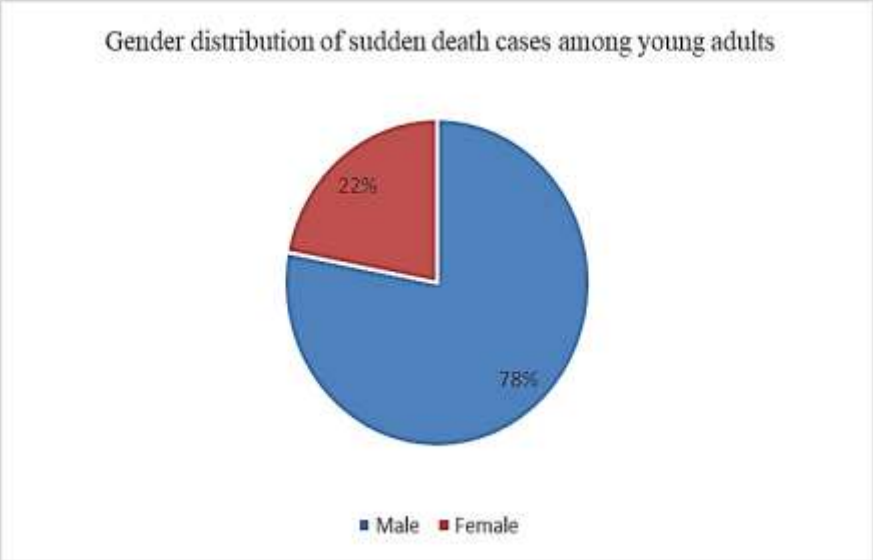
A total of 1199 autopsied specimens were received in the Department of Pathology, Coimbatore Medical College, Coimbatore from a period of January 2018 to June 2019; out of which 100 were sudden deaths which constitutes about 12% of total autopsies studied.

Among these cases, males (78%) were predominant over females(22%) in the ratio of 3.5:1.

TABLE 1 SEX DISTRIBUTION OF SUDDEN DEATH CASES

Gender	Frequency (n)	Percentage (%)
Male	78	78.0
Female	22	22.0

CHART 1 PIECHART SHOWING SEX DISTRIBUTION OF SUDDEN DEATH CASES



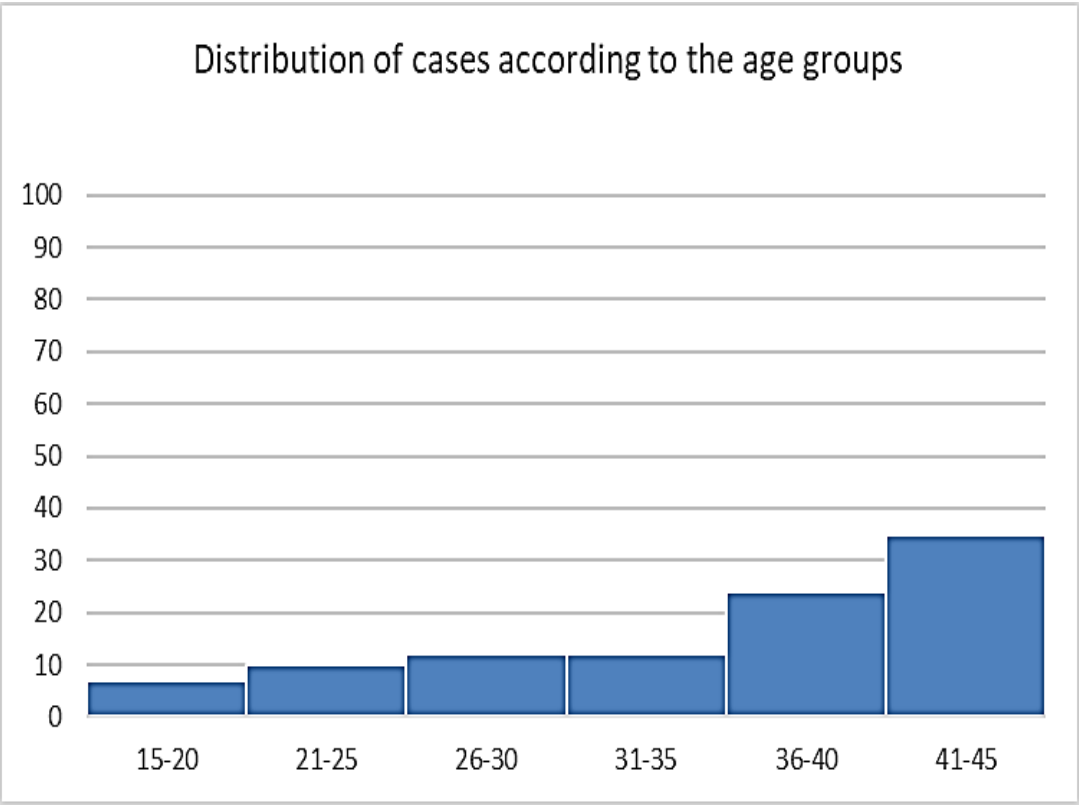
Maximum number of deaths were seen in fourth decade(35%) followed by third decade(24%).

TABLE 2 DISTRIBUTION OF CASES ACCORDING TO AGE GROUPS

Age group	Frequency (n)	Percentage (%)
15-20	7	7.0
21-25	10	10.0
26-30	12	12.0
31-35	12	12.0
36-40	24	24.0
41-45	35	35.0
Total	100	100.0

The mean age of the subjects was 35.57 ± 8.38 (SD) and the minimum and maximum age were 17 yrs & 45 yrs respectively.

CHART 2 BAR DIAGRAM SHOWING DISTRIBUTION OF CASES ACCORDING TO AGE GROUPS



Among the autopsied sudden deaths histomorphologically , most of the deaths were due to cardiovascular causes accounting to 55% of all suddendeaths. Major cardiac cause for sudden death was myocardial infarction (37%)

TABLE 3 HISTOPATHOLOGICAL FINDINGS IN HEART

Pathological findings	**Frequency (n)**	**Proportions (%)**
Ischemic Heart Diseases	**37**	**37**
Acute MI	22	22
Healed MI	15	15
Inflammatory Heart Diseases	**5**	**5**
Myocarditis	1	1
Giant Cell Myocarditis	2	2
Esonophilic myocarditis	2	2
Cardiomyopathy	**4**	**4**
Dilated cardiomyopathy	1	1
Hypertrophic cardiomyopathy	1	1
Endomyocardial fibrosis	2	2
Valvular Heart Diseases	**7**	**7**
Aortic Stenosis	1	1
Mitral Value Prolapse	1	1
Infective endocarditis	2	2
Aortic dissection	1	1
Aortic aneurysm	1	1
Aortitis	1	1
Cysticercosis	1	1
Sarcoidosis	1	1
Normal	41	41
Sample not received	4	4

CHART 3 BAR DIAGRAM SHOWING HISTOPATHOLOGICAL FINDINGS IN HEART

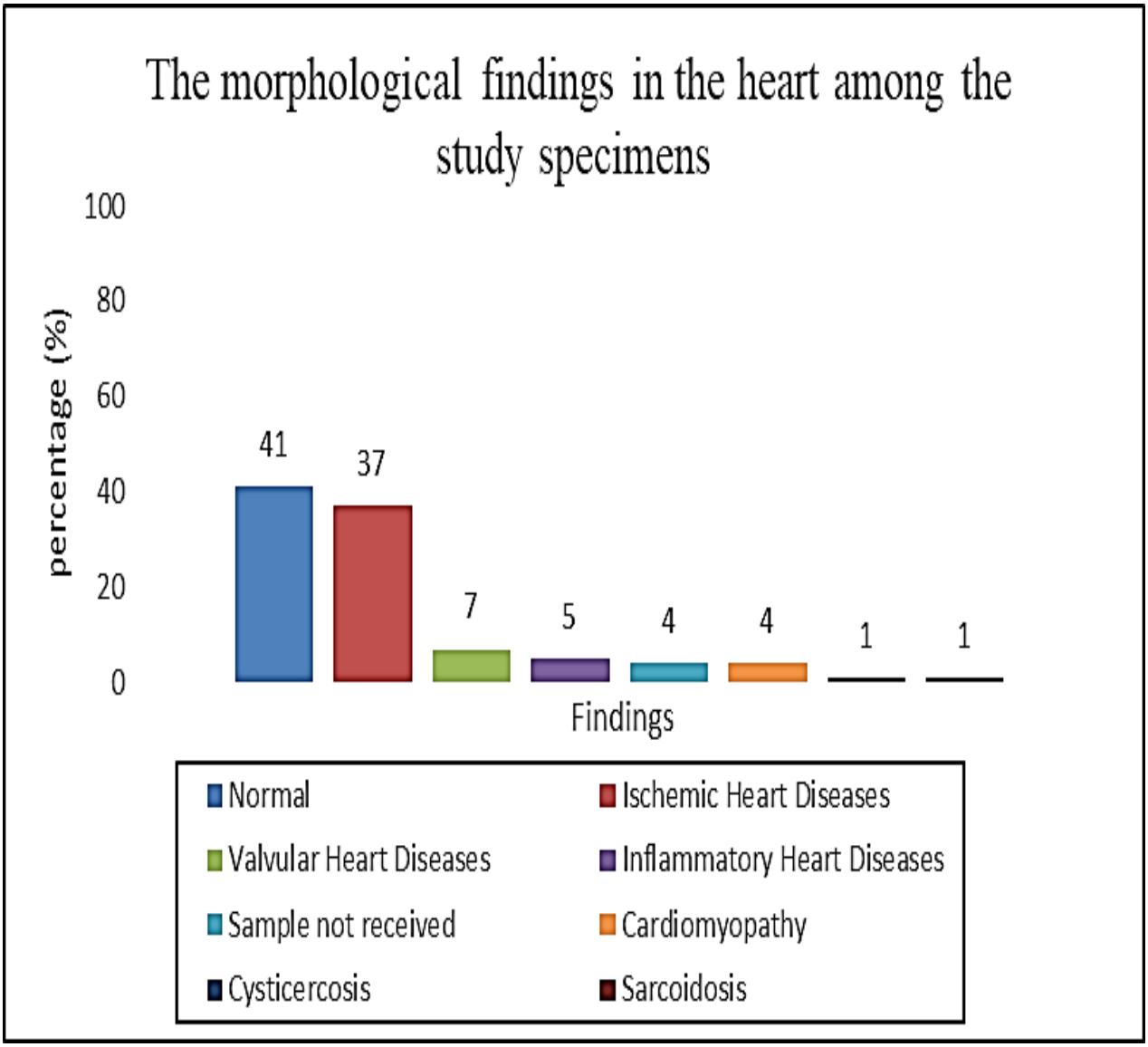


TABLE 4 HISTOPATHOLOGICAL FINDINGS IN LUNG

Findings	**Frequency(n)**	**Percentage(%)**
Congestion	48	48
Pulmonary edema	17	17
Normal	9	9
Sample not received	9	9
PTB	4	4
Pneumonia	3	3
CVC	2	2
Metastasis	2	2
Interstitial pneumonia	1	1
Aspiration pneumonia	1	1
cholesterol granuloma	1	1
DAD	1	1
Emphysema	1	1
Leukemic infiltration	1	1

Noncardiac causes of sudden death were mostly due to pulmonary diseases(11%) followed by intracranial causes(13%). Other noncardiac causes were hepatobiliary causes (6%), renal causes(1%),pancreatic causes(3%) and metastatic deposits(3%).In 7% of causes , the cause of death could not be ascertained even after detailed histopathological examination.

TABLE 5 HISTOPATHOLOGICAL FINDINGS IN LIVER

Findings	**Frequency(n)**	**Percentage(%)**
Congestion	51	51
Normal	25	25
Sample not received	9	9
Cirrhosis	6	6
Fatty liver	5	5
Metastasis	2	2
Hydatid cyst	1	1
Leukemic infiltration	1	1

TABLE 6 CAUSES OF SUDDEN DEATH IN YOUNG ADULTS AGED 15 TO 45 YEARS

Causes of sudden unexpected death	Frequency(n)	Proportions(%)
Cardiovascular	55	55
CNS	13	13
Respiratory	11	11
GIT	9	9
Uncertained causes	7	7
Metastasis	3	3
Reticuloendothelial	1	1
Renal	1	1

CHART 4 PIECHART SHOWING CAUSES OF SUDDEN DEATH IN YOUNG ADULTS AGED 15 TO 45 YEARS

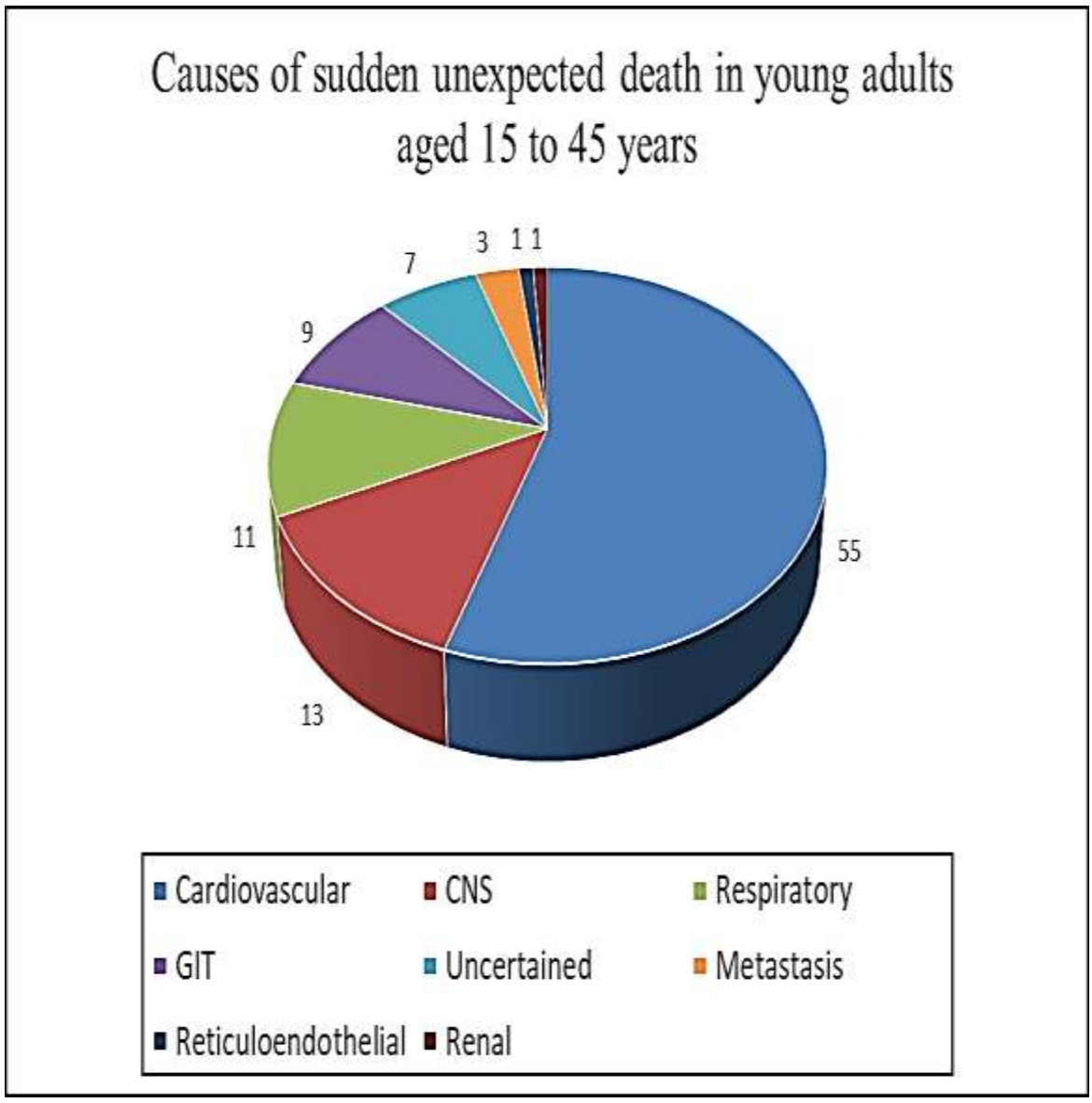


TABLE 7 ASSOCIATION BETWEEN SEX AND HISTOPATHOLOGICAL FINDINGS IN HEART

Association

Gender	**Cardiac pathology**		**Total**	***P value* ***
	Abnormal	**Normal**		
Male	49	25	74	0.001
Female	6	16	22	
Total	55	41	96	

*Chi-square test

TABLE 8 ASSOCIATION BETWEEN AGE AND HISTOPATHOLOGICAL FINDINGS IN HEART

Age group	**Cardiac pathology**		**Total**	***P value* ***
	Abnormal	**Normal**		
15-30	17	11	28	0.664
31-45	38	30	68	
Total	55	41	96	

*Chi-square test

TABLE 9 ASSOCIATION BETWEEN SEX AND ATHEROMATOUS PLAQUES

Gender	Atheromatous plaque		Total	*P value* *
	present	absent		
Male	46	27	73	0.010
Female	7	15	22	
Total	53	42	95	

*Chi-square test

TABLE 10 ASSOCIATION BETWEEN AGE AND ATHEROMATOUS PLAQUES

Age group	Atheromatous plaque		Total	*P value* *
	Present	absent		
15-30	10	18	28	0.011
31-45	43	24	67	
Total	53	42	95	

*Chi-square test

TABLE 11 COMPARISON OF THE INCIDENCE AND PERCENTAGE OF VARIOUS CAUSES OF SUDDEN DEATH OBSERVED IN PRESENT STUDY WITH THAT OBSERVED IN OTHER STUDIES

Parameters	Pandian et al (2014)	Chaturvedi et al (2011)	Present study (2019)
Age (years)	17 -70	18-35	15-45
Duration of study	13	9	1.5
Total cases	120	64	100
Males:Females	6.5:1	3.4:1	3.5:1
Cardiac	67(55.83%)	5(7.8%)	55(55%)
Respiratory	20(16.67%)	8(12.5%)	11(11%)
CNS	4(3.33%)	8(12.5%)	13(13%)
GI,Liver,Pancreas, Renal,Spleen	19(15.77%)	17(26.6%)	10(10%)
Febrile illness	10(8.4%)	14(21.8%)	Not discussed
SADS	Not discussed	12(18.8%)	Not discussed

STATISTICAL ANALYSIS

The data were reported as the mean +/- SD depending on their distribution.

Frequencies were expressed in percentages.

The Chi square test was used to assess difference in categoric variables between gropus.

A p value of <0.05 was taken as being of significance for all statistical tests. All data were analyzed with a statistical software package. (SPSS,version 16.0 for windows)

COLOUR PLATES

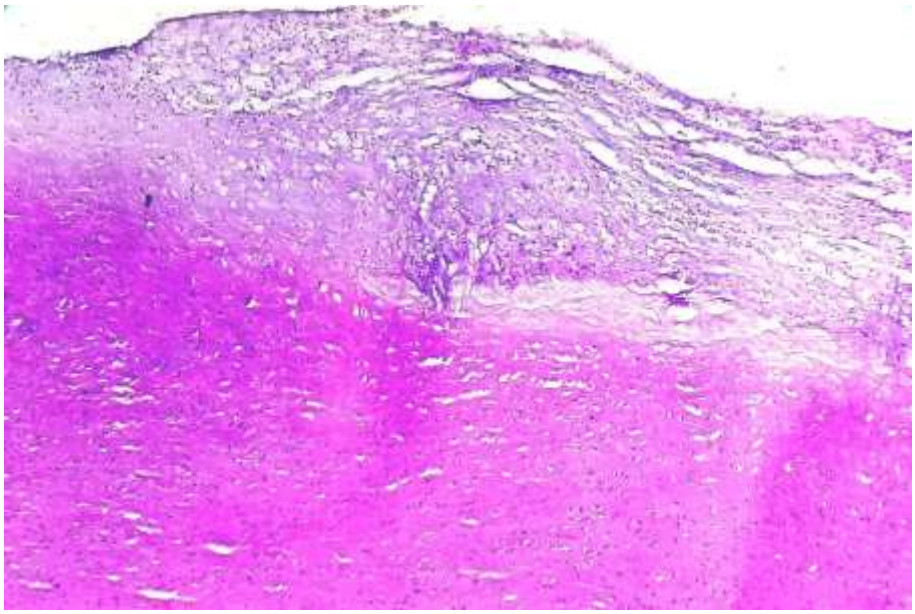


FIG 1A H&E :ATHEROMATOUS PLAQUE(40X)

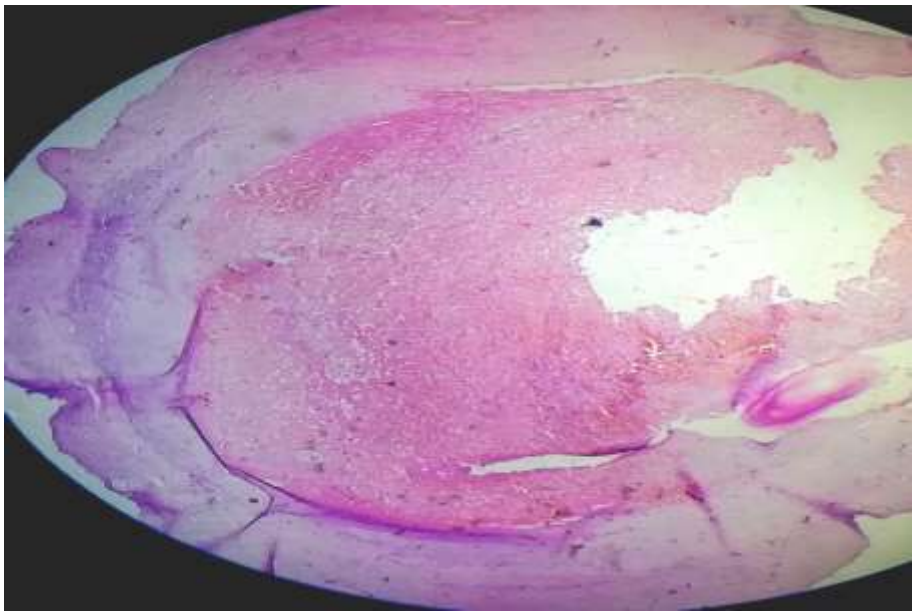


FIG 1B H&E: ORGANIZING THROMBUS(SCANNER VIEW)

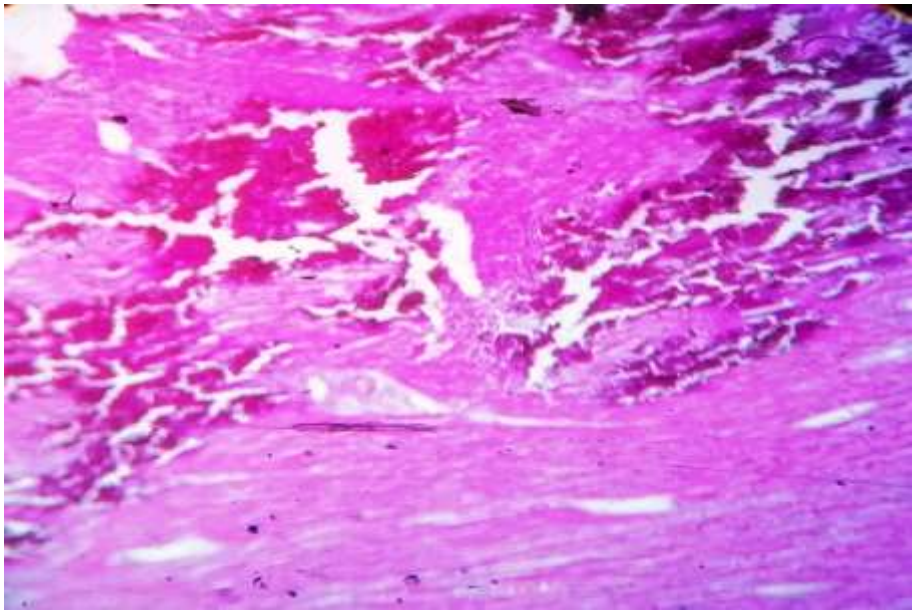


FIG 1C H&E :AORTIC CALCIFICATION(40X)

FIG 2A GROSS:ACUTE MYOCARDIAL INFARCT OF LEFT VENTRICLE AND INTERVENTRICULAR SEPTUM

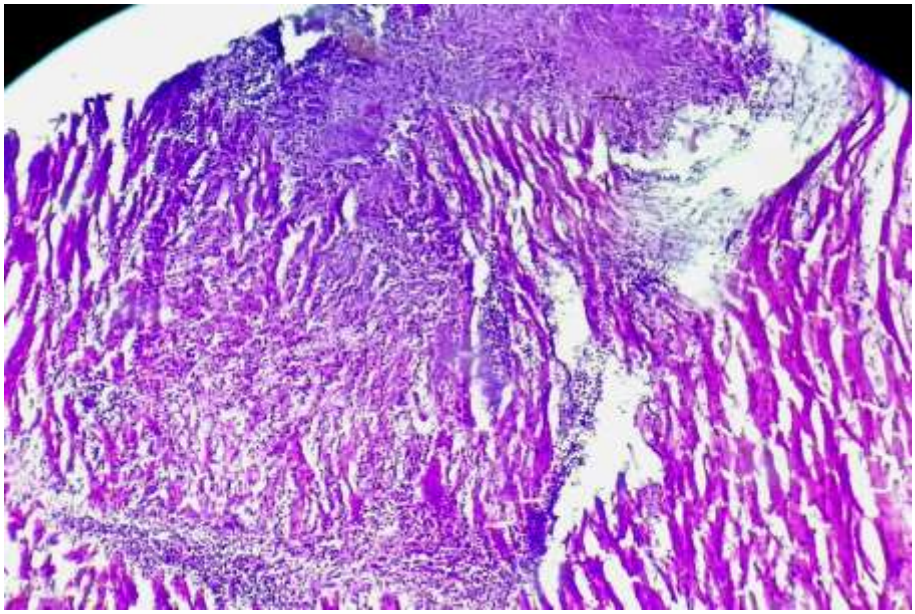


FIG 2B H&E ACUTE MYOCARDIAL INFARCTION(10X)

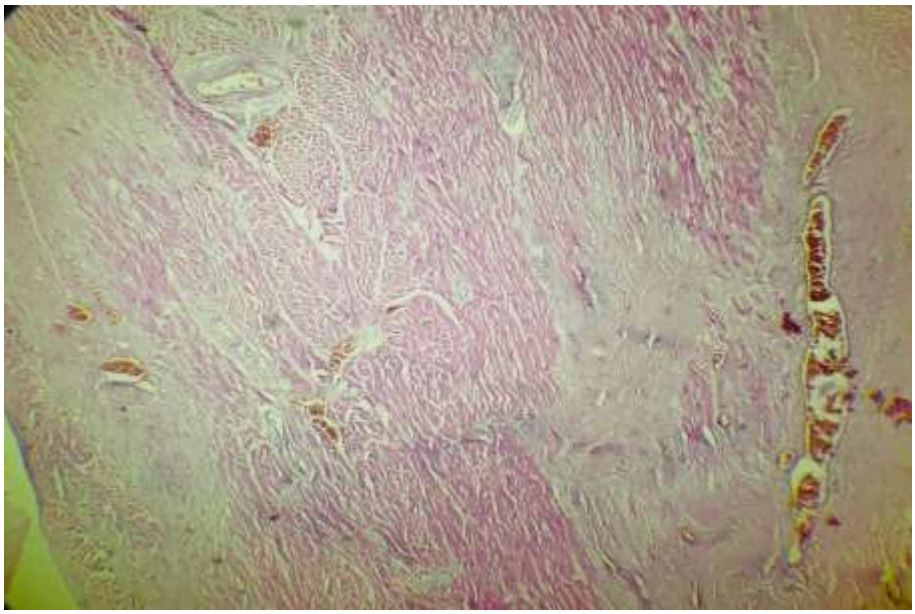


FIG 2C H&E HEALED MYOCARDIAL INFARCTION(10X)

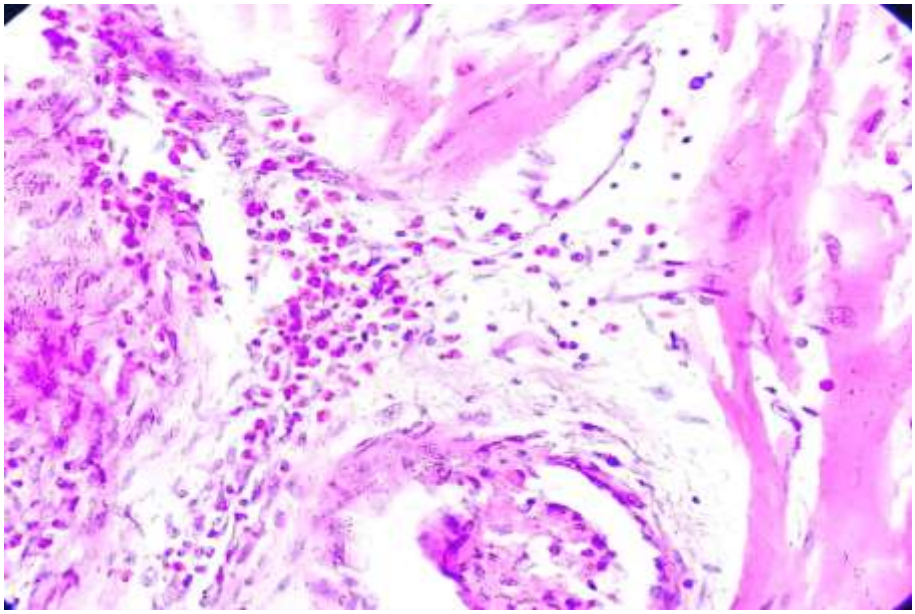


FIG 3 H&E - EOSINOPHILIC MYOCARDITIS(40X)

FIG 4A H&E CARDIAC SARCOIDOSIS (GROSS)

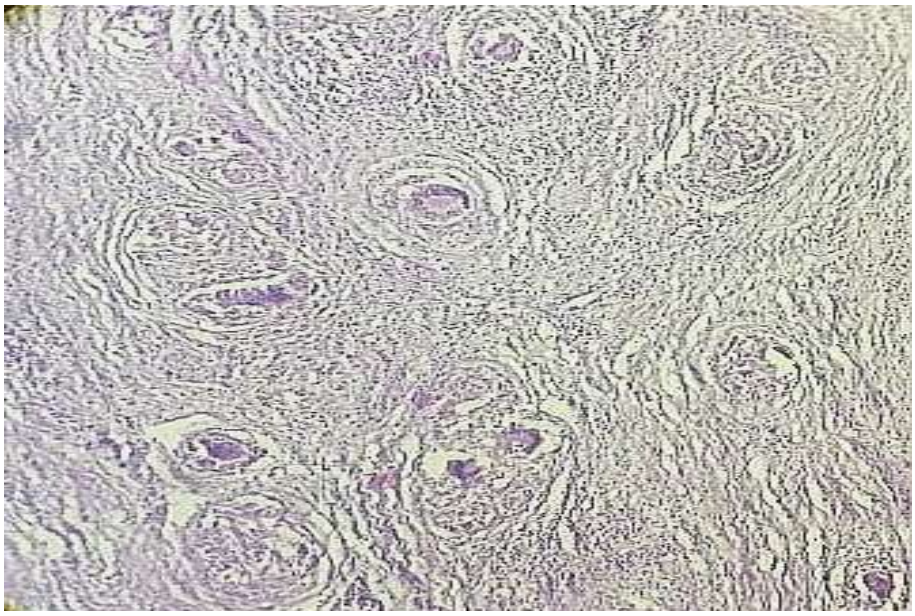


FIG 4B H&E CARDIAC SARCOIDOSIS(10X)

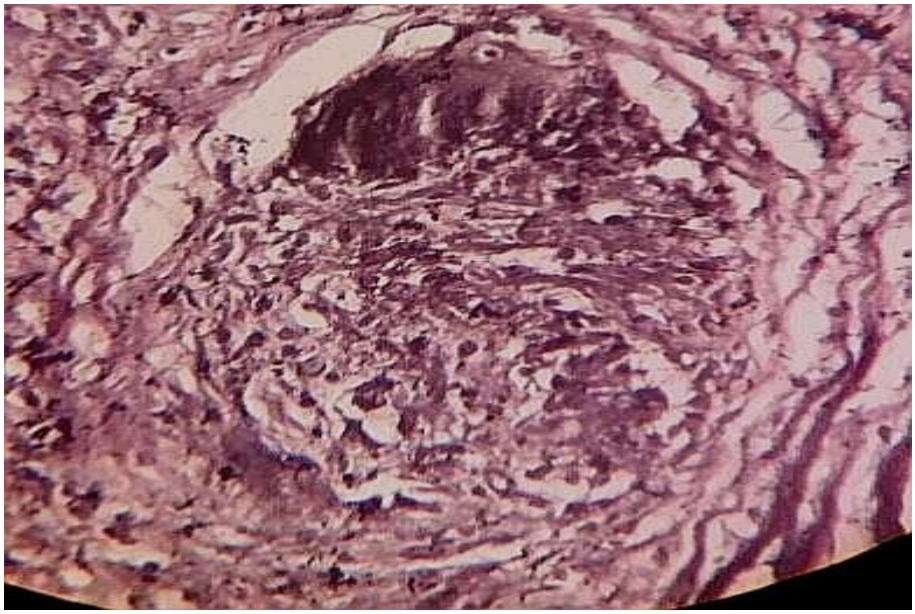


FIG 4C RETICULIN STAIN: CARDIAC SARCOIDOSIS:INTACT BLACK RETICULIN FIBERS IN AND AROUND GRANULOMAS (40X)

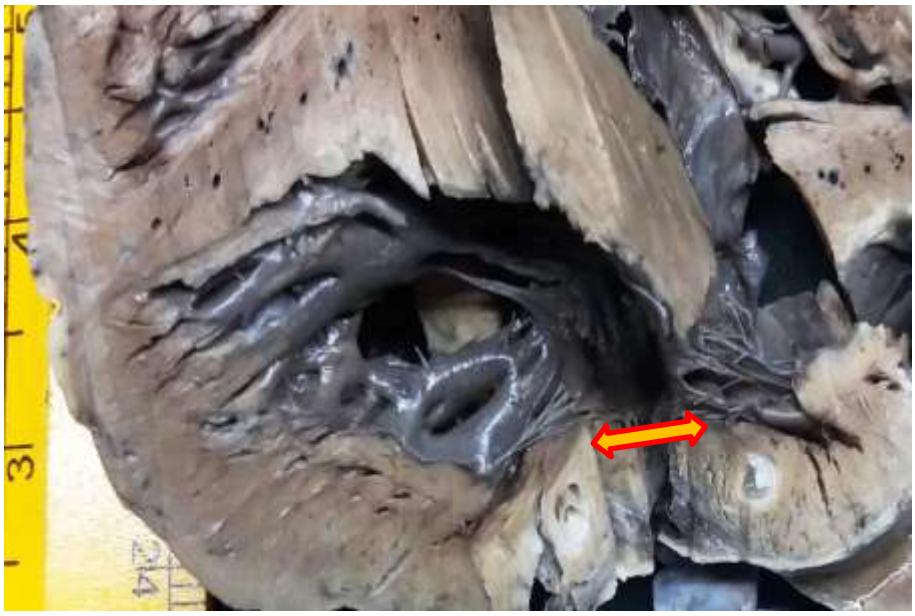


FIG 5A CYST IN THE WALL OF LEFT VENTRICLE (CYSTICERCOSIS)

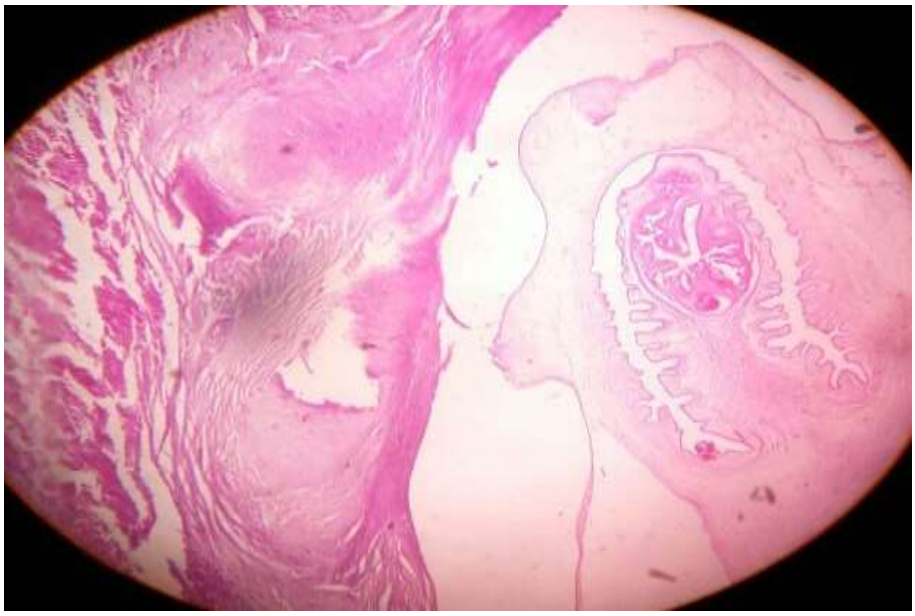


FIG 5B H&E: IRREGULARLY SHAPED MEMBRANOUS FOLDINGS LIKE MICROVILLI AND SCOLICES REPRESENTING CYSTICERCUS LARVAE IN CARDIAC MUSCLE (10X)

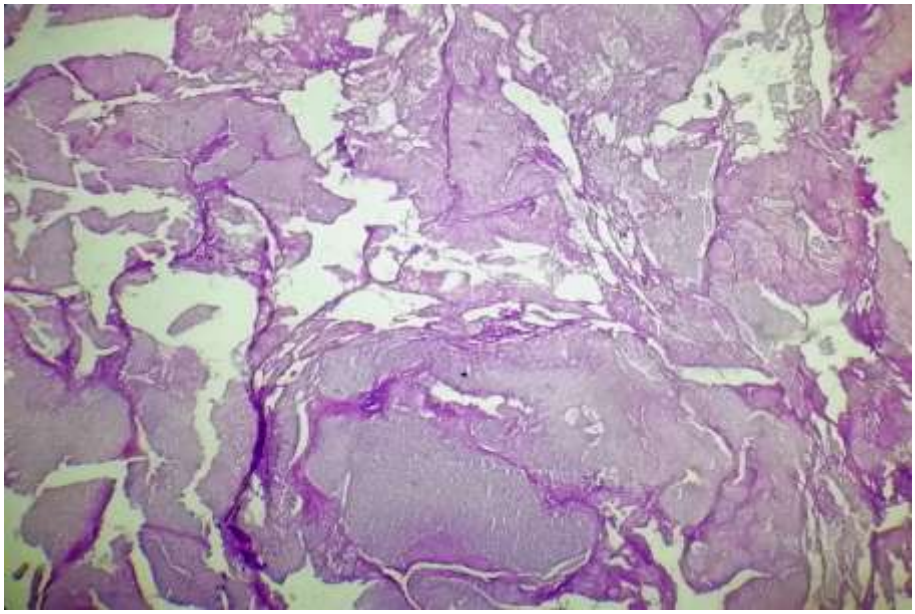


FIG 6AH&E: INFECTIVE ENDOCARDITIS(10X)

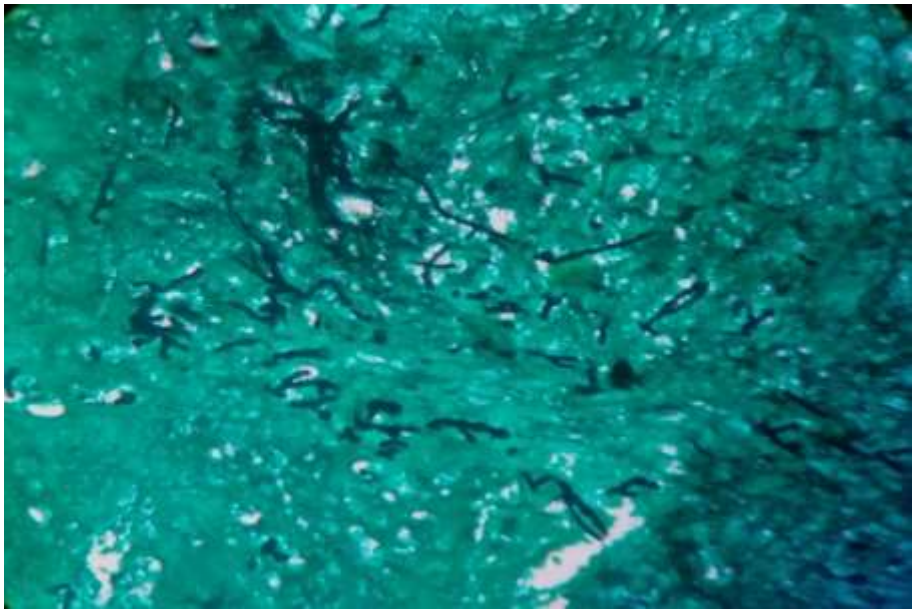


FIG 6B GMS SHOWS SEPTATE HYPHAE WITH ACUTE ANGLE BRANCHING CONSISTENT WITH ASPERGILLUS IN INFECTIVE ENDOCARDITIS(10X)

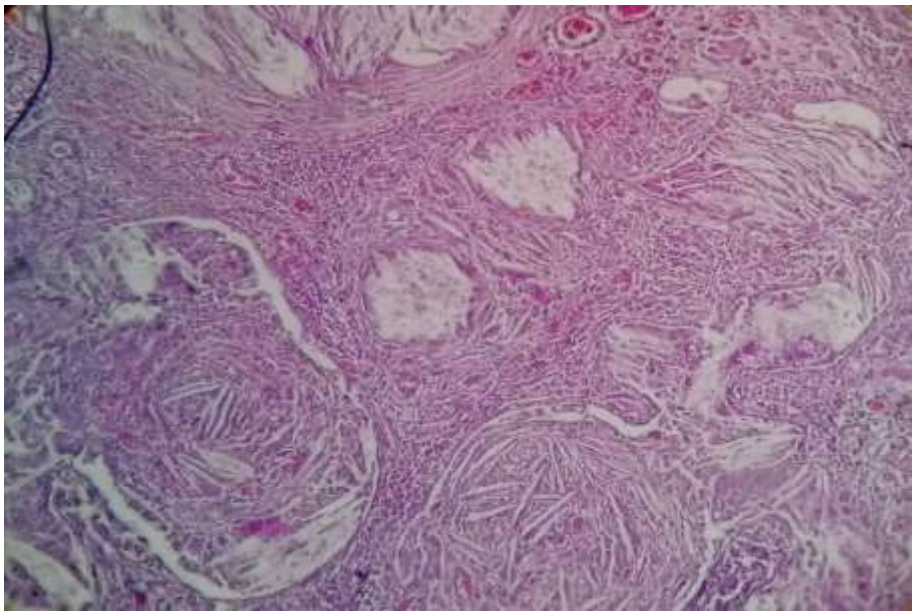


FIG 7 H&E :CHOLESTROL GRANULOMA(10X)

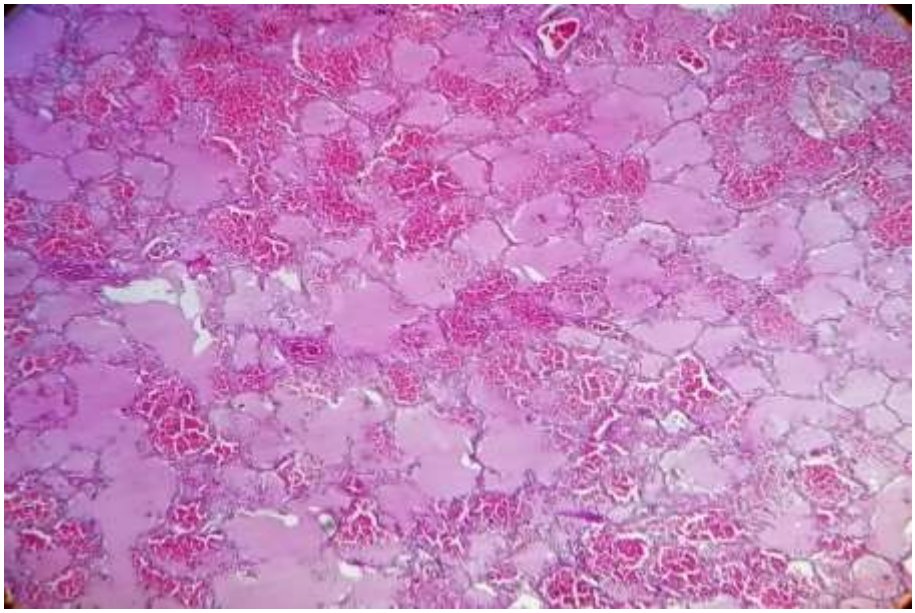


FIG 8 H&E: PULMONARY EDEMA(10X)

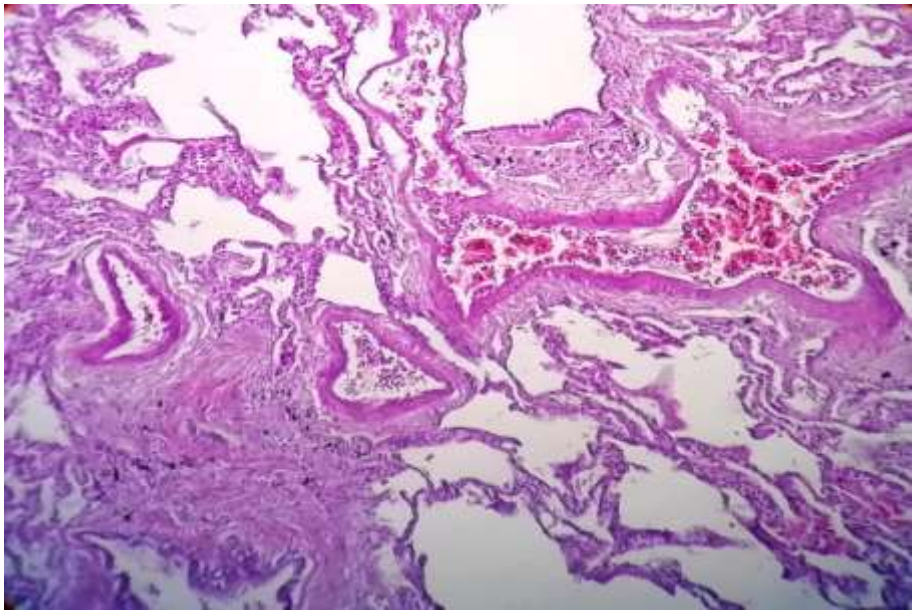


FIG 9 H&E:DIFFUSE ALVEOLAR DAMAGE(10X)

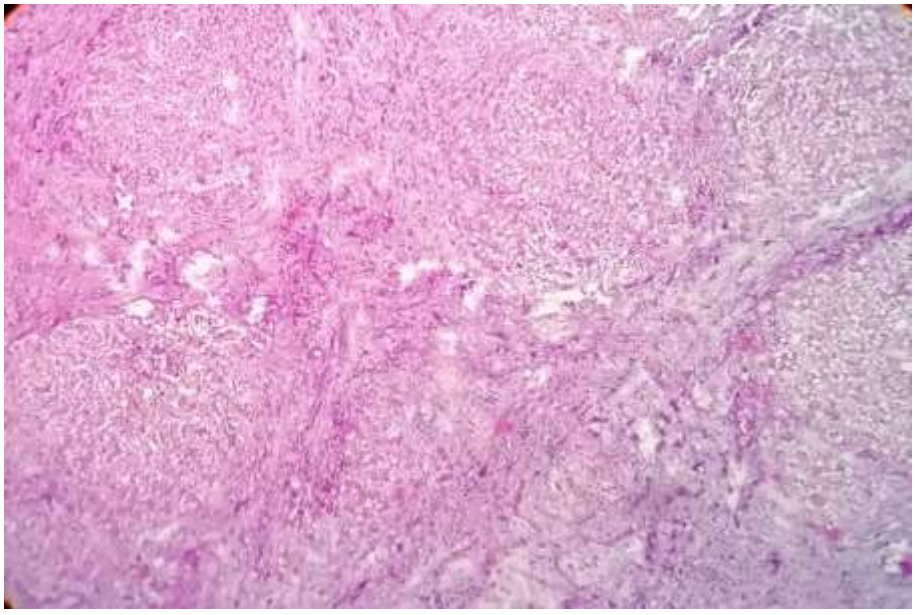


FIG 10 H&E:CIRRHOSIS(10X)

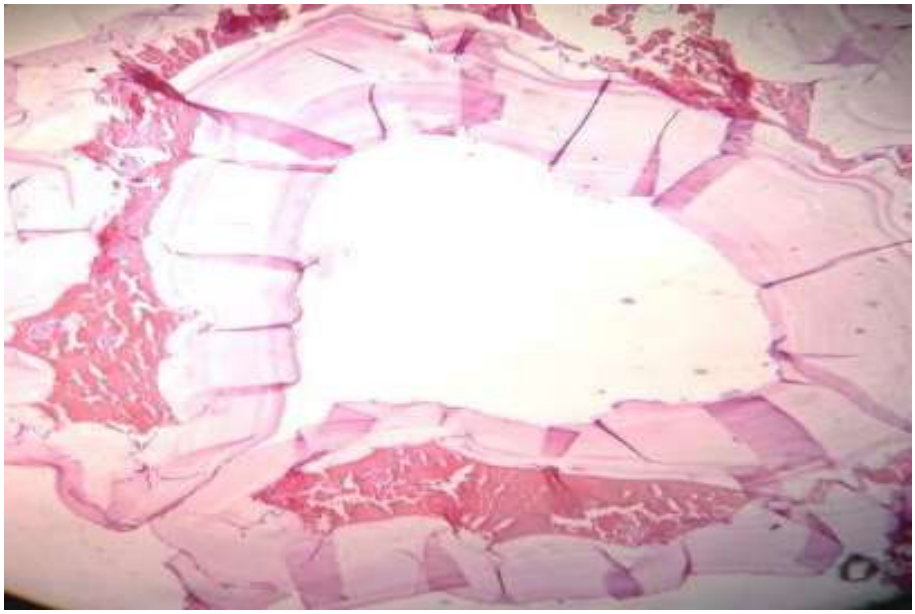


FIG 11 H&E:HYDATID CYST(10X)

FIG 12A MEDULLARY SPONGE KIDNEY (GROSS)

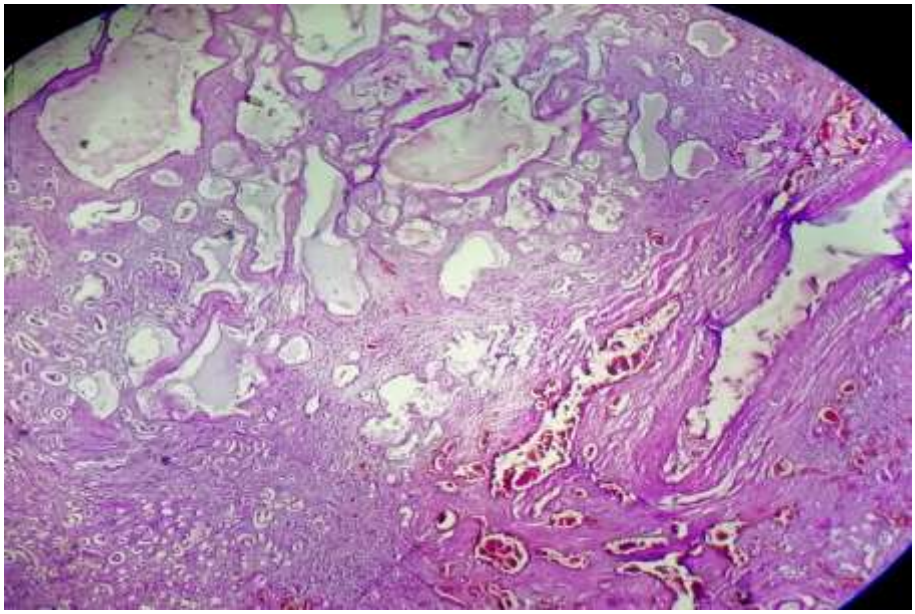


FIG 12B H&E:MEDULLARY SPONGE KIDNEY(10X)

FIG 13A DIAPHGRAMATIC EVENTRATION OF SPLEEN

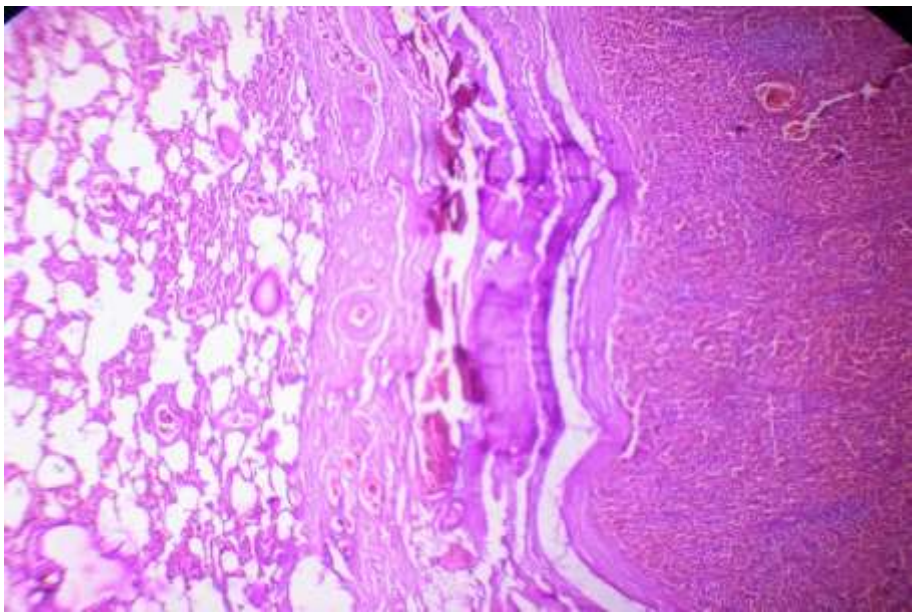


FIG 13B H&E:DIAPHRAGMATIC EVENTRATION OF SPLEEN(10X)

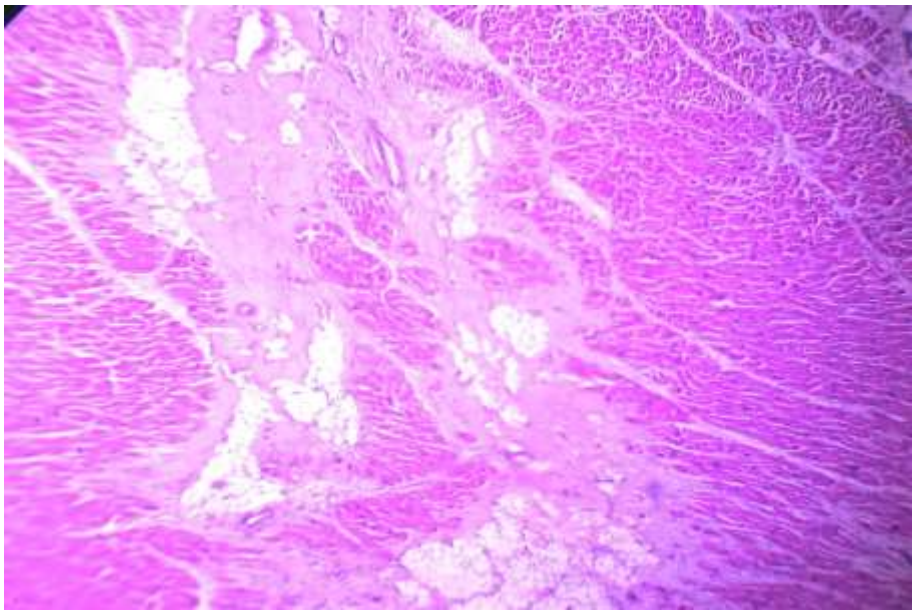


FIG 13C H&E: LIPOMATOUS METAPLASIA OF HEART IN DIAPHRAGMATIC EVENTRATION OF SPLEEN (10X)

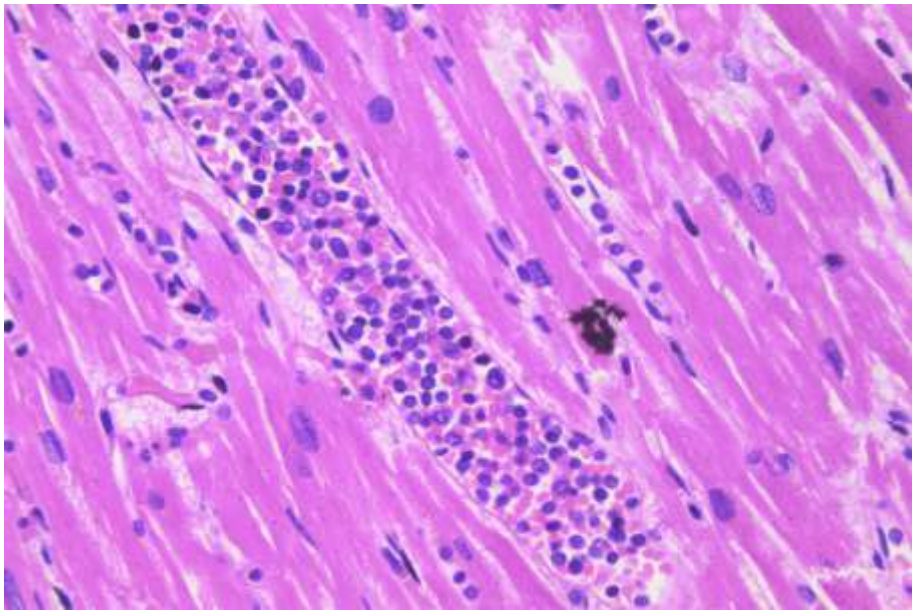


FIG 14A H&E:LEUKEMIC INFILTRATION OF HEART(10X)

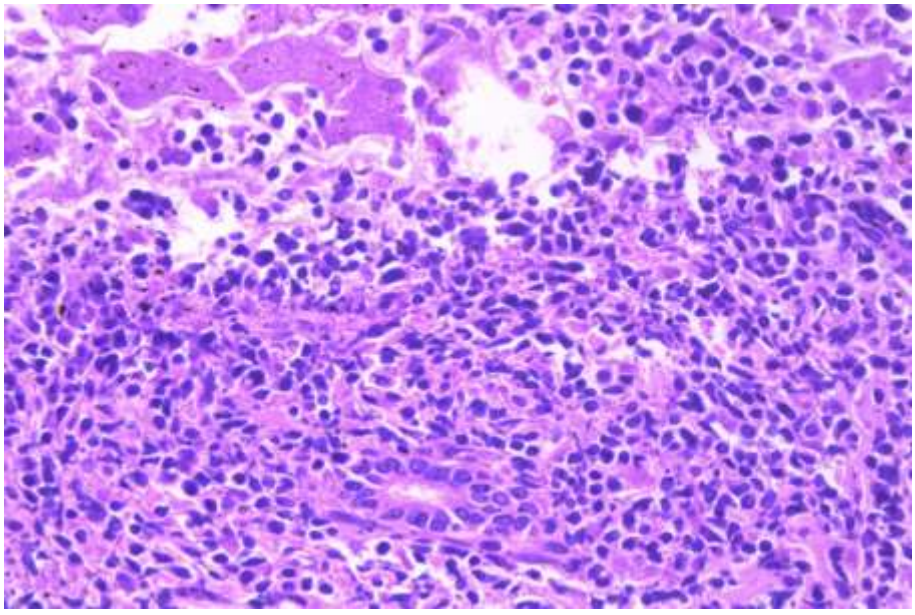


FIG 14B H&E: LEUKEMIC INFILTRATION OF LIVER (10X)

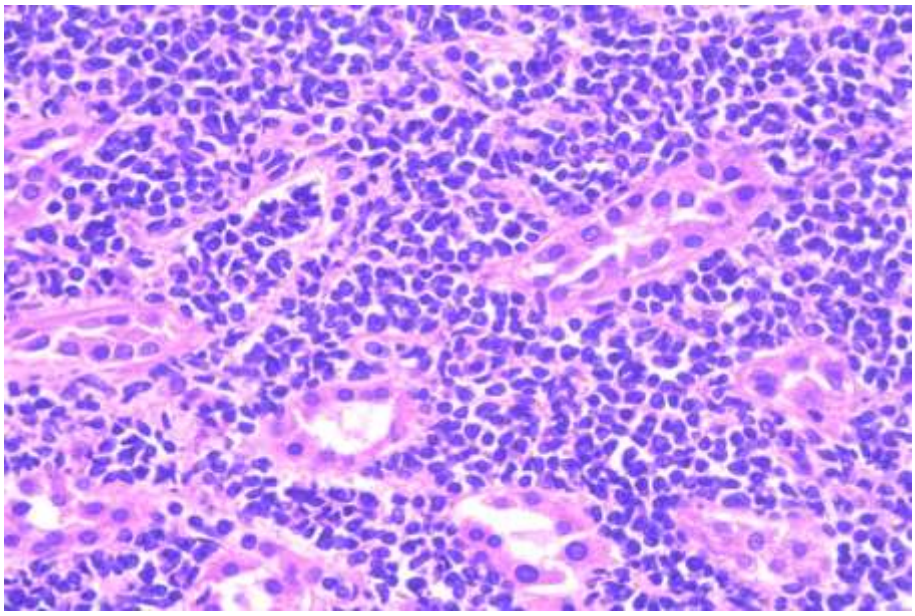


FIG 14C H&E: LEUKEMIC INFILTRATION OF KIDNEY (10X)

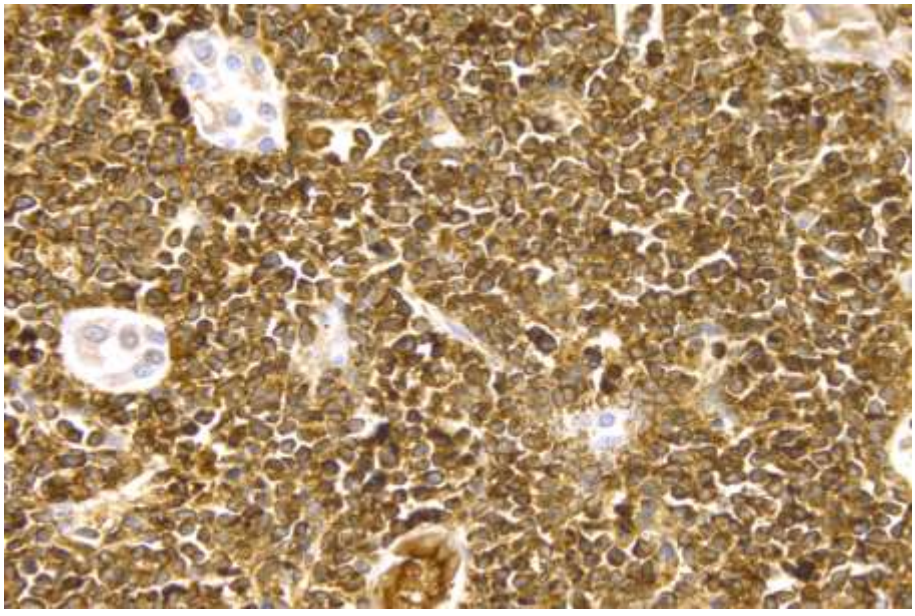


FIG 14D IHC: CD10 DIFFUSE STRONG POSITIVITY IN LEUKEMIC INFILTRATION (10X)

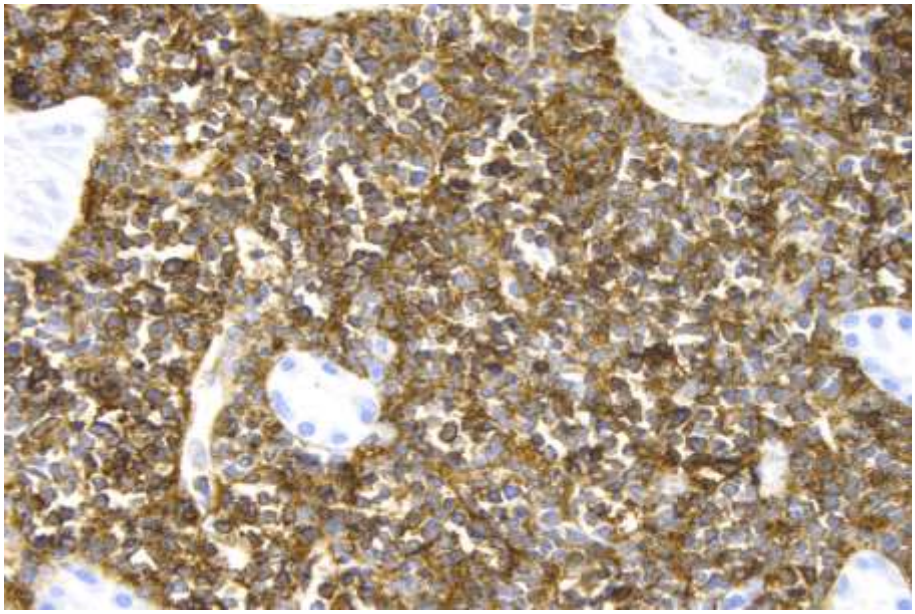


FIG 14E IHC:CD20 DIFFUSE STRONG POSITIVITY IN LEUKEMIC INFILTRATION(10X)

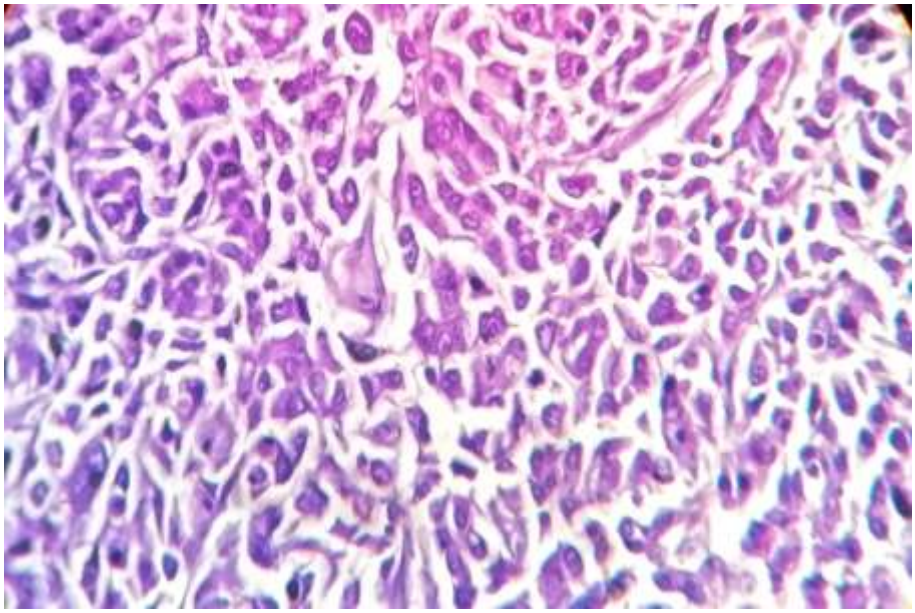


FIG 15 H&E: METASTATIC DEPOSITS IN LUNG FROM BREAST CARCINOMA(10X)

DISCUSSION

DISCUSSION

Sudden death means that the death was caused entirely by the disease and any unnatural events (trauma, poison, etc.,) did not play any part in causation. Outsiders may think that the death has occurred in a sudden and unexpected manner but actually it is not like that according to pathological disease process. The deceased may be asymptomatic or may be unaware of the disease. The deceased may neglect the disease because of fear or low socioeconomic status.

In the present study age ranged from 15 to 45 years ,41-45 years (35%) was the most common age group involved. While Kasthuri et al[41] reported most cases in 31-40 years and a study conducted by Sonawane et al[48] had 41-50 years as the most common age group.

Males were predominantly affected than females. This is in accordance with the study conducted by Kasthuri et al[41].

Cardiovascular pathology(55%) is the most common cause of sudden death. These results were comparable to the study conducted by Farb et al.[40] In the present study, myocardial infarction was observed in 37% of cases. Acute myocardial infarction was the predominant type of myocardial infarction seen in 22 out of 100 cases followed by old healed myocardial infarction in 15 out of 100 cases.

Atheromatous plaques in coronary arteries were noted in 55% of cases. Atheromatous plaque is the main culprit in causing MI. Almost

90% of MI cases revealed atheromatous plaques in aorta and coronary ostium. Of these 3 cases showed organizing thrombus and 3 cases showed critical narrowing (70%) with light microscopic evidence of myocardial infarction in 2 cases. This was comparable to the study conducted by Sree Lakshmi et al[46].Microscopically organizing thrombus showed multiple laminations consisting of platelets and fibrin alternating with layers of RBC (Lines of Zahn).

Non atherosclerotic conditions associated with sudden death include myocarditis (5%),cardiomyopathy(2%)(dilated cardiomyopathy-1, hypertrophic cardiomyopathy-1), valvular heart disease(7%) which was comparable to the study conducted by Ladich et al[43].

Hypertrophic cardiomyopathy presents with heart weighing more than 500 gms. Microscopically myocyte disarray, myocyte hypertrophy with transverse myocyte diameter more than 40 µm and interstitial fibrosis were noted. Sudden death in this case may be due to rhythm disturbances. Endomyocardial fibrosis was observed in 2 cases. Grossly both the atrium were dilated and thickening of the ventricular endocardium noted. Microscopically fibrosis(due to collagen fibers) of the ventricular endocardium and subendocardium noted. Special stains like verhoeff's vangieson stain and masson trichome stain were done which confirmed the diagnosis.

We reported a 42 year old male death due to Mitral valve prolapse. Grossly left atrial dilatation made out with hooding and prolapse of the mitral leaflet into the left atrium.Microscopically there was marked thickening of the spongiosa layer with deposition of mucoid material and attenuation of collagenous fibrosa layer and disorganization of elastin in the atrialis layer.In mitral valve prolapse the mitral valve leaflets prolapse into the left atrium during systole.It usually affects adult females.

We reported a 19 year old male death due to calcific Aortic stenosis. Grossly nodular masses of calcium were seen heaping up within the sinuses of valsalva and the commissures were fused.Left ventricular hypertrophy noted. Microscopically calcification was noted in the valvular fibrosa (outflow surface of the valve).There was mild chronic inflammatory cell infiltrate with osseous metaplasia. Aortic stenosis can be due to age associated wear and tear of either normal valve or congenital bicuspid valve or may be due to postinflammatory scarring(rheumatic heart disease).

Aortic dissection was observed in one of the case (40 year old male).Grossly the heart weighed 350gms and a 1.5 cm oblique intimal tear and intramural hematoma made out in the ascending aorta. Microscopically blood filled channel made out in the media without any inflammation. There was no evidence of cystic medial degeneration. Aortic dissection occurs when blood enters the vessel wall and separates

its layers. The risk factors include hypertension, atherosclerosis, cardiac surgery, connective tissue disorders(Marfan's syndrome, Ehler Danlos syndrome) and syphilis. It is classified into two types.Type A dissection(proximal) involving either ascending and descending aorta or just the descending aorta (type I and II of Debakey classification).Type B(distal) not involving ascending aorta and begins distal to subclavian artery(Type III of Debakey classification).The cause of death is due to rupture of the dissection into the body cavities(pleural, pericardial or peritoneal cavities).

We reported 2 deaths due to Aortic aneurysm and one due to Aortitis.

Infective endocarditis was observed in two cases. In one of the case, grossly large grey white firm vegetation was seen attached to atrial aspect of AV valve extending into adjacent cusp. Microscopically vegetation consist of fibrin, platelets and colonies of fungal organism within necrotic material.Gomori methenamine silver stain revealed septate hyphae branching at 45 degrees (ASPERGILLUS).The deceased had splenic infarct due to the embolus from vegetations.

We reported a 22 year old male death due to cardiac cysticercosis. Cysticercosis is due to ingestion of ova of pork tapeworm (Taenia solium). Ingested ova hatch in alimentary tract , penetrates small intestine and disseminate hematogeneously to various organs like CNS, skeletal

muscle, eyes and skin[96]. Grossly the heart weighs 425 gms and external surface is unremarkable. Cut surface revealed a small cyst of size 0.8cm with focal grey white area in left ventricular wall. Microscopically Cysticercosis larva with irregularly shaped membranous foldings and scolices are seen in cardiac muscle.

One of the decedent (44 year old male) had cardiac sarcoidosis. Grossly grey white fibrotic areas noted in the endocardium ,myocardium and epicardium. Microscopically nonnecrotizing epithelioid cell granulomas, langhans giant cells are noted. Reticulin stain showed network of intact black reticulin fibers in and around the granulomas. Sarcoidosis is a granulomatous disease of unknown etiology. Cardiac sarcoidosis is more fatal.

Pulmonary causes contributed 11 deaths of all sudden deaths. The main causes were tuberculosis(4%) and pneumonia (5%). These results were comparable to the study conducted by Prateek Rastogi et al[74].

One of the decedent revealed after thorough examination vegetable matter within bronchi and bronchioles with adjacent pneumonitis. This is in accordance with the study conducted by Chia-Yu-Chang et al.[55]

We reported a 41 year old male death due to emphysema. Grossly upper part of lung showed dilated airspaces surrounded by relatively spared alveolar spaces. Microscopically abnormal large alveoli are separated by thin septa with focal fibrotic changes.

Pulmonary edema was observed in 17 cases and Chronic venous congestion in 2 cases.

Histopathological examination of a 35 year old male resected lung showed cholesterol granulomas consisting of interstitial and alveolar fibrotic lesions containing needle like cholesterol clefts, foreign body giant cells and scattered lymphocytes.Pulmonary cholesterol granulomas are uncommon findings found in lipoid pneumonia, alveolar proteinosis or as an incidental autopsy finding in severe pulmonary artery hypertension. Since we don't know the previous history, the chest radiographs and CT reports of the decedent, we were not able to find out the actual cause for this cholesterol granuloma.

We reported a 31 year old female death due to Diffuse alveolar damage. Grossly the lungs were red heavy and boggy. Microscopically some of the alveoli are collapsed and some are distended. The alveolar walls are lined by hyaline membrane consisting of fibrin rich edema fluid and remnants of necrotic epithelial cells. There is a sparse interstitial inflammatory cell infiltrate and hyperplasia of pneumocytes.

Hepatobiliary diseases account for 6% deaths of all sudden deaths.Severe hepatic steatosis was the major cause. This was comparable with the study conducted by Rosmorduc et al[82]. Fatty liver was observed in 5 cases.

We reported a 40 year old male death due to hydatid cyst. Hydatid disease is caused by the larval or cystic stage of **Echinococcus granulosus**. After ingestion ,the eggs hatch and the larval oncospheres pass to the liver by the portal vein and form spherical hepatic cyst.[97]It also affects brain and lungs. Histologically the cyst wall shows an outer chitinous (laminar) layer and an inner germinal layer. The cyst wall may be surrounded by either granulation tissue or a fibrous capsule (‘pericyst layer’)[97].Dead cysts has calcification in the pericyst layer. The adjacent liver parenchyma shows portal infiltrate rich in eosinophils. The viable cyst contains daughter cysts and brood capsules with scolices with hooklets of 20–40 μm length. It has communication with the biliary tract.

One of the decedent(35 year old female) had papillary renal cell carcinoma. Grossly kidney showed multifocal tan yellow friable tumour with areas of hemorrhage and necrosis. Microscopically kidney showed a malignant neoplasm composed of papillary structures lined by columnar cells with few papillae having foamy macrophages .Vascular invasion by the tumour is noted.The papillary renal cell carcinoma is thought to arise from distal convoluted tubules and the cytogenetic abnormalities are trisomies 7,17 and loss of Y chromosome. The deceased had metastatic carcinomatous deposits in lung and liver.

A 20 year old female on ayurvedic drugs had sudden death due to Acute tubular necrosis. Acute tubular necrosis is characterized by acute

renal failure and it is due to ischemia or toxicity from endogeneous (myoglobin,haemoglobin,monoclonal light chains etc.,) or exogeneous agents (drugs, dyes,metals etc.,).Microscopically there will be tubular epithelial necrosis and occlusion of tubular lumen by cast.

Medullary sponge kidney was observed in one case (26/M).It is a sporadic cystic disease in adults characterized by bilateral cystic dilatation of medullary collecting ducts with normal cortex. Grossly multiple small cysts in medullary pyramids and papillae giving medulla sponge like appearance. Microscopically the cysts are lined by cuboidal epithelium or urothelium.

Sudden death due to neurological diseases account for 13 deaths.

The main cause of death was due to cerebrovascular accident (7 deaths due to intracranial hemorrhage and 3 due to subarachnoid hemorrhage). Meningitis was noted in 2 cases and encephalitis in one case.

Sudden death due to pancreatic disorders (acute pancreatitis) account for 3 deaths. This was comparable to the study conducted by Tsokos et al.[86]

We reported a 34 year old male death due to diaphragmatic eventration of spleen. Grossly heart showed left ventricular hypertrophy and white fibrous areas in left ventricle and interventricular septum. Thinned out diaphragm was seen adherent to spleen and left lung.

Microscopically cardiac myocytes were hypertrophied with lipomatous metaplasia in left ventricle and interventricular septum.Diaphragm adherent to spleen and lung showed atrophy and was replaced by fibrocollagenous tissue with scattered preserved muscle fibers. The diaphragmatic eventration is the total or partial replacement of the diaphragm muscle fibroblastic tissue ,causing displacement of the hemidiaphragm affected to chest. It affects less than 0.05% of the population ,both children as well as adults and is more common in males. Unilateral involvement is more common than the bilateral. It can be congenital or acquired (phrenic nerve palsy, birth canal compression).The condition is usually asymptomatic but may be the cause of progressive dyspnea and frequent respiratory infections.[98,99]

Metastatic deposits were being the cause of death in 3 cases.

A 23 year old male without any past significant medical history had sudden death. Grossly heart, lung, liver and kidney revealed grey white areas. Microscopically medium to large sized blasts with scant cytoplasm, high N:C ratio, coarse chromatin and 1 to 2 prominent nucleoli were identified in heart, lung, liver and kidney. Immunohischemical stains were done. CD10 and CD20 showed diffuse strong positivity.CD3 was negative. Ki67 (MIB1) showed 20% positivity. Immunohistochemical stains confirmed the diagnosis of B-ALL(Acute lymphoblastic leukemia) infiltration.

Even after detailed histopathologic examination the cause of death could not be ascertained in 7 deaths.

LIMITATIONS OF THE STUDY:

- Although our hospital was in urban area, there were many patients from rural areas nearby. Many of our patients were illiterate and were therefore unaware of the importance of autopsy. Hence many of the sudden deaths goes unreported.
- Since we could not examine organs in fresh state, diseases like pulmonary embolism would have been missed.
- We were not able to detect death due to septicaemia because septic screen culture in body fluids is not possible

SUMMARY & CONCLUSION

SUMMARY

- This study was conducted in the Department of Pathology, Government Medical College Coimbatore.
- The study was done on autopsied specimens of adults aged 15 to 45 years who died suddenly
- A total of 100 cases were studied. Among those cases,78 were males and 22 were females.
- Maximum number of deaths were seen in fourth decade(35%) followed by third decade(24%).
- Cardiovascular pathology (55%)is the most common cause of sudden death in adults.
- Major cardiac cause for sudden death was myocardial infarction (37%).
- Noncardiac causes of sudden death were mostly due to intracranial diseases (13%) followed by pulmonary causes(11%).
- Other noncardiac causes were hepatobiliary causes (6%), renal causes(1%),pancreatic causes(3%) and metastatic deposits(3%).
- The cause of death could not be ascertained even after detailed histopathological examination in 7 cases.

CONCLUSION

Sudden death in adults is an issue of concern and a meticulous post-mortem and histopathological examination is necessary to ascertain its cause. In the present study cardiac causes contributed the major cause of sudden death in adults posing a health concern in our society. Atherosclerosis is the main culprit in causing myocardial infarction. The purpose of the study is to bring attention the various treatable causes of sudden death so that we can reduce the mortality rate. There are many diseases which may remain subtle and yet cause sudden death which will be detected by thorough dissection and examination of organs. Awareness regarding the risk factors, preventive measures, lifestyle modifications and interventions should be made available by the heathcare professionals.

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ANNEXURES

ANNEXURE I

PROFORMA

NAME OF THE DECEASED:

AGE OF DECEASED :

SEX OF DECEASED :

RESIDENCE :

DATE OF DEATH :

PLACE OF DEATH :

FM HPE NO : DATE:

PM NO : DATE:

PAST HISTORY :

GROSS FINDINGS :

HPE FINDINGS :

ANNEXURE II

ABBREVIATION

1.MI	-MYOCARDIAL INFARCTION
2.AV	-ATRIOVENTRICULAR
3.DCM	-DILATED CARDIOMYOPATHY
4.CD	-CLUSTER OF DIFFERENTIATION
5.PDGFRA	-PLATELET DERIVED GROWTH FACTOR ALPHA
6.MVP	-MITRAL VALVE PROLAPSE
7.RHD	-RHEUMATIC HEART DISEASE
8.RF	-RHEUMATIC FEVER
9.IgG4	-IMMUNOGLOBULIN G4
10.TH1	-TYPE 1 T HELPER CELLS
11.TH2	-TYPE 2 T HELPER CELLS
12.IFN-γ	-INTERFERON GAMMA
13.TNF	-TUMOR NECROSIS FACTOR
14.AFB	-ACID FAST BACILLI
15.HIV	-HUMAN IMMUNODEFICIENCY VIRUS
16.COPD	-CHRONIC OBSTRUCTUVE LUNG DISEASE
17.IL	-INTERLEUKIN
18.TGF-β	-TRANSFORMING GROWTH FACTOR BETA
19.UIP	-USUAL INTERSTITIAL PNEUMONIA
20.BOOP	- BRONCHIOLITIS OBLITERANS ORGANIZING PNEUMONIA
21.DIP	-DESQUAMATIVE INTERSTITIAL PNEUMONIA
22.PMF	-PROGRESSIVE MASSIVE FIBROSIS

23.H.PYLORI	-HELICOBACTER PYLORI
24.MALT	-MUCOSA ASSOCIATED LYMPHOID TISSUE
25.PRSS1	-PROTEASE SERINE 1
26.SPINK1	-SERINE PROTEASE INHIBITOR KAZAL TYPE 1
27.EUS	-ENDOSCOPIC ULTRASONOGRAPHY
28.CT	-COMPUTED TOMOGRAPHY
29.CSF	-CEREBROSPINAL FLUID
30.CDC	-CENTRE FOR DISEASE CONTROL
31.CMV	-CYTOMEGALOVIRUS
32.PML	-PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY
33.JC	-JAPANESE ENCEPHALITIS
34.PRP	-PRION PROTEIN
35.CJD	-CREUZFELDT JACOB DISEASE
36.PAS	-PERIODIC ACID SCHIFF
37.CNS	-CENTRAL NERVOUS SYSTEM
38.AVM	-ARTERIOVASCULAR MALFORMATION
39.SUDEP	-SUDDEN UNEXPLAINED DEATH IN EPILEPSY
40.VCAM	-VASCULAR CELL ADHESION MOLECULE
41.E SELECTIN	-ENDOTHELIAL SELECTIN
42.HbS	-HEMOGLOBIN S
43.SD	-STANDARD DEVIATION
44.PTB	-PULMONARY TUBERCULOSIS
45.CVC	-CHRONIC VENOUS CONGESTION
46.DAD	-DIFFUSE ALVEOLAR DAMAGE
47.GIT	-GASTROINTESTINAL SYSTEM

48.SADS -SUDDEN ADULT DEATH SYNDROME

49.H&E -HEMATOXYLIN AND EOSIN

50.IHC -IMMUNOHISTOCHEMICAL STUDY

51.GMS -GOMORI METHENAMINE SILVER

52.RBC -RED BLOOD CELLS

53.N:C -NUCLEAR CYTOPLASMIC RATIO

ANNEXURE III

MASTERCHART

S.NO	HPE NO	CR NO	PM NO	AGE	SEX	HEART	AORTA AND CORONARY OSTIUM	LUNG	LIVER	KIDNEY	CEREBRUM	CEREBELLUM	PANCREAS	SPLEEN
1	13/18	949/17	3046/17	45	M	N	N	PTB	C	N	SNR	SNR	SNR	SNR
2	16/18	345/17	3501/17	44	M	N	N	PTB	N	C	N	N	SNR	SNR
3	32/18	420/17	3704/17	40	M	N	N	C	C	C	SAH	ICH	SNR	SNR
4	41/18	118/18	226/18	24	F	N	N	C	C	C	SNR	SNR	acute pancreatitis	SNR
5	59/18	149/18	359/18	38	M	acute MI	AP	C	C	C	SNR	SNR	SNR	SNR
6	68/18	30/18	413/18	22	M	cysticercosis	N	C	C	C	N	SNR	SNR	SNR
7	69/18	32/18	227/17	37	M	dilated cardiomyopathy	N	N	C	C	N	N	SNR	SNR
8	72/18	21/18	95/18	35	M	N	AP	PE	C	C	SNR	SNR	SNR	SNR
9	80/18	145/18	509/18	40	M	SNR	SNR	SNR	hydatid cyst	SNR	SNR	SNR	SNR	SNR
10	86/18	94/18	184/18	42	F	N	N	C	C	C	ICH	SNR	SNR	SNR
11	95/18	204/18	511/18	45	M	SNR	SNR	C	cirrhosis	N	SNR	SNR	SNR	SNR
12	191/18	249/18	898/18	45	M	acute MI	AP	C	C	C	SNR	SNR	SNR	SNR
13	200/18	368/18	1251/18	40	M	acute MI	AP	C	SNR	SNR	SNR	SNR	SNR	SNR
14	212/18	234/18	911/18	38	M	N	N	C	C	C	ICH	SNR	SNR	SNR
15	222/18	528/18	1282/18	34	M	N	N	PTB	N	SNR	SNR	SNR	SNR	SNR
16	231/18	201/18	982/18	38	F	N	N	METS	N	METS	SNR	SNR	SNR	SNR
17	232/18	191/18	1365/18	40	M	healed MI	AP,Organizing thrombus	C	C	C	SNR	SNR	SNR	SNR
18	234/18	741/18	1383/18	45	M	EMF	AP	C	C	C	SNR	SNR	SNR	SNR
19	241/18	623/18	1454/18	37	M	N	N	C	C	C	SNR	SNR	chronic pancreatitis	SNR
20	252/18	622/18	1510/18	39	M	N	N	C	C	C	ICH	SNR	SNR	SNR
21	255/18	799/18	1485/18	23	M	IE	N	C	C	C	SNR	SNR	SNR	splenic infarct
22	276/18	702/18	1629/18	37	F	Healed MI	AP	SNR	SNR	SNR	SNR	SNR	SNR	SNR
23	278/18	545/18	1716/18	28	M	SNR	SNR	SNR	SNR	Acute tubular necrosis	SNR	SNR	SNR	SNR
24	258/18	173/18	1542/18	45	M	N	N	interstitial pneumonia	C	C	SNR	SNR	SNR	SNR
25	276/18	722/18	1630/18	27	F	Healed MI	AP	PE	C	C	SNR	SNR	SNR	SNR
26	283/18	116/18	287/18	45	M	Healed MI	AP	SNR	SNR	SNR	SNR	SNR	SNR	SNR
27	311/18	227/18	1894/18	36	M	N	N	PE	C	C	Meningitis	SNR	SNR	SNR
28	312/18	212/18	1626/18	45	M	Giant cell myocarditis	AP	C	C	C	SNR	SNR	SNR	SNR
29	315/18	784/18	1892/18	43	M	Acute and healed MI	AP	PE	C	C	N	N	SNR	SNR
30	334/18	595/18	1958/18	45	M	Acute MI	AP	C	C	C	N	SNR	N	SNR
31	345/18	568/18	1972/18	32	M	Eosinophilic myocarditis	AP	C	C	C	SNR	SNR	SNR	SNR
32	350/18	537/18	1957/18	38	F	N	N	C	C	C	N	N	Acute hemorrhagic pancreatitis	SNR
33	353/18	274/18	1215/18	31	M	Acute and healed MI	AP	PE	C	C	SNR	SNR	SNR	SNR
34	363/18	101/18	2066/18	40	M	IE	AP	PE	C	C	N	N	SNR	C
35	369/18	696/18	2107/18	37	M	N	N	C	cirrhosis	C	SNR	SNR	SNR	SNR
36	386/18	599/18	2115/18	19	M	Healed MI	N	C	C	C	N	SNR	SNR	SNR
37	387/18	608/18	2207/18	44	M	Healed MI	AP	C	C	C	SNR	SNR	SNR	SNR
38	391/18	548/18	57/18	43	M	EMF	AP	SNR	SNR	SNR	SNR	SNR	SNR	SNR
39	400/18	126/18	1505/18	26	M	N	N	C	C	C	ICH	SNR	SNR	SNR
40	412/18	187/18	1976/18	35	M	SNR	SNR	SNR	SNR	SNR	ICH	SNR	SNR	SNR
41	440/18	682/18	2600/18	29	M	Acute MI	AP	C	C	C	C	SNR	SNR	SNR
42	463/18	627/18	2225/18	19	F	N	N	PTB	C	C	SNR	SNR	SNR	SNR
43	467/18	1037/18	2710/18	43	F	N	N	C	C	C	SAH	SNR	SNR	SNR
44	501/18	242/18	2635/18	26	F	N	N	C	C	C	Meningitis	SNR	SNR	SNR
45	514/18	604/18	2863/18	21	M	Acute MI	N	C	C	C	SNR	SNR	SNR	SNR
46	518/18	355/18	2900/18	30	F	N	N	C	C	C	SAH	SNR	SNR	SNR
47	549/18	1081/18	3138/18	45	M	N	N	C	cirrhosis	C	ICH	SNR	SNR	SNR
48	607/18	480/18	2949/18	45	M	Healed MI	AP	C	N	N	N	N	SNR	SNR
49	609/18	499/18	3146/18	28	M	N	AP,Organizing thrombus	CVC	C	C	SNR	SNR	SNR	SNR
50	638/18	523/18	3471/18	45	M	Acute MI	AP	C	C	N	N	SNR	SNR	SNR
51	651/18	388/18	3187/18	40	F	Healed MI	AP	C	C	C	C	SNR	SNR	SNR
52	667/18	313/18	3551/18	35	F	N	AP	METS	METS	PAPILLARY RCC	N	SNR	SNR	SNR
53	673/18	309/18	3082/18	30	F	Healed MI	N	PE	C	C	SNR	SNR	SNR	SNR
54	677/18	740/18	3690/18	35	M	N	CRITICAL STENOSIS OF AP	Cholestrol granuloma	fatty liver	C	SNR	SNR	SNR	SNR
55	678/18	728/18	3599/18	19	M	hypertrophic cardiomyopathy	N	N	N	N	ICH	SNR	SNR	SNR
56	701/18	1188/18	3909/18	30	M	Acute MI	AP(70%)	C	C	C	SNR	SNR	SNR	SNR
57	702/18	531/18	3764/18	42	F	N	AP	PE	C	C	SNR	SNR	SNR	SNR
58	703/18	530/18	3849/18	31	F	N	N	N	N	N	SNR	SNR	SNR	SNR
59	708/18	260/18	3943/18	32	M	Acute MI	AP Organizing thrombus	C	C	C	SNR	SNR	SNR	SNR
60	718/18	1262/18	4015/18	41	F	N	AP	PE	fatty liver	N	SNR	SNR	SNR	SNR
61	719/18	324/18	3999/18	41	M	Healed MI	AP Calcification	PE	fatty liver	N	SNR	SNR	SNR	SNR
62	725/18	1539/18	3935/18	39	M	N	N	PNEUMONIA	N	N	SNR	SNR	SNR	SNR
63	13/19	1425/18	4084/18	35	M	N	N	PNEUMONIA	N	N	SNR	SNR	SNR	SNR
64	14/19	573/18	3813/18	25	M	Healed MI	AP	PE	N	N	N	N	SNR	SNR
65	17/19	1007/18	3744/18	21	F	aortitis	N	PE	N	N	SNR	SNR	SNR	SNR

ANNEXURE III

MASTERCHART

66	19/19	1033/18	3796/18	42	M	Acute MI	AP	PE	fatty liver	C	N	SNR	SNR	SNR
67	27/19	13/19	181/19	45	M	N	N	C	cirrhosis	N	SNR	SNR	SNR	SNR
68	29/19	26/19	166/19	41	M	N	N	EMPHYSEMA	N	N	SNR	SNR	SNR	SNR
69	41/19	33/19	222/19	44	M	sarcoidosis	AP Calcification	N	fatty liver	N	SNR	SNR	SNR	SNR
70	46/19	42/19	187/19	36	M	Acute MI	AP	C	N	N	SNR	SNR	SNR	SNR
71	47/19	46/19	238/19	38	M	Acute MI	AP	C	N	N	SNR	SNR	SNR	SNR
72	48/19	72/19	296/19	38	M	Acute MI	AP	SNR	SNR	SNR	SNR	SNR	SNR	SNR
73	51/19	75/19	285/19	34	M	N	N	C	N	N	SNR	SNR	SNR	Diaphragmatic eventration of spleen
74	60/19	139/19	2433/19	40	M	Acute MI	AP	C	N	C	SNR	SNR	SNR	SNR
75	74/19	340/19	4011/19	39	M	Healed MI	AP	C	C	C	N	SNR	SNR	SNR
76	78/19	87/19	431/19	42	M	Healed MI	AP(70%)	C	C	C	SNR	SNR	SNR	SNR
77	79/19	340/19	4014/19	39	M	Healed MI	AP	C	C	C	N	SNR	SNR	SNR
78	80/19	99/19	429/19	32	M	N	AP	C	cirrhosis	N	N	SNR	SNR	SNR
79	85/19	123/19	433/19	42	M	Acute MI	AP	N	N	C	SNR	SNR	SNR	SNR
80	89/19	131/19	117/19	43	M	Acute MI	AP	CVC	N	N	N	N	SNR	SNR
81	93/19	54/19	469/19	19	F	N	N	DAD	N	N	SNR	SNR	SNR	SNR
82	98/19	99/19	368/19	17	F	N	N	Bronchopenumonia	N	N	SNR	SNR	SNR	SNR
83	154/19	118/19	807/19	24	F	N	AP	PE	N	C	Encephalitis	SNR	SNR	SNR
84	155/19	188/19	405/19	45	M	N	AP	PE	METS	C	SNR	SNR	SNR	SNR
85	167/19	165/19	553/19	45	M	Acute and healed MI	AP	C	C	C	SNR	SNR	SNR	SNR
86	170/19	513/19	986/19	44	M	Acute MI	AP	N	N	N	SNR	SNR	SNR	SNR
87	184/19	95/19	1082/19	44	M	N	AP	C	cirrhosis	C	SNR	SNR	SNR	SNR
88	210/19	32/19	1261/19	44	M	Acute MI	AP	C	C	N	SNR	SNR	SNR	SNR
89	260/19	372/19	1428/19	29	M	Healed MI	AP	C	C	C	SNR	SNR	SNR	SNR
90	285/19	542/19	1623/19	40	M	Aortic dissection	N	C	N	C	SNR	SNR	SNR	SNR
91	298/19	47/19	1310/19	45	M	Giant cell myocarditis	AP	N	N	C	SNR	SNR	SNR	SNR
92	318/19	415/19	1749/19	26	M	Acute and healed MI	AP	N	N	Medullary sponge kidney	SNR	SNR	SNR	SNR
93	346/19	248/19	2020/19	19	M	Calcific aortic stenosis	AP	SNR	SNR	SNR	SNR	SNR	SNR	SNR
94	347/19	136/19	1697/19	29	M	N	AP	Aspiration penumonia	C	C	N	N	SNR	SNR
95	361/19	357/19	2071/19	20	F	N	N	N	C	N	SNR	SNR	SNR	SNR
96	434/19	435/19	2435/19	45	M	aortic aneurysm	N	N	N	N	SNR	SNR	SNR	SNR
97	460/19	882/19	2558/19	24	M	Eosinophilic myocarditis	N	C	C	C	SNR	SNR	SNR	SNR
98	468/19	15/19	1341/19	24	F	Myocarditis	N	PE	C	C	SNR	SNR	SNR	SNR
99	470/19	725/19	2424/19	42	M	Mitral valve prolapse	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR
100	471/19	876/19	2876/19	23	M	leukemic infiltration	N	leukemic infiltration	leukemic infiltration	leukemic infiltration	SNR	SNR	SNR	SNR

KEY TO MASTER CHART

M	-MALE
F	-FEMALE
N	-NORMAL HISTOLOGY
C	-CONGESTION
SNR	-SPECIMEN NOT RECEIVED
HPE NO	-HISTOPATHOLOGICAL EXAMINATION NUMBER
CR NO	-CRIME NUMBER
PM NO	-POST MORTEM NUMBER
MI	-MYOCARDIAL INFARCTION
AP	-ATHEROMATOUS PLAQUE
EMF	-ENDOMYOCARDIAL FIBROSIS
IE	-INFECTIVE ENDOCARDITIS
PTB	-PULMONARY TUBERCULOSIS
PE	-PULMONARY EDEMA
CVC	-CHRONIC VENOUS CONGESTION
DAD	-DIFFUSE ALVEOLAR DAMAGE
RCC	-RENAL CELL CARCINOMA
SAH	-SUBARACHNOID HEMORRHAGE
ICH	-INTRACRANIAL HEMORRHAGE